

Association between ophthalmic artery Doppler indices and adverse perinatal outcomes in women with pre-eclampsia in Kano, Nigeria

Hussaini Dede¹, Anas Ismail², Yusuf Lawal², Ayyuba Rabi³, Isa Hassan Muhammad¹

¹Department of Radiology, Yobe State University, Damaturu, Nigeria

²Department of Radiology, Bayero University, Kano, Nigeria

³Department of Obstetrics and Gynaecology, Bayero University, Kano, Nigeria

Corresponding Author: Dr Hussaini Dede Email: dedehussaini@yahoo.com

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Abstract

Background: - Pre-eclampsia (PE) as a pregnancy-related hypertensive disorder poses a significant challenge to maternal and foetal health in low and middle-income countries, like Nigeria. The ophthalmic artery Doppler (OAD) is a tool that has been studied to aid in diagnosing PE, since its pathogenesis is not limited to the placental bed, but extends to cardiovascular and endothelial adaptations during pregnancy. Abnormal maternal ophthalmic artery Doppler velocimetry is associated with poor perinatal outcomes. **Objectives:** - To determine ophthalmic artery Doppler velocimetric indices of patients with pre-eclampsia using ultrasonography and correlate these indices with pregnancy-related outcomes. **Materials and methods:** - This was an observational cohort study carried out at a tertiary hospital in Nigeria. Eighty-two pre-eclamptic patients and an equal number of normotensive-matched pregnant controls were recruited for the study. The ophthalmic artery peak ratio, pulsatility index, and resistive index of both groups were obtained using high-resolution ultrasound Doppler examination. These parameters were then correlated with selected maternal and perinatal outcomes. **Results:** The mean age of pre-eclamptic subjects ($28\text{years} \pm 3.86$) and that of the control subjects ($27.52\text{years} \pm 4.36$) were not statistically different ($p = 0.444$). Gestational ages were also similar between the two groups (pre-eclamptic: mean = $33.24\text{weeks} \pm 2.89$; normotensive: mean $33.41\text{weeks} \pm 3.72$; $p = 0.74$).

The ophthalmic artery RI, PI and PR were significantly associated with adverse perinatal outcomes. These outcomes include: low birthweight ($p = 0.01$) stillbirth ($P < 0.003$) and depressed Apgar score ($p = 0.001$). **Conclusions:** This study found significant association between ophthalmic artery velocimetric indices and adverse perinatal outcomes, suggesting that ophthalmic artery Doppler can enhance risk stratification and improve perinatal outcomes.

Key Words: - Ophthalmic artery, pre-eclampsia, Doppler, velocimetry, perinatal outcomes

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Introduction

Pre-eclampsia (PE) is a pregnancy-related hypertensive disorder occurring usually after 20 weeks of gestation.¹ If left untreated, it progresses to eclampsia.² As estimated by World Health Organization (WHO), the occurrence of PE is seven times higher in developing countries compared to developed countries.³ In Nigeria the prevalence of PE ranges between 2% and 16.7%.⁴ The incidence of eclampsia lies in the range of 0.3 per 1000 deliveries in Calabar (Southern Nigeria) to as high as 9 per 100 deliveries in Birnin Kudu, (Northwestern Nigeria).⁵

Hypertensive disorders are a common complications of pregnancy that put women and their foetuses at disproportionate risk for further complications, as well as life-long sequelae.⁶ Classically, the American College of Obstetrics and Gynaecology (ACOG) defines pre-eclampsia as the presence of hypertension and proteinuria occurring after 20 weeks of gestation in a previously normotensive patient.⁷ However, a significant proportion of women develop systemic manifestations of PE such as low platelets or elevated liver enzymes before the hallmark of proteinuria is detectable resulting in delayed diagnoses.⁶ The common maternal adverse perinatal outcome of PE include: maternal mortality, eclampsia, premature rupture of membrane, presence of antepartum haemorrhage or postpartum haemorrhage (blood loss at birth 500 mL or greater), and admission to the intensive care unit. Foetal adverse outcome include: depressed Apgar score, low birth weight, stillbirth and admission to the neonatal unit.⁸

PE is characterized as mild or severe based on the degree of hypertension, proteinuria and the presence of symptoms resulting from involvement of systemic organs.⁹ Severe PE is a serious clinical type of PE manifested by at least one of the followings: persistent increase in blood pressure ($\geq 160/110$ mmHg), hepatic or renal failure, haemolytic anaemia, elevated liver enzymes and low

platelet count (HELLP syndrome), cerebral or visual disturbances, persistent severe epigastric pain and pulmonary edema.¹⁰ If left untreated, the disorder often leads to serious maternal and perinatal complications.¹¹

Uterine artery and several peripheral vessels Doppler indices have been investigated as a potential marker for the development of pre-eclampsia, among which is ophthalmic artery Doppler (OAD). Evaluating ophthalmic artery with Doppler sonography is easy using standard ultrasound equipment and is unaffected by adiposity. Furthermore, the Doppler velocimetric indices have constant reference ranges throughout trimesters of pregnancy.¹² There is paucity of data regarding the relationships between ophthalmic artery Doppler velocimetric indices and adverse perinatal outcomes in patients with pre-eclampsia.

Although ophthalmic artery Doppler (OAD) ultrasound offers a promising, cost-effective approach to evaluate pre-eclampsia and predict perinatal outcomes¹³, there is paucity of studies on its effectiveness in predicting perinatal outcome of PE in Nigeria.

This study is aimed at evaluating the parameters of the ophthalmic artery Doppler velocimetry in patients with PE and correlate them with perinatal outcome (for both mother and foetus/new-born).

Materials and methods

This hospital based prospective cohort study was carried out in Aminu Kano Teaching Hospital (AKTH). It is a tertiary care facility in Kano, Nigeria. Using a systematic random sampling technique, 82 pregnant women being managed for pre-eclampsia at the obstetrics and gynaecology department of AKTH, and an equal number of matched normotensive pregnant women as controls were recruited into the study. The two groups were matched in terms of maternal age and gestational age.

The study was conducted within 8 months (December, 2023 – July, 2024) after

obtaining institutional ethics board approval from the Aminu Kano Teaching Hospital Health Research Ethics Committee. The first 3 months of the study were used for recruiting the study subjects, obtain ophthalmic artery Doppler velocimetry and other antenatal data as well as perinatal outcome data (for those that deliver within the first 3 months of the study). The last 5 months of the study were used to obtain data on perinatal outcomes. Pregnant women who were not-consenting, smokers, having multiple pregnancies, orbital pathologies and maternal conditions before pregnancy, such as diabetes mellitus, chronic hypertension, and HIV infection, were excluded from both study groups. Informed consents were obtained from the study and control groups. Data were obtained using structured data collection sheet. The maternal age, blood pressure (BP), gestational age and estimated foetal weight (by ultrasound scan) of study group were obtained. Similar information were obtained from the control group. The ophthalmic artery peak ratio (PR), pulsatility index (PI), and resistive index (RI) were obtained for both study and control groups. Both groups were then followed up to the time of delivery and the following perinatal outcomes were recorded: foetal Apgar score, birth weight and stillbirth.

Technique for ophthalmic artery Doppler scan

Ultrasound scanning was performed using HYVission V5 Panascope digital ultrasound machine, equipped with 6.8-15MHz transducer. An acoustic coupling gel was applied on the transducer which was then placed directly and gently on the closed eyelid with the gaze directed at the ceiling.¹⁴ The examiner's hand was rested on the orbital margin to minimize the applied pressure to the globe and the orbit. The insonation angle was kept below 20° with high-pass filter set to its minimum value.⁴ Real time grey scale and colour Doppler scanning was then performed in longitudinal

and transverse planes of both globes. The hypoechoic stripe of the optic nerve was then identified with the ophthalmic artery just medial to it.¹⁵ Using colour Doppler, the ophthalmic artery was further identified by its colour flow and pulsatility at about 15 millimetres from the optic disc (on the medial aspect of the optic nerve). Pulsed-wave Doppler was then applied, with sample volume placed around 15mm behind optic disc, medial to optic nerve; sample volume was about 2mm in length.⁴

The Doppler sample gate (≤ 2 mm) was placed at the centre of the detected vessel to image the spectral pattern. Pulse repetition frequency (PRF) was set at 125 kHz and adjusted as appropriate.¹⁴

The velocimetric indices which include, Resistive index (RI), Pulsatility Index (PI) and peak ratio (PR) were obtained from the ultrasound machine which has the manufacturer calibrated automatic calculator for RI and PI. While the PR was calculated manually by dividing the second peak systolic velocity (P2) with the peak systolic velocity (PSV). Both ophthalmic arteries were insonated and measurement taken three times on both right and left side, and average of each of the three reading were recorded.

Data generated were analysed using IBM statistical product and service solutions (SPSS) statistics software version 22.0 New York, USA. Mean $\pm$ standard deviation was used to summarize quantitative variables. T-test was used to compare continuous with group/categorical variables with two levels. Findings were then presented numerically, graphically and in tabular forms. A p-value of 0.05 or below was considered to be statistically significant.

Ethical consideration

Prior to commencement of the study, ethical approval was obtained from the ethics committee of Aminu Kano Teaching Hospital Kano. Furthermore, an informed consent was obtained from all the members of the study and control groups. Doppler

ultrasonography of the eye is a non-ionizing based imaging modality and considered relatively safer compared to other imaging modalities.⁴² Patient confidentiality was protected by removing identification markers on all images obtained during the study. During the study, the researcher was responsible for any financial burden of the investigation and participants did not pay for any investigation outside the standard of care. Imaging cost were covered by the researcher. Participants with incidental abnormalities detected in the course of the ophthalmic artery Doppler ultrasound scan or the obstetrics scan were referred to the appropriate specialist for further evaluation.

Results

This study was conducted over a period of 8 months from December 2023 to July 2024. A total of 164 subjects were recruited into the study, comprising 82 pre-eclamptic subjects and equal number of normotensive pregnant controls. However, 2 pre-eclamptic subjects were lost to follow-up. As a result, a total of 160 subjects comprising 80 pre-eclamptic and equal number of normotensive control subjects were reviewed for analysis in this study.

Socio-Demographics of the Study Subjects

The age range of pre-eclamptic subjects was 19 – 38 years with a mean age of 28 ± 3.86 years while that of the normotensive pregnant control subjects was 18 – 37 years with a mean of 27.52 ± 4.36 years. The mean age difference between the two groups was not statistically significant ($p = 0.444$). The highest number of the respondents were found in the age range of 25 – 29 years comprising of 37 individuals (46.3%) in both the pre-eclamptic subjects and normotensive pregnant control groups as shown in **Table 1**. The gestational age of the pre-eclamptic group ranges from 28 – 38 weeks with a mean gestational age of 33.24 ± 2.89 weeks, while that of the normotensive pregnant control subjects was 25 – 40 weeks with a mean of 33.41 ± 3.72 weeks. There is no statistically

significant difference between the mean gestational ages of the two groups ($P = 0.74$) as shown in the **Table 1** below.

Table 1: Socio-demographic Characteristics of pre-eclamptic and normotensive pregnant control Subjects:

Variables	Pre-eclamptic subjects n=80 (%)	Normotensive pregnant control n=80 (%)	Total n=160	P-value
Age (Years)				
<20	2 (2.5)	2 (2.5)	4	
20-24	12 (15.0)	12 (15.0)	24	
25-29	37 (46.3)	37 (46.3)	74	
30-34	23 (28.8)	23 (28.8)	46	
35-40	6 (7.5)	6 (7.5)	12	
Mean $\pm$ SD	28 ± 3.82	27.54 ± 4.32		P = 0.444
Gestational age (weeks)				
20 - 24	0	0	0	
25 - 29	9 (11.3)	9 (11.3)	18	
30 - 34	37 (46.3)	37 (46.3)	74	
35 - 40	34 (42.5)	34 (42.5)	68	
Mean $\pm$ SD	33.19 ± 2.88	33.42 ± 3.68		P = 0.740

Correlation between RI, PI and PR with apgar score among pre-eclamptic subjects.

There was statistically significant negative correlation between APGAR score and PR ($P = 0.00008$). On the other hand, statistically significant positive correlation was observed between APGAR score and RI ($P = 0.000017$) and PI ($P = 0.001$)-**Tables 2**

Table 2: Correlation of ophthalmic artery Doppler velocimetric indices (RI, PI and PR) with APGAR score among pre-eclamptic subjects.

APGAR Score			
	Pearson correlation	Sig. (2-tailed)	N

Right Side	RI	0.458	0.001*	80
	PI	0.374	0.001*	80
	PR	-0.568	0.001*	80
Left Side	RI	0.472	0.001*	80
	PI	0.368	0.001*	80
	PR	-0.532	0.001*	80

*Correlation is significant at the $P < 0.05$ level (2-tailed).

Relationship between RI, PI and PR with birthweight among the babies of preeclamptic subjects.

The mean RI, PI and PR values for pre-eclamptic subjects delivered of babies with normal birthweight were 0.62, 1.02 and 0.72 respectively on the right side. The corresponding values on the left were 0.62, 1.04 and 0.71 respectively. The mean RI, PI and PR values for pre-eclamptic subjects delivered of babies with low birth weight were 0.56, 0.83 and 0.76 respectively on the right side. The corresponding values on the left side were 0.56, 0.82 and 0.77 respectively.

The pre-eclamptic subjects that delivered of babies with low birthweight had higher PR with lower IR and PI compared with mothers who delivered babies having normal birthweight ($P < 0.003$) as shown in **Table 3**.

Table 3: Relationships between ophthalmic arteries RI, PI and PR with birthweight among pre-eclamptic subjects.

BIRTHWEIGHT				
		Normal birthweight n = 56	Low birthweight n = 24	P-VALUE
Right Side	RI	0.62	0.56	0.006*
	PI	1.04	0.83	0.003*
	PR	0.71	0.76	0.003*
Left Side	RI	0.62	0.56	0.006*
	PI	1.04	0.83	0.003*
	PR	0.71	0.76	0.003*

RI	0.62	0.56	0.005*
PI	1.02	0.82	0.003*
PR	0.72	0.77	0.010*

*Statistically significant at $p \leq 0.05$

Relationship between RI, PI and PR and rate of stillbirth among the pre-eclamptic subjects.

The mean RI, PI and PR values for pre-eclamptic subjects that had stillbirth were 0.59, 0.93 and 0.74 respectively on the right side. The corresponding values on the left were 0.59, 0.92 and 0.74 respectively. The mean RI, PI and PR values for pre-eclamptic subjects that had live-birth were 0.49, 0.65 and 0.84 respectively on the right side. The corresponding values on the left side were 0.49, 0.65 and 0.84 respectively.

The pre-eclamptic subjects who had stillbirth had statistically significant lower IR and PI with higher PR compared to the pre-eclamptic subjects that had live-birth (all P values < 0.003). **Table 4**.

Table 4: Relationships between ophthalmic arteries RI, PI and PR with the rate of stillbirth among pre-eclamptic subjects.

		Live birth, n = 11	Stillbirth, n = 69	P-VALUE
Right Side	RI	0.59	0.49	0.001*
	PI	0.93	0.65	0.003*
	PR	0.74	0.84	0.001*
Left Side	RI	0.59	0.49	0.001*
	PI	0.92	0.65	0.003*
	PR	0.74	0.84	0.001*

*Statistically significant at $p \leq 0.05$

Discussion

A total of 80 pre-eclamptic subjects were evaluated in this study with an equal number of normotensive pregnant control groups summing up to 160 participants. The mean

age of the pre-eclamptic subjects is 28 ± 3.86 years with an age range of 19 – 38 years. Similarly, the control group has a mean age and range of 27.52 ± 4.36 years and 18 – 37 years respectively. The modal age for both the study and control groups is 25 – 29 years. The difference between the mean age of the study and control groups was not statistically significant (P- value = 0.444), because they were matched. The mean age obtained in this study (27.52 ± 4.36 years) was similar one Nigerian study, by *Mustapha et al*¹⁶ in Northwestern Nigeria (at 27.24 ± 4.16) and another Asian study by *Rani et al*¹⁷ in India (at 26.58 ± 4.30). However, *Olatunji et al*⁴ in Southwestern Nigeria and *Sapantzoglou et al* in United Kingdom obtained higher mean age values in their studies at 32.4 ± 4.7 years and 34.95 ± 4.95 years. These differences were likely due to socio-cultural variation in terms of the time of marriage and childbearing among the regions. The modal age of this study was also in agreement with what was reported by *Melese et al*¹⁰ in Ethiopia.

The mean gestational age of the pre-eclamptic group was 33.24 ± 2.89 , while that of the control group was 33.41 ± 3.72 weeks. The modal gestational age for the two groups was 25 – 29 weeks. While the literature confirmed that there are no changes in ophthalmic artery Doppler indices as gestation advances,^{12,13} there was no statistically significant difference between the mean gestational age of pre-eclamptic subjects and their control groups (P value = 0.74). The modal gestational age presented in this study was similar to what was found by *Olatunji et al*⁴ in Southwestern Nigeria where a gestational age of less than 30 weeks was reported. The mean gestational age of the pre-eclamptic group was also similar to what was recorded by *Mustapha et al*¹⁶ in Northwestern Nigeria at 33.20 ± 3.74 weeks.

This study found statistically significant negative correlation between the APGAR score of babies of pre-eclamptic subjects and maternal ophthalmic artery P2 (P = 0.03),

EDV (P = 0.028) and PR (P = 0.00008), with statistically significant positive correlation observed between the APGAR score and RI (P < 0.001) and PI (P = 0.001). There is paucity of data, correlating maternal ophthalmic artery Doppler velocimetric indices with the new-born APGAR score.

This study also demonstrated that pre-eclamptic subjects that were delivered of babies having low birthweight had higher PSV (P = 0.009), EDV (P = 0.001), P2 (P = 0.002) and PR (P = 0.003) with lower RI (P = 0.006) and PI (P = 0.003) compared with pre-eclamptic mothers that were delivered of babies having normal birthweight. Similar findings are reported from a Brazilian study by *Maria et al*,¹⁸ where pre-eclamptic mothers with higher PR had the smallest babies. Similarly *Gyokova et al*¹⁹ in Bulgaria and *Manchu et al*²⁰ in India reported statistically significant negative correlation between PR and birth weight in patients with preeclampsia.

The pre-eclamptic subjects who had stillbirth (in this study) had statistically significant lower RI (P < 0.001) and PI (P = 0.003) with a higher PR (P < 0.001) compared to the pre-eclamptic subjects that had livebirth. The PSV, EDV and P2 had no statistically significant difference between the two groups (P = 0.99, 0.164 and 0.299). There is paucity of data interrogating direct relationships between the rate of stillbirth and ophthalmic artery Doppler velocimetric indices among preeclamptic subjects. However, *Maria et al*,¹⁸ in Brazil and *Gyokova et al*²¹ in Bulgaria reported relationships between higher ophthalmic artery peak ratio (PR) and adverse perinatal outcomes.

One of the strengths of this study was being a prospective study. The findings underscore the potential of ophthalmic artery Doppler velocimetry as a valuable tool in predicting adverse perinatal outcomes in patients with pre-eclampsia.

The limitation of this study include the fact that it was conducted at a single centre, highlighting the potential for selection bias due to its limited geographic scope. While the findings regarding ophthalmic artery Doppler parameters are significant, the results may not fully represent the broader population. Secondly, long term perinatal complications were not addressed in this study due to time and resource limitation.

Conclusions

From findings in this study, it was observed that ocular vascular resistance among pre-eclamptic subjects determined by Doppler velocimetric indices was significantly lower than in the normotensive pregnant control group. There was a statistically significant relation between ophthalmic artery Doppler velocimetric indices and adverse perinatal outcomes. The ophthalmic artery Doppler velocimetry has the potential to improve risk stratification, and overall perinatal outcomes.

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