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SERVICES FOR SCIENCE AND EDUCATION

Prediction of Preeclampsia and Other Adverse Pregnancy Outcomes in Women of Advanced Maternal Age: The Use of Mid Trimester Uterine Artery Doppler Velocimetry

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ABSTRACT

Background: Adverse pregnancy outcomes such as pre-eclampsia, gestational diabetes, and low birth weight are significant contributors to maternal and fetal morbidity. The use of Doppler ultrasonography, particularly pulsatility index (PI) and the presence of a notch, has been explored as a predictive tool for identifying pregnancies at risk of these complications. Objectives: This study aimed to evaluate the association between uterine artery Doppler findings, specifically PI and notching, with adverse maternal and fetal outcomes among pregnant women. Methodology: A cross-sectional study was conducted among 141 pregnant women at Irrua Specialist Teaching Hospital, Nigeria. Doppler ultrasonography was used to assess PI and the presence of a notch. Participants were followed up to delivery, and data on outcomes, including pre-eclampsia, gestational diabetes, low birth weight, and pre-term delivery, were analyzed. Statistical analysis was performed using SPSS 23.0, with significance set at $p < 0.05$. Results: Women with abnormal PI were four times more likely to develop pre-eclampsia compared to those with normal PI. Abnormal PI was also associated with twice the risk of gestational diabetes and three times the likelihood of delivering a low-birth-weight infant. The presence of a notch was significantly associated with pre-eclampsia, doubling the risk compared to cases without a notch. However, neither abnormal PI nor notching demonstrated significant associations with caesarean section rates, ICU admission, or poor APGAR scores. Conclusion: Doppler findings, particularly abnormal PI and notching, are valuable in identifying pregnancies at risk for complications like pre-eclampsia and low birth weight. Routine integration of Doppler screening into antenatal care is recommended to enable early detection and timely interventions, thereby improving maternal and fetal outcomes.

Keywords: Doppler Ultrasonography, Preeclampsia, Pregnancy Outcomes Pulsatility Index, Uterine Artery.

BACKGROUND

Adverse maternal outcomes during pregnancy are a significant global concern, particularly in women of advanced maternal age (AMA), typically defined as 35 years or older[1]. AMA increases the risk of complications such as hypertensive disorders, gestational diabetes, preterm birth, and fetal growth restriction (FGR), often due to impaired placentation and reduced uterine blood flow, which lead to placental insufficiency, negatively impacting maternal and fetal health[2,3].

Preeclampsia, a hypertensive disorder that occurs after the 20th week of gestation, is one of the leading causes of maternal and fetal morbidity and mortality worldwide[4]. It affects 5% to 7% of pregnancies globally and contributes to over 70,000 maternal deaths and approximately 500,000 fetal deaths annually[5,6].

In the United States, Black women are particularly vulnerable, experiencing up to70% higher incidence of preeclampsia compared to White women, with more severe outcomes such as kidney damage and increased maternal mortality[7,8]. Risk factors for preeclampsia include first pregnancies, hypertension, chronic kidney disease, diabetes, obesity (BMI ≥ 35 kg/m^2), history of preeclampsia, and age > 40 years[9,10].

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In sub-Saharan Africa, including Nigeria, preeclampsia and other adverse pregnancy outcomes are prevalent, with a pooled incidence of 13% in the region[11]. In Nigeria, the maternal mortality rate associated with preeclampsia is high at 6.04%, while fetal mortality stands at 16.73%[12,13]. Limited access to healthcare, inadequate antenatal care, and lack of early screening contribute to delayed diagnoses and poor outcomes[14].

Women of AMA are also at increased risk of gestational diabetes (GDM) with women over 40 years having almost two-fold risk of developing GDM[15,16]. GDM is associated with complications such as macrosomia, preterm birth, and cesarean delivery[17]. Additionally, AMA increases the risk of placenta previa, placental abruption, and preterm birth, all of which heighten the risk of maternal hemorrhage and severe fetal morbidity[18,19]. Fetal growth restriction is also more common in pregnancies complicated by preeclampsia and AMA, due to inadequate placental blood supply[20,21].

In Nigeria and other sub-Saharan African countries, addressing the risks of AMA is key. Non-invasive methods like uterine artery Doppler velocimetry have shown promise in identifying pregnancies at high risk of adverse outcomes, including preeclampsia, FGR, and preterm birth[22,23]. Uterine artery Doppler measures blood flow in the uterine arteries using ultrasound and can detect impaired placental perfusion, an early indicator of preeclampsia and FGR[24].

Research has shown that uterine artery Doppler velocimetry significantly improves the prediction of preeclampsia. The presence of a diastolic notch and an elevated resistance index (RI) in the uterine arteries can indicate a higher risk of adverse outcomes, as considering both the diastolic notch and an RI > 0.65 increases the detection rate for preeclampsia by up to 87.51%[25,26]. Additionally, uterine artery Doppler, when combined with other markers, can detect up to 75% of preterm preeclampsia cases.[27] Early detection through Doppler allows for timely interventions such as closer monitoring, prophylactic treatment, and, when necessary, early delivery to reduce risks for both mother and fetus[28].

The non-invasive nature of Doppler ultrasound makes it particularly valuable in resource-limited settings like Nigeria, where access to more invasive diagnostic methods may be limited. As a cost-effective and accessible screening tool, uterine artery Doppler velocimetry plays a crucial role in identifying high-risk pregnancies, improving maternal and fetal health outcomes by enabling better management of preeclampsia and gestational diabetes.

METHODOLOGY

Study Area

The study was conducted at the Obstetrics and Gynaecology Department of Irrua Specialist Teaching Hospital (ISTH), located in Irrua, the local government headquarters of Esan Central Local Government Area in Edo State, Nigeria. Established in 1991, the hospital served as a major referral center for two of the three senatorial districts of Edo State (Edo Central and Edo North), as well as for neighboring states, including Delta, Ondo, and Kogi. ISTH provided a wide range of maternal and child health services, including antenatal care and delivery, and had an average annual delivery rate of 1800. The Obstetrics and Gynaecology Department was equipped with 48 obstetric beds and 42 gynecological beds. Antenatal clinics were held three times a week, where ultrasound equipment with Doppler capabilities was routinely used, and this equipment played a key role in the study.

Study Population

The study population comprised pregnant women who met the inclusion criteria for participation. These women were recruited from the Obstetrics and Gynaecology Department of ISTH. All participants were either referred for antenatal care or voluntarily booked for delivery, and they met the necessary gestational and age requirements as stipulated by the inclusion criteria.

Study Technique

This research utilized a cross-sectional study design with cohort selection. This design allowed for the identification of pregnant women based on specific inclusion criteria, enabling the selection of cohorts based on factors such as maternal age and gestational age. The cohort approach allowed for thorough follow-up of participants throughout their pregnancies, from recruitment to delivery, and for the documentation of pregnancy outcomes in relation to Doppler ultrasonographic findings.

Data Collection

Data collection was carried out in several phases. Initially, a structured questionnaire was administered to the participants to gather information on their sociodemographic background and medical history. Following this, ultrasound scans were performed to determine gestational age and estimate fetal weight. Doppler ultrasonography was employed to assess uterine artery blood flow, with specific focus on identifying abnormal Doppler patterns such as an elevated Pulsatility Index (PI) or the presence of a diastolic notch. Participants were followed up throughout their pregnancy, and relevant data on adverse pregnancy outcomes such as preeclampsia, preterm delivery, gestational diabetes, and low birth weight were recorded. At the time of delivery, neonatal outcomes including birth weight, APGAR scores, and respiratory distress were also documented, providing a comprehensive dataset for analysis.

Ethical Considerations

Ethical approval for the study was obtained from the ethics committee of ISTH, with formal approval being granted through the Head of the Obstetrics and Gynaecology Department. Informed written consent was sought from all participants, ensuring they understood the study's purpose, procedures, and any potential risks. Participants were assured of their right to withdraw from the study at any point without any repercussions. To protect participant confidentiality, data were coded using study numbers instead of personal identifiers. All measures were taken to ensure privacy and minimize any potential discomfort or harm to participants during the research process.

Data Analysis

The data collected during the study were analyzed using IBM SPSS version 23.0 software. Descriptive statistics were used to summarize key sociodemographic characteristics and pregnancy outcomes. The sensitivity and specificity of Doppler indices were calculated to assess the diagnostic utility of the Doppler measurements in predicting adverse pregnancy outcomes. The Chi-square test was employed to test for associations between Doppler findings and pregnancy complications, with statistical significance set at $p < 0.05$. The results were presented in tabular format, and all data were stored securely, with plans for data destruction set for three years after the study's completion.

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RESULTS

Maternal Complications and Mode of Delivery

Out of 141 women, 37 (26.2%) experienced maternal complications. Gestational diabetes was the most common, affecting 19 women (51.4%), followed by pregnancy-induced hypertension in 18 women (48.6%) and preeclampsia in 12 women (32.4%). Other complications included abruptio placentae (3, 8.1%), eclampsia (2, 5.4%), and placenta previa (2, 5.4%).

Regarding delivery, spontaneous vaginal delivery occurred in 111 women (78.7%), while caesarean section was performed in 30 women (21.3%). Among those with caesarean section, the main indications were fetal distress (9, 30.0%), CPD (6, 20.0%), and maternal request (1, 3.3%), with 14 cases (46.7%) categorized as "other".

Doppler Findings Among Respondents

Among the 141 women, pulsatility index (PI) values indicated that 103 women (73.0%) had a PI below the 95th percentile, while 38 women (27.0%) had a PI at or above the 95th percentile. The presence of an early diagnostic notch was noted in 27 women (19.1%), with 114 women (80.9%) showing an absent notch. Of those with a notch, 10 women (37.0%) had a notch on the right side only, 7 women (26.0%) had a notch on the left side only, and 10 women (37.0%) had a notch on both sides.Doppler anomalies were categorized as follows: 38 women (27.0%) had a PI greater than the 95th percentile, 27 women (19.1%) had the presence of a notch, and 24 women (17.0%) had both anomalies.

Fetal Outcomes Among Respondents

Of the 141 pregnancies, 129 women (91.5%) delivered at term, while 12 women (8.5%) had pre-term deliveries.

Regarding birth weight, 21 infants (14.9%) had a birth weight of less than 2.5 kg, while the majority, 120 infants (85.1%), had a birth weight of 2.5 kg or greater. In terms of APGAR score at the 1st minute, most infants had scores between 7-10 (126, 89.4%), followed by scores of 6 (9, 6.4%), 4-5 (5, 3.5%), and only 1 infant (0.7%) had a score between 0-3. At the 5th minute, 137 infants (97.2%) scored between 7-10, while 3 infants (2.1%) had a score of 6, 1 infant (0.7%) scored 4-5, and no infants had a score between 0-3.

Regarding special care baby unit (SCBU) admission, 11 infants (7.8%) required admission. The most common indications for SCBU admission were neonatal respiratory distress syndrome (RDS) in 5 infants (45.4%), followed by prematurity in 4 infants (36.4%), low birth weight in 1 infant (9.1%), and neonatal sepsis in 1 infant (9.1%).

Finally, perinatal mortality was reported in 1 case (0.7%), while the remaining 140 infants (99.3%) survived.

Association between Pulsatility Index and Outcomes

The analysis compares the frequency of outcomes in cases with a normal PI (n=103) and an abnormal PI (n=38).

Among women with a normal PI, 4 (33.3%) had pre-eclampsia, while 8 (66.7%) of those with an abnormal PI had the condition. The odds ratio (OR) for abnormal PI being associated with

pre-eclampsia is 0.15 [0.04-0.51], with a p-value of 0.001, suggesting a significant association. The sensitivity is 66.7% and specificity is 76.7%.

Of those with a normal PI, 21 (70.0%) underwent caesarean section, compared to 9 (30.0%) with an abnormal PI. The OR for abnormal PI and caesarean section is 0.83 [0.34-1.98], with a p-value of 0.671, indicating no significant association. Sensitivity is 30.0%, and specificity is 73.9%.

Among women with a normal PI, 9 (47.4%) had gestational diabetes mellitus, while 10 (52.6%) of those with an abnormal PI had the condition. The OR for gestational diabetes with an abnormal PI is 0.27 [0.10-0.71], with a p-value of 0.007, suggesting a significant association. Sensitivity is 52.6%, and specificity is 77.0%.

Among those with a normal PI, 7 (33.3%) delivered low birth weight infants, while 14 (66.7%) with an abnormal PI had low birth weight infants. The OR for abnormal PI and low birth weight is 0.12 [0.05-0.34], with a p-value of <0.001, indicating a significant association. Sensitivity is 66.7%, and specificity is 93.2%.

The relationship between PI and poor APGAR scores is not statistically significant, with an OR of 1.40 [0.38-5.07] and a p-value of 0.624. Sensitivity is 7.9%, and specificity is 89.3%.

The OR for ICU admission with an abnormal PI is 0.45 [0.14-1.49], with a p-value of 0.203, suggesting no significant association. Sensitivity is 23.1%, and specificity is 72.7%.

For pre-term delivery, the OR is 0.62 [0.18-2.13], with a p-value of 0.464, indicating no significant association. Sensitivity is 41.7%, and specificity is 74.4%.

Overall, a normal PI is significantly associated with lower risks of pre-eclampsia, gestational diabetes, and low birth weight, while no significant associations were found for caesarean section, poor APGAR score, ICU admission, or pre-term delivery.

Association between Presence of Notch and Outcome

The analysis compares the frequency of outcomes in cases with a notch absent (n=103) and a notch present (n=38). For pre-eclampsia, 5 (41.7%) of those with an absent notch had the condition, while 7 (58.3%) of those with a present notch were affected. The odds ratio (OR) for the presence of a notch being associated with pre-eclampsia is 0.23 [0.07-0.73], with a p-value of 0.010, indicating a significant association. Sensitivity is 58.3%, and specificity is 84.5%.

Regarding caesarean section, 19 (63.3%) with an absent notch underwent the procedure, while 11 (36.7%) with a present notch had a caesarean section. The OR for the association between a present notch and caesarean section is 0.56 [0.24-1.30], with a p-value of 0.182, suggesting no significant association. Sensitivity is 35.6%, and specificity is 40.7%.

For gestational diabetes mellitus, 11 (57.9%) of those with an absent notch had the condition, while 8 (42.1%) with a present notch were affected. The OR is 0.45 [0.17-1.19], with a p-value of 0.109, indicating no significant association. Sensitivity is 42.1%, and specificity is 84.4%.

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In terms of low birth weight, 12 (57.1%) with an absent notch delivered low birth weight infants, while 9 (42.9%) with a present notch had low birth weight infants. The OR for low birth weight with a present notch is 0.42 [0.17-1.09], with a p-value of 0.075, suggesting no significant association. Sensitivity is 42.9%, and specificity is 85.0%.

The relationship between the presence of a notch and poor APGAR scores is not statistically significant, with an OR of 0.91 [0.28-2.99] and a p-value of 0.885. Sensitivity is 28.6%, and specificity is 81.9%.

The odds ratio for ICU admission with a present notch is 0.98 [0.26-3.69], with a p-value of 0.980, indicating no significant association. Sensitivity is 23.1%, and specificity is 81.3%.

For pre-term delivery, the OR is 0.33 [0.10-1.05], with a p-value of 0.060, suggesting a borderline association. Sensitivity is 50.0%, and specificity is 84.0%. In summary, the presence of a notch is significantly associated with pre-eclampsia, while no significant associations were observed for caesarean section, gestational diabetes, low birth weight, poor APGAR scores, ICU admission, or pre-term delivery.

Table 1: Maternal complications and mode of delivery

Variable	Frequency (n=141)	Percentage (%)
Maternal Complications (n=37)		
Gestational diabetes	19	51.4
Pregnancy Induced Hypertension	18	48.6
Preeclampsia	12	32.4
Abruptio placentae	3	8.1
Eclampsia	2	5.4
Placenta previa	2	5.4
Mode of delivery		
Spontaneous vaginal delivery	111	78.7
Caesarean section	30	21.3
Indication for CS (n=30)		
Fetal distress	9	30.0
CPD	6	20.0
Maternal request	1	3.3
Others	14	46.7

Table 2: Doppler findings

Variable	Frequency (n=141)	Percentage (%)
Pulsatility Index (PI)		
$<95^{th}$ percentile	103	73.0
$\geq 95^{th}$ percentile	38	27.0
Early diagnostic notch		
Present	27	19.1
Absent	114	80.9
Form of early diagnostic notch (n=27)		
Right only	10	37.0
Left only	7	26.0
Both	10	37.0

Doppler anomalies		
PI > 95th percentile	38	27.0
Presence of notch	27	19.1
Both	24	17.0

Table 3: Fetal outcomes

Variable	**Frequency (n=141)**	**Percentage (%)**
Gestational age at delivery		
Term	129	91.5
Pre-term	12	8.5
Birth weight (kg)		
<2.5	21	14.9
≥2.5	120	85.1
APGAR score (1st minute)		
0-3	1	0.7
4-5	5	3.5
6	9	6.4
7-10	126	89.4
APGAR score (5th minute)		
0-3	0	0.0
4-5	1	0.7
6	3	2.1
7-10	137	97.2
SCBU admission		
Yes	11	7.8
No	130	92.2
Indication for SCBU admission (n=11)		
Prematurity	4	36.4
Low birth weight	1	9.1
Neonatal RDS	5	45.4
Neonatal sepsis	1	9.1
Perinatal Mortality		
Yes	1	0.7
No	140	99.3

Table 4: Association between pulsatility index and outcomes

Variables	**Pulsatility Index**		**OR [95% CI]**	**p-value**	**Sensitivity (%)**	**Specificity (%)**
	Normal PI (n = 103) n (%)	**Abnormal PI (n = 38) n (%)**				
Pre-eclampsia						
Yes	4 (33.3)	8 (66.7)	0.15 [0.04-0.51]	0.001	66.7	76.7
No	99 (76.7)	30 (23.3)				
Caesarean Section						
Yes	21 (70.0)	9 (30.0)				

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No	82 (73.9)	29 (26.1)	0.83 [0.34-1.98]	0.671	30.0	73.9
Gestational DM						
Yes	9 (47.4)	10 (52.6)	0.27 [0.10-0.71]	0.007	52.6	77.0
No	94 (77.0)	28 (23.0)				
Low birth weight						
Yes	7 (33.3)	14 (66.7)	0.12 [0.05-0.34]	<0.001	66.7	93.2
No	96 (80.0)	24 (20.0)				
Poor APGAR score						
Yes	11 (78.6)	3 (21.4)	1.40 [0.38-5.07]	0.624	7.9	89.3
No	92 (72.4)	35 (27.6)				
ICU admission						
Yes	6 (54.5)	5 (45.5)	0.45 [0.14-1.49]	0.203	23.1	72.7
No	93 (72.7)	35 (27.3)				
Pre-term						
Yes	7 (63.6)	4 (36.4)	0.62 [0.18-2.13]	0.464	41.7	74.4
No	96 (73.8)	34 (26.2)				

Table 5: Association between presence of notch and outcome

Variables	**Notching**		**OR [95% CI]**	**p-value**	**Sensitivity (%)**	**Specificity (%)**
	Notch Absent (n = 103) n (%)	**Notch Present (n = 38) n (%)**				
Pre-eclampsia						
Yes	5 (41.7)	7 (58.3)	0.23 [0.07-0.73]	0.010	58.3	84.5
No	98 (76.0)	31 (24.0)				
Caesarean Section						
Yes	19 (63.3)	11 (36.7)	0.56 [0.24-1.30]	0.182	35.6	40.7
No	84 (75.7)	27 (24.3)				
Gestational DM						
Yes	11 (57.9)	8 (42.1)	0.45 [0.17-1.19]	0.109	42.1	84.4
No	92 (75.4)	30 (24.6)				
Low birth weight						
Yes	12 (57.1)	9 (42.9)	0.42 [0.17-1.09]	0.075	42.9	85.0
No	91 (75.8)	29 (24.2)				

Poor APGAR score			0.91 [0.28-2.99]	0.885		
Yes	10 (71.4)	4 (28.6)			28.6	81.9
No	93 (73.2)	34 (26.8)				
ICU admission						
Yes	8 (72.7)	3 (27.3)	0.98 [0.26-3.69]	0.980	23.1	81.3
No	95 (73.1)	35 (26.9)				
Pre-term						
Yes	6 (50.0)	6 (50.0)	0.33 [0.10-1.05]	0.060	50.0	84.0
No	97 (75.2)	32 (24.8)				

DISCUSSION

The findings from this study emphasize the significant associations between Doppler findings, particularly pulsatility index (PI) and the presence of a notch, with adverse pregnancy outcomes. Women with an abnormal PI were more than four times as likely to develop pre-eclampsia compared to those with a normal PI. This aligns with studies by Guzmánet al. in 2021[29], which highlighted abnormal PI as a strong predictor of pre-eclampsia, with mothers with abnormal PI having about 6 times the risk, likely due to impaired placental blood flow. The health significance of these findings lies in the potential for early detection of pre-eclampsia, allowing for closer monitoring and timely intervention. Doppler ultrasound screening should be integrated into routine antenatal care, particularly for pregnancies at high risk.

The relationship between PI and caesarean section, however, did not show a significant difference. Caesarean rates were only slightly higher in women with a normal PI compared to those with an abnormal PI, suggesting that factors other than Doppler findings, such as fetal distress or maternal preference, may play a larger role. Jo et al.[30] in 2018 reported contrasting results, indicating that Doppler findings may independently influence delivery methods. This emphasizes the importance of a comprehensive evaluation when determining delivery plans, with doppler studies being indispensable.

Women with an abnormal PI were twice as likely to have gestational diabetes mellitus compared to those with a normal PI. This supports previous research showing a link between impaired placental perfusion and vascular dysfunction in GDM[31,32]. Early identification of abnormal PI in women with GDM is crucial for preventing complications such as macrosomia and pre-term delivery through targeted interventions. Doppler assessments, complementing routine glucose screening in high-risk pregnancies, can enhance early detection and management.

Low birth weight was also notably associated with abnormal PI. Women with an abnormal PI were three times more likely to deliver low-birth-weight infants compared to those with a normal PI. This finding is consistent with studies by Matthewlynn et al.[33] in 2022, which demonstrated that reduced placental blood flow compromised fetal growth, leading to a five-fold increment in the risk of low birth weight, and almost ten-fold increase in the risk of growth restriction. Addressing this risk requires intensified monitoring and interventions in

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pregnancies with abnormal PI to prevent adverse neonatal outcomes. Routine Doppler screening for fetal growth restriction should be prioritized in antenatal care protocols.

The presence of a notch was associated with nearly twice the likelihood of developing pre-eclampsia compared to cases where the notch was absent. This finding highlights the clinical relevance of notching as an indicator of increased uterine artery resistance and poor placentation. A similar study by Espinoza et al.[34] in 2011 corroborates this association, emphasizing the role of notch evaluation in identifying pregnancies at risk for pre-eclampsia. Integrating notch assessment into standard Doppler protocols, particularly during early gestation, could enable the implementation of preventive measures like low-dose aspirin therapy to mitigate risk.

Conversely, the presence of a notch did not show significant associations with other outcomes such as caesarean section, gestational diabetes, or poor APGAR scores. This finding contradicts prior research, which suggested that notching alone was an independent predictor of the development of low APGAR score, high caesarean section rates, preterm birth and intrauterine growth restriction[25,35]. This highlights the need for a multi-parametric approach combining Doppler findings with maternal and fetal clinical assessments to improve predictive accuracy.

These findings reaffirm the clinical utility of Doppler ultrasound, particularly abnormal PI and notching, in identifying pregnancies at higher risk of complications like pre-eclampsia, GDM, and low birth weight. While their predictive value for other outcomes remains limited, integrating Doppler findings into routine antenatal care will significantly enhance early risk stratification and intervention, improving maternal and fetal outcomes, especially in high-risk populations.

CONCLUSION

Doppler ultrasonography, particularly pulsatility index (PI) and notching, is a valuable tool for predicting complications like pre-eclampsia, gestational diabetes, and low birth weight. While its predictive value for outcomes such as caesarean section and poor APGAR scores is limited, integrating Doppler screening into routine antenatal care can enhance early detection and management of high-risk pregnancies. This approach will enable timely interventions, improving maternal and neonatal outcomes. Further research should aim to refine Doppler protocols and combine them with other diagnostic tools to enhance predictive accuracy.

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AUTHORS CONTRIBUTIONS

Conceptualization of the study and study design was done by Dr Ngwu and Prof Eigbefoh, Literature review was done by Dr Ngwu, Dr Omorogbe and Dr Njoku, data collection and analysis were done by Dr Ngwu, Dr Aikpopo and Dr Enodiana, The Doppler scans were under the tutelage of Dr Akhigbe while the final editing was done by Dr Okome and Dr Olugbenga. All the authors reviewed and approved the manuscript for publication.

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