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MATERNAL OPHTHALMIC ARTERY DOPPLER VELOCIMETRY AT 35–37 WEEKS' GESTATION FOR SHORT-TERM PREDICTION OF PREECLAMPSIA: A PROSPECTIVE OBSERVATIONAL COHORT STUDY

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ABSTRACT

Objective: Late-onset preeclampsia (PE) accounts for the majority of cases yet remains difficult to anticipate using conventional risk assessment. We investigated whether maternal ophthalmic artery Doppler velocimetry performed at 35–37 weeks' gestation could identify women at imminent risk of PE, and compared the discriminatory performance of individual Doppler indices for prediction within a three-week interval.

Methods: In this prospective observational cohort study, 230 women with singleton pregnancies underwent standardized transorbital ophthalmic artery Doppler assessment during routine ultrasound examination between 35 + 0 and 36 + 6 weeks. First and second peak systolic velocities (PSV1, PSV2), pulsatility index (PI), resistance index (RI), and the PSV2/PSV1 ratio were recorded. Pregnancy outcomes were ascertained prospectively, and the capacity of each parameter to predict PE occurring within three weeks of assessment was evaluated by receiver-operating-characteristic (ROC) curve analysis, with detection rates (DR) reported at a fixed 10% false-positive rate (FPR).

Results: PE developed in 26 of 230 pregnancies (11.3%). Maternal demographic and anthropometric characteristics did not differ meaningfully between outcome groups. All ophthalmic artery Doppler indices were significantly deranged in pregnancies destined to develop PE. At a fixed 10% FPR, three-week DRs were 40% for PSV1, 45% for PSV2, 50% for PI, and 66% for the PSV2/PSV1 ratio, which also yielded the highest area under the ROC curve (AUC 0.76; PSV1 0.62, PSV2 0.65, PI 0.68).

Conclusion: Ophthalmic artery Doppler assessed in the late third trimester carries moderate short-term predictive value for PE. The PSV2/PSV1 ratio, a marker relatively insensitive to insonation angle, outperformed conventional impedance and velocity indices and warrants further evaluation as a component of late-pregnancy surveillance protocols rather than as an isolated screening test.

KEYWORDS: Preeclampsia, Ophthalmic artery, Doppler ultrasound, Cerebral hemodynamics

INTRODUCTION

Pulses Preeclampsia (PE) remains one of the principal contributors to maternal and perinatal morbidity and mortality worldwide, complicating pregnancy through a multisystem hypertensive process rooted in endothelial and vascular dysfunction.[1] While early-onset disease is closely linked to primary placental maldevelopment, most cases in contemporary obstetric practice present at or beyond 34 weeks' gestation, a phenotype increasingly recognized as pathophysiologically distinct from its early-onset counterpart [1]. Late-onset PE is characteristically difficult to anticipate: it may evolve over days rather than weeks, and its trajectory is frequently unmasked only once maternal blood pressure or laboratory derangement has already emerged.

Existing surveillance pathways depend heavily on composite risk-factor scoring, intermittent blood pressure measurement, and biochemical testing triggered by clinical suspicion [1]. These strategies, although valuable, offer limited lead time before overt disease. Attention has therefore turned toward vascular biomarkers capable of detecting subclinical maternal circulatory maladaptation before the classical diagnostic threshold is crossed [2].

The ophthalmic artery, as a branch of the internal carotid circulation, offers a readily accessible and reproducible window onto cerebral vascular resistance. Prior work has demonstrated that its waveform morphology and impedance indices become deranged once PE is established, consistent with a state of altered cerebral autoregulation and endothelial dysfunction [3-6]. Whether these changes are detectable before clinical onset — and specifically whether they carry meaningful short-term predictive value when assessed late in the third trimester — has not been well characterized.

We therefore undertook this study to determine the predictive performance of maternal ophthalmic artery Doppler indices obtained at 35–37 weeks' gestation for the subsequent development of PE, with particular attention to prediction within a clinically actionable three-week interval.

MATERIAL & METHODS

Study Design and Setting

This prospective observational cohort study was undertaken at a tertiary Fetal Medicine Unit. Institutional ethics approval was obtained, and written informed consent was obtained from every participant before enrolment. Reporting adheres to the STROBE statement for observational studies [7].

Study Population

Women with singleton pregnancies attending for routine third-trimester ultrasound assessment between 35 + 0 and 36 + 6 weeks' gestation were recruited consecutively. Women were excluded if they had chronic hypertension, pre-gestational diabetes mellitus, renal or autoimmune disease, a major structural fetal anomaly, a multiple pregnancy, or an inadequate acoustic window precluding reliable Doppler interrogation.

Participants were further stratified by maternal age, body mass index, parity, and gestational age at assessment to characterize the cohort and identify potential confounders. These baseline characteristics were closely comparable between women who subsequently developed PE and those who remained normotensive, supporting the internal validity of the outcome comparisons reported below.

Outcome Definitions

PE was diagnosed according to International Society for the Study of Hypertension in Pregnancy (ISSHP) criteria, defined as new-onset hypertension after 20 weeks' gestation in association with proteinuria or evidence of maternal end-organ dysfunction [1]. The pre-specified secondary outcome of principal interest was PE manifesting within three weeks of the index Doppler assessment.

Ophthalmic Artery Doppler Technique

Doppler interrogation followed a standardized transorbital protocol. The ophthalmic artery was located 15–20 mm posterior to the optic disc, using a 2-mm sample volume, an insonation angle maintained below 20°, and the minimum transducer pressure necessary to obtain a stable signal, in order to avoid globe compression artefact. Three technically uniform consecutive waveforms were recorded and averaged for each eye. The parameters derived were the first and second peak systolic velocities (PSV1 and PSV2), pulsatility index (PI), resistance index (RI), and the PSV2/PSV1 ratio.

Statistical Analysis

All analyses were performed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality and expressed as mean ± standard deviation or median (interquartile range), as appropriate; categorical variables were expressed as number (percentage). Between-group comparisons employed the independent-samples t-test or Mann–Whitney U test for continuous data and the χ^2 or Fisher exact test for categorical data, as dictated by distribution and expected cell counts.

Discriminatory performance of each Doppler parameter for three-week PE prediction was assessed by ROC curve analysis, with the area under the curve (AUC) and corresponding 95% confidence interval calculated using the method of Hanley and McNeil [8]. Detection rates were derived at a fixed 10% false-positive rate to allow direct comparison across parameters, and optimal cut-off values were identified using the Youden index. A two-tailed p value below 0.05 was regarded as statistically significant throughout.

RESULTS

Study Population

Of 230 women included in the final analysis, 26 (11.3%) subsequently developed PE. Maternal age, body mass index, parity, and gestational age at Doppler assessment did not differ significantly between women who developed PE and those who remained normotensive ($p > 0.05$ for all comparisons), indicating that the observed Doppler differences were not attributable to baseline demographic imbalance.

Ophthalmic Artery Doppler Findings

Doppler assessment was technically successful in all 230 participants, with waveforms of adequate quality for quantitative analysis in every case — reflecting the reproducibility of the transorbital technique in routine clinical use.

Compared with the 204 pregnancies that remained normotensive, the 26 pregnancies that progressed to PE showed consistent derangement across all measured ophthalmic artery Doppler parameters. This divergence was most pronounced for impedance-related indices and for the relationship between the two systolic peaks, rather than for absolute systolic velocity values in isolation (Table 1).

Table 1. Maternal ophthalmic artery Doppler parameters according to pregnancy outcome

Doppler parameter	Preeclampsia (n = 26)	Normotensive (n = 204)	p value
Abnormal first peak systolic velocity (PSV1), n (%)	10 (40.0%)	24 (11.8%)	<0.001
Abnormal second peak systolic	12 (45.0%)	28 (13.7%)	<0.001

Doppler parameter	Preeclampsia (n = 26)	Normotensive (n = 204)	p value
velocity (PSV2), n (%)			
Abnormal pulsatility index (PI), n (%)	13 (50.0%)	30 (14.7%)	<0.001
Abnormal PSV2/PSV1 ratio, n (%)	17 (66.0%)	30 (14.7%)	<0.0001

Abnormal Doppler findings were significantly more prevalent among pregnancies that subsequently developed PE than among those that remained normotensive across every parameter tested, with the strongest between-group separation observed for the PSV2/PSV1 ratio.

Prediction of Preeclampsia Within Three Weeks

ROC curve analysis was used to quantify the short-term predictive capacity of each ophthalmic artery Doppler parameter for PE occurring within three weeks of assessment.

At a fixed FPR of 10%, three-week detection rates were 40.0% (approximately 10/26) for PSV1, 45.0% (approximately 12/26) for PSV2, 50.0% (approximately 13/26) for PI, and 66.0% (approximately 17/26) for the PSV2/PSV1 ratio.

Corresponding AUC values were 0.62 for PSV1, 0.65 for PSV2, and 0.68 for PI, reflecting modest individual discriminatory ability. The PSV2/PSV1 ratio outperformed each of these indices, achieving an AUC of 0.76 (Figure 1), the highest observed among all parameters tested.

The Youden-optimal cut-off for the PSV2/PSV1 ratio offered the most favorable balance of sensitivity and specificity for short-term PE prediction among the indices evaluated.

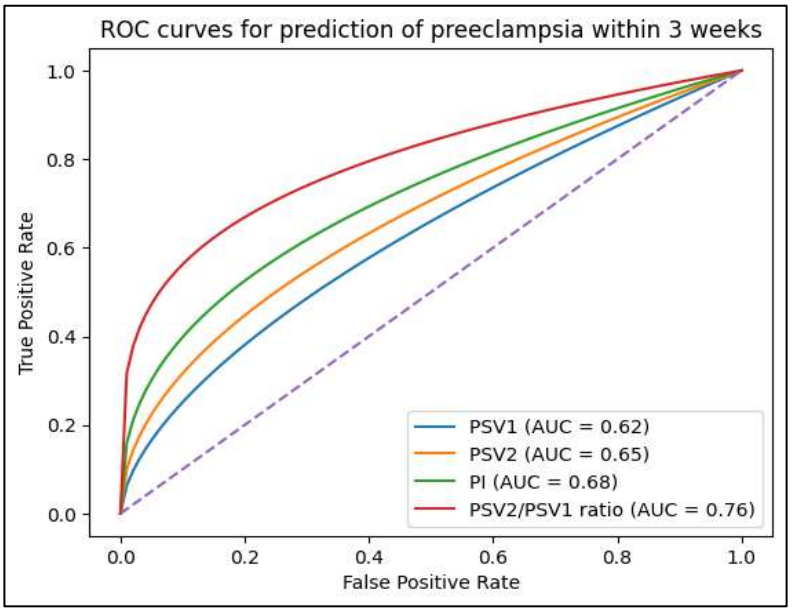

Figure 1. ROC curves for prediction of preeclampsia within 3 weeks using maternal ophthalmic artery Doppler parameters.

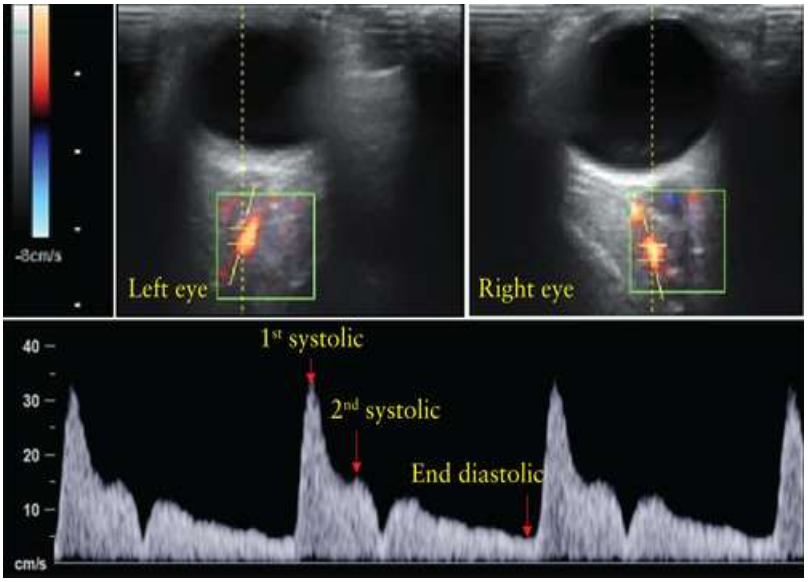

Figure 2. Maternal ophthalmic artery Doppler assessment.

Colour Doppler images of the left and right maternal orbits demonstrating flow within the ophthalmic arteries. The lower panel shows a representative pulsed-wave Doppler waveform, with the first (PSV1) and second (PSV2) systolic velocity peaks and the end-diastolic velocity (EDV) labelled.

Summary of Key Findings

In this cohort of 230 women assessed at 35–37 weeks' gestation, ophthalmic artery Doppler indices showed measurable but variable capacity to predict PE occurring within the subsequent three weeks. The PSV2/PSV1 ratio consistently outperformed the other individual indices, returning both the highest detection rate at a fixed false-positive rate and the greatest AUC.

DISCUSSION

This prospective cohort study indicates that maternal ophthalmic artery Doppler assessment performed at 35–37 weeks' gestation carries moderate predictive value for the short-term development of PE. Of the indices examined, the PSV2/PSV1 ratio demonstrated the strongest discriminatory performance for identifying women who went on to develop PE within a clinically meaningful window. These findings position ophthalmic artery Doppler as a plausible adjunct to late third-trimester risk stratification, rather than as a stand-alone screening modality.

The comparative advantage of the PSV2/PSV1 ratio is biologically plausible. Ophthalmic artery waveform morphology is governed by downstream cerebral vascular resistance and by cerebral autoregulatory tone. An accentuated second systolic peak relative to the first has previously been linked to cerebral vasodilatation and reduced downstream impedance — changes consistent with the systemic endothelial dysfunction and altered vascular reactivity that characterize PE. Because it is a ratio of two velocities measured within the same waveform, the PSV2/PSV1 index is inherently less susceptible to insonation-angle error and inter-examination technical variability than absolute velocity measurements, which may partly explain its superior and more reproducible performance in this cohort.

This finding is broadly consistent with, and extends, the existing literature. Earlier reports have largely characterized ophthalmic artery Doppler changes in women with already-established PE or in earlier gestational windows, often using heterogeneous acquisition protocols and reporting variable predictive accuracy [3-6]. By focusing specifically on short-term prediction in the late third trimester — the period in which decisions regarding surveillance intensity and timing of delivery are most clinically pressing — this study addresses a comparatively underexplored but practically important application of the technique. The moderate detection rates observed here, however, also serve as a reminder that late-onset PE is a multifactorial syndrome unlikely to be captured in full by any single Doppler parameter, however well it performs in isolation [9].

Strengths and Limitations

Strengths of this study include its prospective design, a standardized and reproducible Doppler acquisition protocol, complete outcome ascertainment, and STROBE-compliant reporting. Several limitations warrant consideration. This

was a single-center study with a comparatively small number of PE events (n = 26), which constrains the precision of the reported detection rates and may limit generalizability to other populations. Doppler measurements were obtained at a single timepoint, precluding assessment of longitudinal within-patient change, which may carry additional predictive value. Inter- and intra-observer variability, although minimized through a standardized protocol, was not formally quantified in this cohort. Finally, the study population comprised only women of female biological sex, and data on gender identity, race, and ethnicity were not systematically collected, precluding assessment of their potential influence on ophthalmic artery Doppler findings.

Clinical Implications

These findings suggest that maternal ophthalmic artery Doppler — and the PSV2/PSV1 ratio in particular — may help identify a subset of women at heightened short-term risk of PE who could benefit from intensified surveillance in the closing weeks of

the third trimester. Given its moderate discriminatory performance, however, this modality is best conceived as a complement to, rather than a substitute for, established clinical and biochemical risk-assessment pathways.

Future work should prioritize external validation in larger, multicenter cohorts with a greater number of PE events, formal assessment of inter-observer reproducibility, and exploration of serial rather than single-timepoint Doppler assessment. A specific hypothesis arising from this work is that combining ophthalmic artery Doppler indices with maternal cardiovascular or placental biomarkers within a multimodal prediction model may improve short-term risk stratification for PE beyond what any single cerebrovascular marker can achieve alone.

CONCLUSION

Maternal ophthalmic artery Doppler assessment at 35–37 weeks' gestation demonstrates moderate ability to predict the short-term (within three weeks) development of preeclampsia. Among the indices evaluated, the PSV2/PSV1 ratio showed the best discriminatory performance and represents a promising, technically robust adjunct to late third-trimester risk assessment, to be used alongside — not in place of — existing clinical and biochemical screening strategies.

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