## **Original article**



# Ultrasound Evaluation of the Impact of Disparities of the Pulsatility Indices on Fetal Outcomes in Preeclamptic Pregnancies: A Pilot Study from a Tertiary Hospital in South South Nigeria

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## **Summary**

**<u>Objective</u>:** To examine the relationships between fetal Doppler indices and perinatal outcomes in women with preeclampsia and normotensive controls. <u>**Methods:**</u> Middle cerebral artery (MCA) pulsatility index (PI), umbilical artery (UA) PI, and cerebroumbilical PI ratio were measured in women with preeclampsia (n=50) and normotensive controls (n=50). Associations with birth weight, gestational age at delivery, and 1- and 5-minute Apgar scores were evaluated. Predictive accuracy of indices for adverse outcomes was also assessed. <u>**Results:**</u> In pre-eclamptics, MCA PI correlated with birth weight, Apgar scores, and gestational age (p<0.05). UA PI correlated negatively with all outcomes (p<0.05). Cerebroumbilical ratio correlated positively with birth weight and Apgar scores, and negatively with gestational age and 1-minute Apgar (p<0.05). UA PI demonstrated high sensitivity and specificity for predicting outcomes except prematurity. Cerebroumbilical ratio showed balanced sensitivity and specificity except for stillbirths. <u>**Conclusions:**</u> Fetal Doppler indices provide valuable prognostic information in preeclampsia. UA PI may be optimal for predicting adverse outcomes. Cerebroumbilical ratio balances sensitivity and specificity. Larger multicenter studies are needed to standardize criteria and validate predictive accuracy across disease severity. Fetal Doppler surveillance warrants further research to optimize preeclampsia management.

Keywords: Preeclampsia, Doppler Pulsatility Indices, cerebroumbilical pulsatility index ratio (CUmR), Nigeria.

## Introduction

The significance of ultrasonography in the field of obstetrics has undergone significant development throughout time, and its efficacy in predicting unfavourable perinatal outcomes has been recognised as crucial in preserving lives during complex gestations <sup>[1]</sup>. The issue of hypertension during pregnancy has been a longstanding concern for obstetricians throughout the years <sup>[1,2]</sup>. Ultrasound has emerged as a significant instrument in contemporary obstetric practice as a result of advancements in technology and computer processing <sup>[3]</sup>. These advancements enable the visualisation and identification of various anatomical structures such as the placenta, membranes, fluid, and foetal abnormalities <sup>[1,3]</sup>.

Doppler velocimetry examinations of the placental and foetal circulation can provide crucial information about the health of the foetus, offering a chance for positive perinatal outcomes in patients with preeclampsia <sup>[2]</sup>. The application of Doppler interference to examine the foetal vascular system facilitates an indirect assessment of placental resistance.

Preeclampsia poses significant challenges in obstetric care due to its association with hypertension and organ dysfunction during pregnancy <sup>[4]</sup>. Fetal well-being assessment is critical in managing preeclamptic pregnancies to mitigate risks related to uteroplacental insufficiency and impaired fetal growth <sup>[5]</sup>. Doppler ultrasound studies measuring the pulsatility indices of the middle cerebral artery (MCA) and umbilical artery (UA) play a pivotal role in evaluating fetal circulation and health status. The Cerebroumbilical Pulsatility Index (C/U PI) ratio is composed of the pulsatility indices of two key vessels: the middle cerebral artery (MCA) and the umbilical artery (UA) [6-8]. By incorporating the pulsatility indices of the MCA and UA into the C/U PI ratio calculation, healthcare providers can derive a value that reflects the differences in resistances between the fetal brain circulation (represented by the MCA) and the placental circulation (represented by the UA). This ratio provides crucial information about fetal hemodynamics and can serve as a valuable indicator of fetal wellbeing and potential risks in conditions such as preeclampsia. The cerebroumbilical pulsatility index ratio (CUmR), derived from these

Doppler measurements, reflects differential resistances in fetal brain and placental circulation, serving as a potential marker for altered fetal hemodynamics and adverse outcomes in preeclamptic pregnancies. Understanding the impact of CUmR disparities on fetal outcomes is essential for timely risk stratification and intervention to optimize perinatal care <sup>[9,10]</sup>. These adverse perinatal outcomes in this study are defined as any of these: Birth weight:-low birth weight<2.5kg, very low birth weight<1.5kg, extreme low birth weight<1kg; Still birth/IUFD-baby born with no signs of life at or after 28weeks gestation/death in-utero or perinatal deaths (early neonatal deaths); APGAR score less than seven at five minutes and Prematurity <37weeks; others are special care baby unit (SCBU)Admission; Duration of stay in SCBU; and also evaluation of the mode of delivery that is Assisted vaginal delivery or Caesarean Section.

This study aims to explore the relationship between CUmR variations and perinatal outcomes in preeclamptic pregnancies. By elucidating the associations between Doppler parameters and complications like fetal growth restriction, preterm birth, and adverse neonatal outcomes.

Therefore, the objective of this research is to assess the Cerebroumbilical pulsatility index ratio (CUmR), in preeclamptic and normotensive pregnancies at Braithwaite Memorial Specialist Hospital (BMSH), located in Port-Harcourt. The aim is to utilise this measurement to forecast and contrast the perinatal results of the two groups, with the goal of promptly intervening and enhancing overall perinatal outcomes. Moreover, there exists a scarcity of research about the efficacy of this pulsatility marker in forecasting unfavourable perinatal outcomes within the regions of Nigeria and West Africa.

## **Materials and Method**

## Study Area/Site/Study Population

A tertiary hospital situated in the southern area of Nigeria was the site of the study. Pregnant women who were attending the antenatal clinic of the hospital were recruited into the study.

## **Study Design**

This hospital-based prospective cohort study included preeclamptic and normotensive pregnant women. Eligibility for preeclamptic pregnant women were the following: Singleton pregnancy with known GA due to LMP or early ultrasound before 24 weeks; Pregnant age 28-36 weeks. G.A.; Preeclamptic individuals have BP 140/90mmhg or a fast rise of 30/15mmhg with proteinuria or oedema.

*Inclusion criteria* for normotensive pregnant women were -a singleton pregnancy with known GA (LMP or early ultrasound before 24 weeks); Pregnant age 28-36 weeks. G.A.; BP under 120/80mmhg is normal; Normal dipstick urinalysis.

*Exclusion criteria* for preeclamptic and normotensive pregnant women were: Single Umbilical artery; Chronic hypertension patient - Pre-pregnancy hypertension; Gestational hypertension: post-20 weeks GA without proteinuria; Diabetes during pregnancy; Patient with cardiac disease; Multiple pregnancies; Congenital abnormalities; First Doppler examination reveals intrauterine foetal demise; positive tobacco history

#### **Study Duration**

The research was carried out for a duration of twelve months. (January 2021-December 2021) Follow-up was conducted using the medical records, which provide access to such information.

Furthermore, telephone calls were made and regular visits to the labour ward were conducted concurrently.

## Sample Size Calculation

This study calculated sample size using the two-group comparison formula <sup>[11]</sup>.  $n = 2 (Z\alpha + Z\beta)2 p q d^2 n =$  minimum sample size per group

 $Z\alpha$  = intended statistical significance, set at 95% = 1.96.

 $Z\beta = 90\%$  power, about 1.28 p = proportion of interest from prior study; preeclampsia prevalence in Nigeria is 2%-16.7%, averaging 9.35% (0.094).16-19 q= 1 - p; 1 - 0.094 = 0.906 d= 0.2 precision n= 2 (1.96 + 1.28)0.094X 0.906= 44.7 (0.2)<sup>2</sup> = 44.7 approximately 45.

The 10% non-response allowance was derived using the formula.

Adjusted sample size (Na = n) 1 - non-response.

The minimum sample size is 45, and the non-response rate is 10% (0.1).1- 0.1

Hence, 50 preeclamptic and 50 normotensive pregnant women were recruited into the study making a total sample size of 100.

#### Sampling Technique

A sampling interval-based systematic sampling strategy identified normotensive pregnant women. Divide the average number of normotensive pregnant women in the clinic by the sampling size to calculate the sampling interval. The antenatal clinic attendance averaged 40 normotensive pregnant women, which was enough to meet the sample size every clinic week over three months (50/12=4.2), or four. The sample fraction (k) was derived by dividing the average number of normotensive pregnant women each clinic (40) by the weekly recruitment rate (4), which is 10. Thus, every 10th normotensive pregnant woman at the antenatal clinic was recruited. The first patient of a clinic day was chosen by balloting the first 10 patients. After that, every 10th patient would be recruited. The technique continued until the desired sample size was reached. The study's eligible participants were recruited sequentially after signing consent.

#### Study Procedure/ Methodology

Confirmatory blood pressure check and protein levels in urine was done with dipstick urine test, as well as random blood sugar check was carried out on both the pre-eclamptic cases and controls. The sociodemographic and obstetric information were obtained.

**Scanning Technique:** All women underwent normal obstetric ultrasounds in a semi-recumbent position to prevent IVC pressure and hypotension <sup>[12]</sup>. All scans were done by the researcher utilising a 3-5MHz transabdominal probe on a Diagnostic Ultrasound Machine (LOGIQ, Model V5 SN 617848WXO, YEAR 2017). After removing air with coupling gel, a full obstetric scan confirmed gestational age. Before Doppler, foetal anomalies and other parameters were checked.

Middle cerebral artery (MCA)identification and measurement: The technique used to identify middle cerebral artery waveforms was a combination of colour and pulsed Doppler imaging, following ISUOG standards <sup>[13]</sup>. A enlarged axial view of the foetal brain, including the thalami and sphenoid bone wings. The circle of Willis and proximal MCA were identified using colour flow mapping. Next, the pulsed-wave Doppler gate was put in the MCA's proximal third, near its origin in the internal carotid artery <sup>[12]</sup>. Ultrasound beam-blood flow angle was kept as close as 0 degree. There was limited foetal activity during Doppler interrogations. Analysing spectral waveforms and automatically/manually tracing them generated Doppler parameters after freezing. To reduce intraobserver error, at least three measurements were taken and averaged.

**The umbilical artery (UmA)measurement:** Colour and pulsed Doppler imaging identified the umbilical artery. A free-floating cord loop during minimal foetal activity was used to identify the umbilical artery and collect flow velocity waveforms. We used 2mm samples and the smallest velocity scales. To obtain a clear spectrum waveform with low noise, the pulse repetition frequency was modified to 1–5 KHz. A minimum of four roughly similar waveforms were recorded. To reduce intra-observer error, three measurements were taken and averaged. Keeping the Doppler insonation angle below 60 degrees.

Following measurements, the coupling gel was removed, and the subject was helped up from the examination couch. The mean results were analysed statistically.

Three waveforms from the middle cerebral and umbilical arteries were averaged to compute the PI to reduce intra-observer variability. Machines generated pulsatility indices (UmA PI) Following, the cerebroumbilical pulsatility index ratio was manually determined using the formula MCA/UmA PI=CUmR and was seen as abnormal when the CUmR<1.087

## Data Analysis

Microsoft Excel spreadsheets were used to enter data and export it to SPSS version 21 for statistical analysis.

## Result

#### Socio-Demographic Characteristics

The study recruited a cohort of 100 pregnant women, consisting of 50 pregnant women with pre-eclampsia and 50 normotensive pregnant women. Among the sample of 50 individuals diagnosed with preeclampsia, 9 (28.0%) had moderate preeclampsia, while 41 (82.0%) presented with severe preeclampsia. The pre-eclamptic group showed a mean age of  $32.20\pm4.99$ , while the control group had a mean age of  $31.50\pm5.49$  (P=0.503).

The basic and clinical characteristics of the groups are shown in Table 1. There was significant difference in gestational age at ultrasound scan (weeks) between pre-eclamptic and normotensive pregnant women. The mean GA of the pre-eclamptic group was  $30.68\pm2.26$ , while that of control was  $34.02\pm1.56$  (P=0.001). It also shows that both the systolic and diastolic blood pressures measurements were significantly higher in the pre-eclamptic group, with mean systolic and diastolic blood pressure of 122.82mmHg and 74.56mmHg respectively for the case group, and 102.38mmHg and 64.54mmHg respectively for the control group. (P=0.0001).

Table 1: Comparison of obstetric-related and clinical characteristics between pre-eclamptic and normotensives women in the study.
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	Study group	Study group			
	Pre-eclampsia Normotensive				
Variable	Mean ±SD	Mean ±SD	t	p-value	
Gestational age by USS (weeks)	30.68±2.26	34.02±1.56	8.644	0.001*	
Gravidity	3.04±2.49	2.40±1.81	1.471	0.145	
Parity	1.26±1.35	0.86±1.07	1.641	0.104	
Systolic blood pressure (mmHg)	122.82±28.86	102.38±9.36	4.763	0.0001*	
Diastolic blood pressure (mmHg)	74.56±14.77	64.54±6.81	4.356	0.0001*	

SD: Standard deviation\*Statistically significant

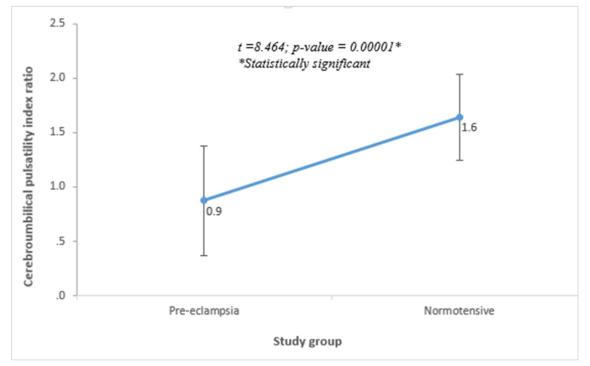


Figure 2: Error bar showing mean Cerebroumbilical pulsatility index ratio between Pre-eclampsia and Normotensive women in the study

The cerebroumbilical pulsatility index ratio was lower in the preeclamptic group  $(0.90\pm0.51)$  and normal in the control group  $(1.60\pm0.39)$  (P=0.00001) as seen in Figure 2.

Table 2: Comparison of proportion of abnormal and normal Cerebroumbilical pulsatility index ratio between Pre-eclampsia and Normotensive women in the study

Cerebroumbilical pulsa	Cerebroumbilical pulsatility index ratio			
Abnormal	Normal	Total		
n (%)	n (%)	n (%)		
42 (84.0)	8 (16.0)	50 (100.0)		
1 (2.0)	49 (98.0)	50 (100.0)		
43 (43.0)	57 (57.0)	100 (100.0)		
	Abnormal n (%) 42 (84.0) 1 (2.0)	Abnormal Normal   n (%) n (%)   42 (84.0) 8 (16.0)   1 (2.0) 49 (98.0)		

*Chi Square=68.584, p-value=0.00001\*; Odds ratio=257.250, 95% CI (30.90 – 2141.72); \*Statistically significant* 

Table 2 shows the comparison of the proportion of abnormal and normal cerebroumbilical pulsatility index ratio in the study population and it was statistical significance. Out of the 50 preeclamptic patients 42(84.0%) had abnormal values and 8(16.0%) had normal values respectively. Those with abnormal cerebroumbilical pulsatility index ratio among the pre-eclamptic group; four (9.5%) were mild and 38(90.5%) were severe preeclamptic cases. Also, out of the 50 normotensive pregnant women 1(2.0%) had abnormal values and 49(98.0%) had normal values respectively.

Table 3: Comparison of perinatal outcomes between pre-eclamptic and normotensives women in the s	tudy

Variable	Pre-Eclamptic	Normotensive	Total	Chi Square	p-value
	N=50	N=50	N=100		
	n (%)	n (%)	n (%)		
Mode of delivery					
SVD	8 (16.0)	35 (70.0)	43 (43.0)	35.312**	0.001*
SVD with IOL	1 (2.0)	2 (4.0)	3 (3.0)		
Assisted vaginal delivery	1 (2.0)	0 (0.0)	1 (1.0)		
Elective CS	5 (10.0)	4 (8.0)	9 (9.0)		
Emergency CS	35 (70.0)	9 (18.0)	44 (44.0)		
Birth weight					
Normal	20 (40.0)	50 (100.0)	70 (70.0)		
Low birth weight	13 (26.0)	0 (0.0)	13 (13.0)	46.659**	0.0001*
Very low birth weight	12 (24.0)	0 (0.0)	12 (12.0)		
Extremely low birth weight	5 (10.0)	0 (0.0)	6 (6.0)		
Still birth					
Yes	5 (10.0)	1 (2.0)	6 (6.0)	**	0.204
No	45 (90.0)	49 (98.0)	94 (94.0)		
Early neonatal death(N=94)					
Yes	7 (15.6)	0 (0.0)	7 (7.5)	**	0.004*
No	38 (84.4)	49 (100.0)	87 (92.5)		
SCBU Admission (N=94)					
Yes	29 (64.4)	7 (14.3)	36 (38.3)	**	0.0001*
No	16 (35.6)	42 (85.7)	58 (61.7)		
Duration of SCBU admission (N=	-36)				
<24hours	1 (3.4)	0 (0.0)	1 (2.8)	3.627**	0.387
1 – 5 days	7 (24.1)	3 (42.9)	10 (27.8)		
6 – 10 days	7 (24.1)	3 (42.9)	10 (27.8)		
>10 days	14 (48.4)	1 (14.2)	15 (41.7)		

\*\*Fisher's exact test \*Statistically significant SVD=Spontaneous vaginal/vertex delivery, AVD=Assisted vaginal delivery, IOL=Induction of labour

Table 3 displays the comparison of perinatal outcomes between preeclamptic and normotensive women in the study. The modes of delivery between the pre-eclamptic and normotensive groups were compared. Out of the 50 pre-eclamptic patients 8(16.0%) had SVD, 1(2.0%) had SVD with IOL, 1(2.0%) had AVD, 5(10%) had elective CS and 35(70%) had emergency CS respectively. In the control group 35(70%) had SVD, 2(4.0%) had SVD with IOL, none had AVD, 4(8.0%) had elective CS and 9(18%) had emergency CS. The difference observed among the study groups were of statistical significance (P=0.0001).

The mean birth weights of babies born to preeclamptic and normotensive mothers in the study were  $2.18\pm0.95$ kg and

 $3.29\pm0.53$ kg respectively. This difference in mean birth weight was significant (t=7.191; p=0.0001). Twenty (40%) had normal birth weight (>2.5kg) in the preeclamptic group versus 50(100%) in the control group, thirteen (26.0%) had low birth weight (P=0.0001) and twelve (24.0%) had very low birth weight in the preeclamptic group and none (0.0%) in the control group, extreme low birth weight was 5(10.0%) in the case group and none in the control group. Early neonatal death was noted in the preeclamptic group 7(15.6%) versus 0(0.0%) in the control group (P=0.004). Twenty-nine (64.4%) neonates in the preeclamptic group was admitted into the SCBU versus 7(14.3%) in the normotensive group (P=0.0001).

#### Table 4: Comparison of mode of delivery between mild and severe pre-eclamptic patients in the study

	Pre-eclampsia	Pre-eclampsia		
Mode of delivery	Mild	Severe	Total	
	n (%)	n (%)	n (%)	
SVD	3 (33.3)	5 (12.2)	8 (16.0)	
SVD with IOL	0 (0.0)	1 (2.4)	1 (2.0)	
Asst vaginal delivery	0 (0.0)	1 (2.4)	1 (2.0)	
Elective CS	1 (11.1)	4 (9.8)	5 (10.0)	
Emergency CS	5 (55.6)	30 (73.2)	35 (70.0)	
Total	9 (100.0)	41 (100.0)	50 (100.0)	

Fishers Exact=35.312, p-value=0.0001\* \*Statistically significant; SVD: spontaneous vertex delivery; IOL – Induction of labour

The mode of delivery of the pre-eclamptic subgroups were compared in Table 4. Out of the 50 pre-eclamptic patients 3(33.3%) had SVD, none had SVD with IOL and AVD, 1(11.1%) had elective CS and 5(55.6%) had emergency CS respectively in the mild group.

In the severe group 5(12.2%) had SVD, 1(2.4%) had SVD with IOL, 1(2.4%) had AVD, 4(9.8%) had elective CS and 30(73.2%) had emergency CS. The difference observed among the subgroups were of statistical significance (P=0.0001).

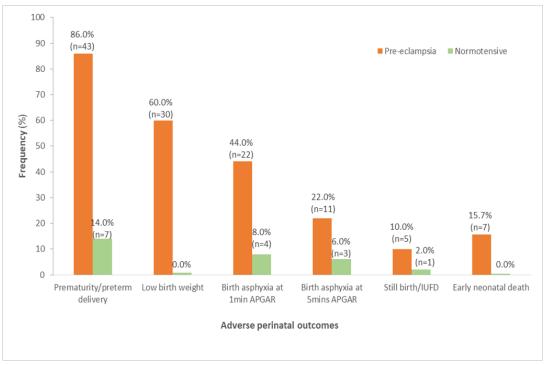
Table 5: Correlation between cerebroumbilical pulsatility index ratio and perinatal outcomes among pre-eclamptic and normotensi	ve
pregnancies.	

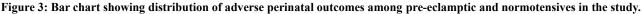
	Pre-eclampsia		Normotensive		
	Cerebroumbilical pulsatility index ratio		Cerebroumbilical pulsatility index ratio		
	<b>Pearson Correlation</b>	p-value	Pearson Correlation		
Perinatal outcomes	co-efficient (r)		co-efficient (r)	p-value	
Birth weight	0.535	0.0001*	0.265	0.063	
1 min APGAR	0.458	0.001*	-0.032	0.828	
5 mins APGAR	0.444	0.001*	0.019	0.897	
Gestational age at delivery	-0.408	0.004*	-0.117	0.472	

\*Statistically significant

Table 5 displays the correlation between the cerebroumbilical pulsatility index ratio and perinatal outcomes among the study population. There was a positive correlation between the perinatal outcomes (birth weight, Apgar score at 1 and 5 minutes respectively (p<0.05) and a negative correlation with GA at delivery and cerebroumbilical pulsatility index ratio (p<0.05) in the precelamptic

group. In the control group, birth weight and Apgar score at 5 minutes shows positive correlation with the cerebroumbilical pulsatility index ratio and Apgar score at 1 minute as well as GA at delivery shows negative correlation with cerebroumbilical pulsatility index ratio. These findings were not statistically significant.





The above Figure 3 showed that LBW and early neonatal deaths were seen solely in the pre-eclamptic while prematurity and SCBU admission was more in the case compared to the normotensive group. Birth asphyxia at one minute was more in both case and

control in comparison to that obtained at five minutes. Still births/IUFD was more in the pre-eclamptic when compared to the normotensive.

Validity of pulsatility index of fe	etal MCA PI in identif	ying adverse perinatal	outcomes	
Adverse perinatal outcomes	Sensitivity (%)	Specificity (%)	Positive predictive value PPV (%)	Negative predictive value NPV (%)
Low birth weight	36.7	84.3	50.0	75.6
Birth asphyxia	26.3	80.2	22.7	88.5
Still birth/IUFD	33.3	78.7	9.1	94.9
Prematurity	42.0	98.0	95.5	62.8
Validity of pulsatility index of fe	etal umbilical artery in	ı identifying adverse p	erinatal outcomes	
Adverse perinatal outcomes	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Low birth weight	73.3	87.1	71.0	88.4
Birth asphyxia	71.4	75.6	32.3	94.2
Still birth/IUFD	83.3	72.3	16.1	98.6
Prematurity	56.0	94.0	90.3	68.1
Validity of Cerebroumbilical pu	llsatility index ratio in	identifying adverse pe	erinatal outcomes	
Adverse perinatal outcomes	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Low birth weight	96.7	80.0	67.4	98.2
Birth asphyxia	78.6	62.8	25.6	94.7
Still birth/IUFD	83.3	59.6	11.6	98.2
Prematurity	82.0	96.0	95.3	84.2

Table 6 shows that the MCA PI is demonstrates specificity but low sensitivity for all outcomes. It had the highest specificity for birth asphyxia (80.2%), stillbirths/IUFD (78.7%) and prematurity (98.0%). The highest PPV was for prematurity (95.5%) and lowest PPV for stillbirths/IUFD (9.1%).

UmA PI demonstrated high specificity for all outcomes as well as high sensitivity except for prematurity. PPV and NPV were higher for LBW and prematurity, while NPV was higher than PPV for birth asphyxia and stillbirths/IUFD.

CUmR revealed high sensitivity for all outcomes except stillbirths/IUFD. It showed the highest sensitivity and NPV for LBW (96.7%, 98.2%), birth asphyxia (78.6%, 94.7%) and prematurity (95.3%, 84.2%). PPV and NPV were both high for LBW and prematurity, while NPV was higher than PPV for birth asphyxia and stillbirths/IUFD.

## Discussion

Relationship between fetal Doppler indices (middle cerebral artery pulsatility index, umbilical artery pulsatility index, and cerebroumbilical pulsatility index ratio) and perinatal outcomes was examined in women with preeclampsia and normotensive controls. Fetal middle cerebral artery PI showed correlations with birth weight, APGAR scores, and gestational age at delivery, with gestational age being statistically significant in preeclamptics. Umbilical artery PI showed negative correlations with all outcomes in preeclamptics and no significant correlations in controls. Cerebroumbilical PI ratio showed positive correlations with birth weight and APGAR scores and negative correlations with gestational age and APGAR score at one minute.

Several previous studies support our findings. A study in Egypt found similar associations between severe preeclampsia and adverse perinatal outcomes <sup>[14]</sup>. A study examining Doppler indices and perinatal outcomes in preeclampsia agreed with our findings regarding birth weight, gestational age, and APGAR scores <sup>[15]</sup>. Studies from Nigeria, <sup>[16]</sup> Egypt, <sup>[14]</sup> and India <sup>[17]</sup> reported outcomes matching our findings for prematurity, low birth weight, and APGAR scores in preeclamptics. Studies from multiple countries

found cerebroumbilical PI ratio to be a better predictor of outcomes than umbilical or middle cerebral artery PI alone <sup>[17-19]</sup>.

Some studies disagreed with aspects of our findings. A study in Egypt found lower sensitivity for umbilical artery PI in predicting outcomes compared to our results, potentially due to only examining severe preeclampsia <sup>[14]</sup>. Studies also reported lower specificity for middle cerebral artery PI <sup>[20]</sup> and higher sensitivity for both umbilical artery <sup>[21]</sup> and middle cerebral artery PI <sup>[18,22]</sup>. The se discrepancies may relate to differences in study populations, inclusion of less severe preeclampsia cases, and analytic methods between studies.

A few studies contradicted our observation that cerebroumbilical PI ratio had high validity. A study including gestational hypertensive cases reported lower sensitivity than our findings <sup>[21]</sup>. Others documented cerebroumbilical PI ratio as having low sensitivity and diagnostic accuracy, <sup>[23,24]</sup> conflicting with our results. These divergent results could stem from examining milder disease cases <sup>[25]</sup> and inclusion of small-for-gestational age, <sup>[23]</sup> potentially diluting associations with preeclampsia.

We further evaluated the validity of the Doppler indices for predicting perinatal complications. Middle cerebral artery PI showed higher specificity but lower sensitivity, predicting outcomes best for prematurity. Umbilical artery PI showed high sensitivity and specificity for all outcomes except prematurity. Cerebroumbilical PI ratio demonstrated high sensitivity and specificity except for stillbirths. Previous studies from Egypt, <sup>[14]</sup> India, <sup>[26]</sup> and Nigeria <sup>[20]</sup> agreed with our findings of high specificity and low sensitivity for middle cerebral artery PI. Studies from multiple countries supported umbilical artery PI and cerebroumbilical PI ratio as valuable predictors of adverse outcomes in preeclampsia <sup>[19,26,28]</sup>.

The cerebroumbilical pulsatility index ratio is more of predictive value for all variables (LBW, birth asphyxia, still birth/IUFD and prematurity) than either the middle cerebral artery or umbilical artery pulsatility index alone. The umbilical artery pulsatility index is a better indicator than fetal middle cerebral artery. Hence, the single best vessel interrogation for evaluation of adverse perinatal outcomes in preeclampsia is umbilical artery.

The results of this study show that pulsatility index of fetal middle cerebral and umbilical arteries and their corresponding cerebroumbilical pulsatility index ratio are very useful in predicting perinatal outcomes in patients with pre-ecalmpsia and so this study recommends that, Doppler evaluation of middle cerebral and umbilical arteries pulsatility indices as well as the manually calculated cerebroumbilical pulsatility index ratio should be done before decision regarding delivery and management options for preeclamptic patients are reached to avoid undue delays or unnecessary interventions.

In conclusion, fetal Doppler indices show potential as predictive tests for adverse perinatal outcomes in preeclampsia. While some inconsistencies exist between studies, cerebroumbilical PI ratio appears to have the best balance of predictive accuracy demonstrating the best balance of sensitivity and specificity. These findings could help identify at-risk pregnancies for targeted surveillance and management. However, larger, multicenter studies are needed to standardize Doppler criteria and validate findings across populations and disease severity strata. Stratifying preeclampsia subtypes may also clarify discrepant results between studies. Fetal Doppler surveillance warrants further investigation as a tool to optimize perinatal management in hypertensive pregnancies.

# Limitations

As a single-center study, our population may not be broadly generalizable. Examining Doppler indices as continuous variables versus dichotomized cut-offs could influence sensitivity and specificity calculations between studies.

Loss of patients to follow-up leading to attrition. This was compensated for by collecting more data to ensure the sample size was reflected in the analysis.

Confounding factors like maternal comorbidities, socioeconomic status, or treatment interventions received were often not well accounted for.

Long-term follow up into childhood is lacking, so predictive value for later morbidity remains uncertain.

# Recommendation

Conduct large, well-powered multicenter prospective studies to validate Doppler indices for predicting perinatal outcomes across diverse populations.

Develop multidisciplinary consensus guidelines outlining optimal Doppler protocols and incorporation into routine preeclampsia care.

While most studies focused on outcomes like LBW, prematurity and birth asphyxia, longer term follow up of infants exposed to preeclampsia in utero may reveal longer-lasting effects on development and health. Doppler findings could predict later developmental risks.

## List of Abbreviations

APGAR: Appearance, Pulse, Grimace, Activity, Respiration CPR: Cerebroplacental Pulsatility Index Ratio CumR: Cerebroumbilical Pulsatility Index Ratio IUGR: Intrauterine Growth Restriction IUFD: Intrauterine Fetal Death MCA: Middle Cerebral Artery NPV: Negative predictive value PPV: Positive predictive value PI: Pulsatility Index SGA: Small for gestational age SBCU: Special Baby Care Unit SVD: Spontaneous Vaginal Delivery

UmA: Umbilical Artery

UmV: Umbilical Vein

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## Contributors

Akagbue Vivian N -Data collection, data analysis, conceptualization, literature search, review and editing; Ugboma EW-Conceptualization, review and editing. The final manuscript has been reviewed and approved by all the authors.

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# **Competing Interests**

The authors do not have any conflict of interest in this research.

# **Ethics Approval**

The research work was approved by Rivers State Health Research Ethics Committee and informed consent obtained from all participants.

# Data Availability Statement

All the relevant data in this study have been analyzed and reported in the article but data set can be availed on request.

# **Supplemental Material**

Not Applicable.

## **Declaration of conflicting interests**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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