IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 24, Issue 7 Ser.1 (July 2025), PP 18-24
www.iosrjournals.org

Role of Ophthalmic Artery Doppler in The Prediction of Pre-Eclampsia At 35 – 37 Weeks of Gestation in A Tertiary Care Center

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Abstract
Background: *Pre-eclampsia (PE) is a major cause of maternal and fetal morbidity worldwide. Early detection and management are essential for reducing associated risks. Traditional methods of diagnosing PE, including blood pressure measurement and proteinuria assessment, are limited, especially when the disease progresses in the late third trimester. This study explores the utility of ophthalmic artery Doppler ultrasonography as a predictive tool for pre-eclampsia between 35-37 weeks of gestation.*
Methods: *This prospective cohort study was conducted in the* ***Department of Radiodiagnosis*** *at* ***BGS GIMS Hospital, Bangalore****. The study included women at 35-37 weeks of gestation who were considered at high risk for pre-eclampsia due to factors such as a history of hypertension, prior pre-eclampsia, multiple gestations, or advanced maternal age. A total of 200 participants were included in this study. Ophthalmic artery Doppler ultrasonography was performed with color and pulsed Doppler capabilities. Data were analyzed using SPSS software (version 21).*
Results: *On assessing the baseline parameters, BMI was found to be similar in preeclampsia and non preeclampsia group. However, previous hypertension, advanced maternal age and multiple gestation were linked with the presence of preeclampsia. Among the ophthalmic artery Doppler indices, the systolic/diastolic ratio, resistance index, and pulsatility index differs remarkably with the presence of preeclampsia with premising AUC values.*
Conclusion: *Our findings suggest that ophthalmic artery Doppler indices—mean S/D ratio, mean RI and mean PI remarkably differs with the presence of preeclampsia.—can provide valuable insights into the prediction of PE in the late third trimester, offering a non-invasive, reliable method for early detection.*
Key words: *ophthalmic artery, preeclampsia, Doppler*

Date of Submission: 20-06-2025 Date of Acceptance: 03-07-2025

I. Introduction

Preventive measures can be implemented to lower morbidity and death rates for expectant mothers and their unborn children by identifying high-risk pregnancies[1]. One of the main causes of maternal mortality in the globe is preeclampsia[2-5]. Between 5% and 10% of people get preeclampsia[6]. Preeclampsia has remained common despite improvements in prenatal care[5]. Furthermore, there is disagreement about whether preventing preeclampsia itself—as opposed to preventing its complications—is a worthwhile objective, and there is no one predictor of preeclampsia among women who are at low or greater risk of developing the condition[7]. The goal of preeclampsia treatment must be to identify women at risk of negative outcomes as soon as possible[5].

Eclampsia is the most serious consequence of preeclampsia[3]. At least 75% of maternal fatalities in preeclampsia are caused by acute cerebral complications, including cerebral edema, intracranial hemorrhage, and eclampsia[8]. It is debatable whether preeclampsia is caused by hemodynamic changes in the central nervous system[6]. Preeclampsia-eclampsia syndrome meets the criteria for posterior reversible encephalopathy syndrome due to its neurologic involvement[810]. Investigations are still ongoing to determine the pathophysiologic cause of posterior reversible encephalopathy syndrome. According to the more recent and widely accepted view, severe hypertension causes vasodilatation and breakthrough brain edema when it beyond the limits of cerebral autoregulation[11]. Cerebral circulation assessment is difficult. The use of noninvasive methods is growing, particularly transcranial Doppler sonography[10]. The ophthalmic artery can be studied for central territory vascular flow during pregnancy using a noninvasive technique called Doppler sonography[3,6].

Ocular artery ultrasonography may be characterized as a noninvasive technique for examining cerebral vascular areas since the ocular artery is a direct branch of the internal carotid artery and shares similarities with the small diameter intracranial artery in development, architecture, and function[12,13]. Ophthalmic Artery Doppler (OAD) can then be used to assess the hemodynamic activity of tiny central arteries in order to help diagnose preeclampsia[14]. Although several research have lately evaluated the usefulness of OAD measures as preeclampsia predictors, the findings are inconsistent, and there is still no clear agreement on their precise use in clinical practice[15,16]. In this study, the predictive value of ophthalmic artery Doppler for pre-eclampsia at 35–37 weeks gestation is evaluated.

Methods

This prospective cohort study was conducted at **BGS GIMS** hospital, Bangalore in the department of Radiodiagnosis and OBGY. The study included women at 35-37 weeks of gestation who were considered at high risk for pre-eclampsia due to factors such as a history of hypertension, prior pre-eclampsia, multiple gestations, or advanced maternal age. Women aged between 18-40 years, gestational age between 35 and 37 weeks and high risk for pre-eclampsia (previous pre-eclampsia, chronic hypertension, multiple gestations, or history of fetal growth restriction) were included in this study. Pre-existing ophthalmic conditions, any retinal artery disease or abnormalities, non-viable pregnancies and pregnancy complications other than pre-eclampsia were excluded. A total of 200 participants were included in this study.

Ophthalmic artery Doppler ultrasonography was performed with color and pulsed Doppler capabilities. Doppler flow velocities were measured from the ophthalmic arteries of both eyes. The key Doppler indices assessed were:

- **Systolic/diastolic ratio (S/D ratio)**: Reflects the ratio between peak systolic and end-diastolic flow velocities.
- **Resistance index (RI)**: Measures vascular resistance, calculated as RI = (Systolic velocity – Diastolic velocity) / Systolic velocity.
- **Pulsatility index (PI)**: Represents the variation in blood flow velocity during the cardiac cycle, calculated as PI = (Systolic velocity – Diastolic velocity) / Mean velocity.

Pre-eclampsia was diagnosed based on the following criteria:

- Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two separate occasions, at least four hours apart
- Proteinuria ≥300 mg/24 hours or 1+ on a urine dipstick
- Evidence of end-organ damage, such as elevated liver enzymes or impaired renal function
- Fetal growth restriction or abnormal umbilical artery Doppler velocimetry

Data were analyzed using SPSS software (version 21). Descriptive statistics were used to summarize baseline characteristics. The comparison of OAD indices between the pre-eclampsia group and controls was performed using independent t-tests or Mann-Whitney U tests for continuous variables. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of ophthalmic artery Doppler indices in predicting pre-eclampsia was assessed using receiver operating characteristic (ROC) curves.

II. Results

A total of 200 pregnant women were enrolled in the study, with 40 diagnosed with pre-eclampsia (20%) and 160 without (80%). The overall mean age of participants was 30.2 years, with a BMI of 26.4 kg/m². The most common risk factors for pre-eclampsia included previous hypertension, advanced maternal age and multiple gestation.

Table 1: Comparison of baseline clinical profile

Parameters	PE - Present	PE- Absent	p value
Mean age	33.4±3.1	28.7±3.6	0.0317*
Mean BMI	26.8±1.4	27.1±1.2	0.1963
Hypertension			
Present	31	15	<0.0001*
Absent	9	145	
Advanced maternal age			
Present	24	12	<0.0001*
Absent	16	148	
Multiple gestation			
Present	22	18	<0.0001*
Absent	18	142	

*Significant

Doppler Findings

The Doppler ultrasound measurements of the ophthalmic artery revealed significant differences between the pre-eclampsia group and the control group:

- **S/D ratio**: The mean S/D ratio in the pre-eclampsia group was 3.45 ± 0.42, significantly higher than the 2.83 ± 0.35 observed in the control group ($p < 0.001$).
- **Resistance index (RI)**: The average RI in the pre-eclampsia group was 0.74 ± 0.05, compared to 0.63 ± 0.06 in the control group ($p < 0.001$).
- **Pulsatility index (PI)**: The mean PI for the pre-eclampsia group was 1.78 ± 0.31, significantly higher than the 1.36 ± 0.28 in the control group ($p < 0.001$).

Table 2: Comparison of parameters of OAD

Parameters	PE - Present	PE- Absent	p value
Mean S/D Ratio	3.45±0.42	2.83±0.35	< 0.001*
Mean RI	0.74±0.05	0.63±0.06	< 0.001*
Mean PI	1.78±0.31	1.36±0.28	< 0.001*

*Significant

Predictive Accuracy of Ophthalmic Artery Doppler

The ROC analysis demonstrated that ophthalmic artery Doppler indices had good predictive value for pre-eclampsia:

- The **S/D ratio** at a cutoff value of 3.2 had a sensitivity of 87.5% and specificity of 80%, with an area under the curve (AUC) of 0.89.
- The **Resistance index (RI)** at a cutoff of 0.71 had a sensitivity of 75% and specificity of 82%, with an AUC of 0.84.
- The **Pulsatility index (PI)** at a cutoff of 1.5 had a sensitivity of 79% and specificity of 78%, with an AUC of 0.85.

Combined use of these three Doppler parameters resulted in an overall sensitivity of 91% and specificity of 86% for predicting pre-eclampsia.

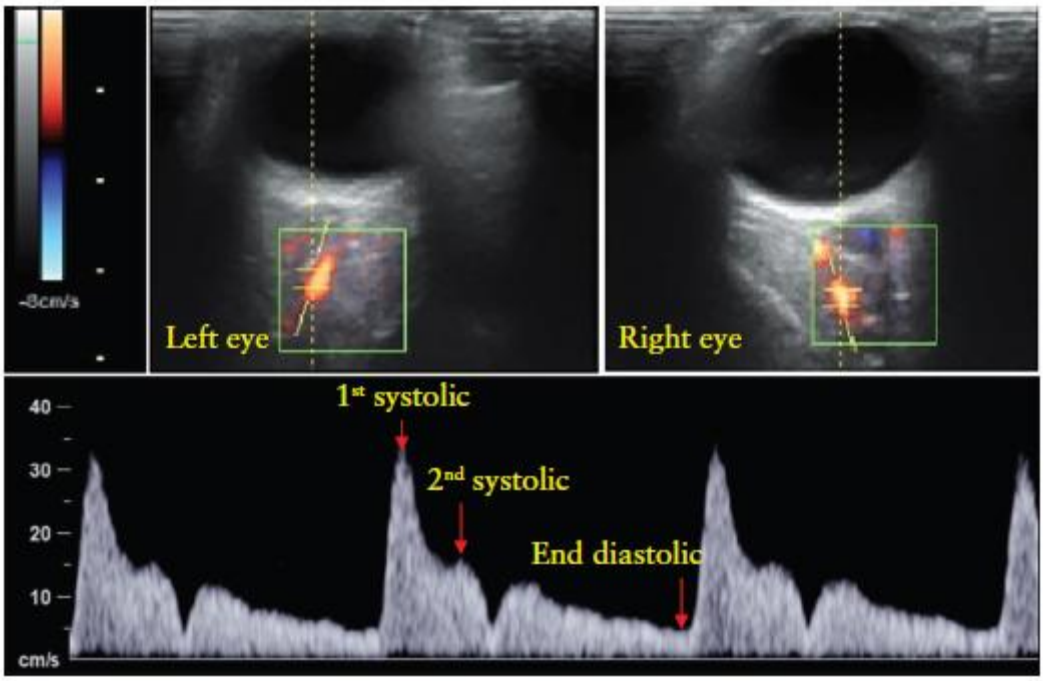

Figure 1: OAD - Left and Right Pulsed-wave Doppler flow velocity waveform from the ophthalmic artery, which displays the first and second peaks of the systolic and end-diastolic velocities, is shown at the bottom

III. Discussion

The alterations observed in ophthalmic artery Doppler indices can be attributed to the systemic endothelial dysfunction and impaired vasodilation seen in pre-eclampsia. These vascular changes lead to increased resistance and decreased perfusion in various organs, including the eye. As the ophthalmic artery shares similar pathophysiological changes with other systemic vessels, such as the uterine and umbilical arteries, Doppler findings in the ophthalmic artery can serve as an early indicator of the disease.

Ophthalmic artery Doppler provides a non-invasive, easily accessible, and reproducible method for identifying women at risk of developing pre-eclampsia in the late third trimester. The high sensitivity and specificity observed in this study suggest that ophthalmic artery Doppler could be integrated into routine clinical practice for high-risk pregnancies, particularly as a complementary tool alongside blood pressure monitoring and urine protein testing. The findings of this study were comparable with the following studies. The possible importance of OAD characteristics in preeclamptic women was discovered by Dai X et al[17]. Peak systolic velocities (PSV) had a pooled standardized mean difference (SMD) of 0.12. For mean peak velocities (MV), the total SMD was 1.8. The pooled SMD for the PI was -2.05. End-diastolic velocities (EDV) had an overall SMD of 1.1. The peak ratio (PR) and RI pooled SMDs were 1.46 and −.18, respectively. Chaves MTP et al[18] investigated the relationship between preeclampsia and poor pregnancy outcomes using the ratio of velocity peaks (PR), an OAD measure. As the PR values rose, adverse maternal outcomes were increasingly common. Additionally, PR levels were positively correlated with the incidence of hypertensive crisis following hospitalization. Although women in the severely aberrant PR group had the earliest births and the smallest neonates, PR levels were not linked to worse perinatal outcomes. The outcome was negative for every woman in the extremely abnormal PR group. They asserted that in preeclampsia, maternal OA Doppler PR > 0.99 may help identify women who are more likely to experience unfavorable maternal outcomes and pregnancies with the highest risk of premature delivery.

In the second trimester, Matias DS et al[19] reported OAD parameters in pregnant females at risk for preeclampsia; compare these parameters to reference values reported in women with healthy pregnancies. They said that when compared to the reference values, noticeably greater OAD velocimetric parameters were found. These metrics had mean values of 37.9 cm/s for peak systolic velocity, 7.2 cm/s for end-diastolic velocity, 0.81 for RI, 2.17 for PI, and 0.53 for peak ratio. The Doppler measurements and gestational age did not correlate. According to their findings, women at risk for preeclampsia have ophthalmic Doppler parameters that are noticeably higher than the normal range for healthy pregnancies. This might be a symptom of a poor vascular response to ongoing peripheral resistance. In pregnant women at risk for preeclampsia, OAD values are not correlated with gestational age throughout the second trimester. In another study, to link the OAD indicators of hypertensive pregnant women with those of healthy pregnant women, Oliveira CA et al[20] evaluated the indices of women with singleton pregnancies complicated by hypertension. They stated that when comparing the RI, PI, and peak ratio of women with severe preeclampsia to the other groups, they discovered notable variations. In women with severe preeclampsia, the RI, PI, and pulse ratio averages were 0.63, 1.13, and 0.89, respectively. ROC showed that the best cutoff values for the RI, PI, and peak ratio for identifying women with severe preeclampsia were 0.657, 1.318, and 0.784. They asserted that in pregnant women with severe preeclampsia, OAD revealed central over perfusion. The best metric for differentiating between moderate and severe preeclampsia or chronic hypertension was the peak ratio. Using OAD indices, Diniz ALD et al[21] found that moderate and severe pre-eclamptic women behaved differently in terms of orbital flow than healthy pregnant women. When comparing women with moderate and severe pre-eclampsia, they discovered that PR, PSV, and EDV OAD differed statistically significantly. All of the research group's Doppler indices showed statistically significant differences from those of healthy expectant mothers. Severe pre-eclamptic subjects had considerably greater ophthalmic PR, PSV, and EDV, but no change was seen in other index values. When pre-eclampsia become severe, diastolic and systolic flow increased. In contrast to moderate pre-eclamptic and healthy pregnant women, they found that severe pre-eclamptic women had orbital vascular impedance decrease with orbital hyperperfusion.

In consistent with this study, Nicolaides KH et al[22] sought to summarize results from the clinical application of such assessment in preeclampsia prediction. Notably, two small studies in high-risk pregnancies, one at 11 to 14 weeks and another at 20 to 28 weeks, found differences in OAD between preeclamptic women and unaffected pregnancies, suggesting that this is a useful biomarker for preeclampsia screening. Another small study in high-risk gestational periods at 18 to 23 weeks showed no discernible difference in OAD indices between women with preeclampsia and unaffected groups. The waveform from the ophthalmic arteries is characterized by two systolic peaks, and the ratio of the second to the initially peak systolic velocity was increased in women who developed preeclampsia, according to two recent, large empirical investigations in unselected pregnancies at 19 to 23 and 35 to 37 weeks' gestation, respectively. For consistent results, waveforms from both eyes must be recorded; Third, the peak systolic velocity ratio outperformed the uterine artery PI, mean arterial pressure, serum placental growth factor, and soluble fms-like tyrosine kinase-1 as individual biomarkers in the prediction of both preterm and term preeclampsia. Additionally, the peak systolic velocity ratio enhanced the prediction of preeclampsia provided by all other biomarkers. Fourth, in the study conducted at 35 to 37 weeks of gestation, the peak systolic velocity ratio enhanced the estimation of subsequent progression of preeclampsia provided by maternal factors alone and combinations of maternal factors with mean arterial pressure, uterine artery PI, placental growth factor, and serum placental growth factor. The OAD offers a valuable biomarker for preeclampsia prediction. Melo PFM et al[23] assessed the accuracy of various OAD parameters in the complementary diagnosis of preeclampsia (PE) and found that peak ratio and second systolic velocity peak (P2)

performed better as diagnostic tools than the other indexes, with a ROC of 0.926 for the P2 and a PR of ROC of 0.926 for the OAD. RI, PI, and EDV demonstrated good performance and consistency across studies, but had lower ROC values of 0.83, 0.79, and 0.77, respectively.

Additionally, in order to predict pre-eclampsia, Alves JAG et al[24] evaluated the effectiveness of a multiparametric test that included maternal risk variables, uterine artery Doppler, and OAD in the first trimester of pregnancy. They reported that 7% of individuals experienced PE, with 5% experiencing late PE and 2% requiring delivery before 34 weeks. The PE and control groups differed remarkably in the mean values of the OAD's initial diastolic peaks (PD1) and UtA-PI. Both UtA-PI and PD1 obtained a 67% detection rate for early PE in a multiparametric model; however, the total detection rate only rose to 68%. In the first trimester, ophthalmic artery PD1 was about as effective as UAD as a prognostic marker for the later development of PE. According to Matias DS et al[25], 40 of the 347 women who were recruited went on to acquire PE. Peak systolic and diastolic velocity, peak mesodiastolic velocity (PMDV), and peak ratio were among the metrics exhibiting statistically significant differences between women with and without PE. With an AUC of 0.73, only PMDV was still statistically significant after controlling for confounding factors. With sensitivity of 70%, specificity of 75%, PPV of 28%, and NPV of 95%, the optimal cut-off for PE prediction was a PMDV of >22.11 cm/s. When the PMDV was included in a prediction model based on clinical factors, the AUC rose from 0.72 to 0.78, indicating that this marker improved the algorithm's capacity for discrimination. When it came to PE prediction, OAD and UtA Doppler performed similarly. Furthermore, when the PMDV was included to the model that included clinical factors and UtA Doppler indices, the AUC rose noticeably from 0.82 to 0.88. In the second trimester of pregnancy, a high ophthalmic artery PMDV is a distinct indicator of PE that improves the discriminatory power of clinical markers and models that incorporate UtA Doppler indices and clinical factors. For the prediction of early-onset PE, Kalafat E et al[26] observed that the initial diastolic peak velocity of OAD at a cut-off of 23.3 cm/s demonstrated a moderate level of sensitivity and specificity. For the prediction of late-onset PE, the initial diastolic peak velocity had a lower AUC, comparable specificity, and a much lower sensitivity. At any PE cut-off, the ocular artery's PI did not exhibit clinically meaningful sensitivity or specificity. An AUC of 0.67 for early-onset PE and 0.57 for late-onset illness indicated that a peak ratio greater than 0.65 had diagnostic accuracy comparable to that of first diastolic peak velocity. OAD is a straightforward, precise, and impartial method that has independent predictive value for the emergence of early-onset PE on par with UAD assessment.

According to Sapatzoglou I et al[27]., 2.7% of the 2853 pregnancies in the research population had PE, with 0.6% of those deliveries occurring with PE at less than 37 weeks' gestation. Early PE deviated more from normal than late PE, and the PE impact was dependent on gestational age at birth. The ocular artery PSV ratio was considerably elevated in PE pregnancies. Although the impact was independent of gestational age at delivery, PE pregnancies also showed an increase in the second peak of systolic velocity. PE had no discernible effect on the initial peak of systolic velocity or PI, the other two OAD parameters. Larger research is required to confirm their assertion that the ophthalmic artery PSV ratio at 19–23 weeks of gestation, both alone and in conjunction with other biomarkers, may be helpful in predicting the development of PE later on, particularly preterm PE. According to Sarno M et al[28]., 2.6% of the 2287 pregnancies in the research group had PE, with 0.8% of those deliveries occurring with PE less than three weeks following the evaluation. Following evaluation by maternal factors alone, maternal factors and MAP, maternal factors, MAP and PlGF, and maternal factors, MAP, PlGF and sFlt-1, the PSV ratio enhanced the prediction of PE with delivery at any stage, with an FPR of 10%. The prediction of PE with delivery at less than three weeks following evaluation by maternal variables alone, maternal variables and MAP, maternal factors, MAP and UtA-PI, and maternal factors, MAP and PlGF was further enhanced by the PSV ratio. The predicted findings and the observed results for DR at a 10% FPR agreed. Using MAP and PSV ratio in conjunction with maternal variables to screen for gestational hypertension also identified 59.4% of cases with birth at any point after assessment and 86.7% of those with delivery within three weeks of evaluation. They came to the conclusion that OAD could enhance the effectiveness of screening for PE at 35–37 weeks, particularly impending PE with delivery within 3 weeks after evaluation; however, more research is required to confirm this conclusion. According to Gana N et al[29]., 2.8% of the 4066 pregnancies in the study cohort had PE, with 0.6% of those deliveries occurring with PE at less than 37 weeks' gestation. Pregnancies with PE had a considerably higher PSV ratio, and the effect of PE varied according to the gestational age at birth, with early PE showing a larger departure from normal than late PE. According to modeling, the detection rate of preterm PE supplied by maternal risk factors alone, maternal factors, MAP, and UtA-PI, as well as maternal factors, MAP, UtA-PI, and PlGF, was increased by 10% FPR with the inclusion of PSV ratio. The term PE prediction offered by any combination of biomarkers was not enhanced by the PSV ratio. Larger investigations are required to support their assertion that the ophthalmic artery PSV ratio at 11–13 weeks of gestation is a potentially valuable biomarker for predicting the eventual development of preterm PE.

Notably the limitation of this study is that it was conducted in a single center, and findings may not be universally applicable; Doppler measurements are operator-dependent, and variability in technique could affect

results and Further multicenter studies are necessary to validate these findings in diverse populations and confirm the optimal cutoff values for clinical use.

IV. Conclusion

Ophthalmic artery Doppler ultrasonography is a promising tool for predicting pre-eclampsia at 35-37 weeks of gestation. Significant differences in Doppler indices, including the S/D ratio, resistance index, and pulsatility index, were observed between women who developed pre-eclampsia and those who did not. The high sensitivity and specificity of these indices make ophthalmic artery Doppler a valuable adjunctive method for the early detection of pre-eclampsia, facilitating timely intervention and better outcomes for both mothers and infants. Hence we recommend OAD should be considered as part of the standard screening for pre-eclampsia in high-risk pregnancies at 35-37 weeks of gestation. Future studies with larger, multi-center cohorts are needed to establish the generalizability of these findings and to refine cutoff values for clinical use. Training healthcare professionals to standardize Doppler techniques will improve the reliability and accuracy of this diagnostic tool.

Declarations
Funding: no funding source
Conflict of interest: none declared
Ethical approval: this study was registered with institutional human ethical committee.

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