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Original article

Fetal Umbilical Artery Velocimetry Indices and Pregnancy Outcome Among Preeclamptic Women at the Federal Teaching Hospital, Abakaliki, Southeast Nigeria

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Abstract

An accurate tool to identify fetuses at risk of in-utero compromise in women with Preeclampsia is unknown. We studied the hemodynamic changes in the fetal umbilical and middle cerebral arteries and their association with pregnancy outcomes. This was a cross-sectional study among eligible pregnant women with Preeclampsia. We conducted a Doppler evaluation of the fetal umbilical and middle cerebral artery indices. The neonatal APGAR scores, birth weight, NICU admission and perinatal deaths were documented. Maternal complications were documented. Data analysis was undertaken with Statistical Package for Social Sciences (IBM-SPSS, version 22, Chicago II, USA). Means were compared using the Z-test for continuous variables, while categorical variables were compared with Chi-square. Relationships were assessed using Pearson's correlation, with significance at $P< 0.05$. The accuracy of Doppler indices was calculated using contingency tables. There was a statistically significant association between fetal complications and Doppler indices but not with maternal complications. The Sensitivity of Doppler indices was higher with fetal umbilical artery Doppler indices, while the middle cerebral artery indices were more specific. Accuracy is better when Doppler indices are combined with the cerebro-placental ratio. In women with normal Doppler indices, the indices decreased with advancing gestational age, but values were higher when compared with nomograms. In conclusion, we found an association between fetal Doppler indices of the umbilical artery and adverse fetal outcomes. Abnormal umbilical artery Doppler indices suggest fetal compromise, while normal middle cerebral artery Doppler is reassuring.

Keywords: ***Fetal, Umbilical Artery, Velocimetry, Indices, Preeclampsia***

Introduction

Worldwide, Preeclampsia complicates about 5-10% of all pregnancies. It is one of the leading causes of maternal and perinatal mortality, fetal growth restriction and prematurity [1-9]. According to World Health Organization (WHO), Preeclampsia is about seven times higher in developing countries [10]. A combination of poor health-seeking attitudes, lack of uniform protocols for case management, poverty and ignorance are the main culprits [3,4]. Identifying at-risk fetuses in developing countries where the perinatal mortality rate is about 14 times higher than in developed countries is vital to improving perinatal outcomes [5]. Some studies have found that haemodynamic indices of the fetal umbilical artery (UmA) and Middle cerebral artery (MCA) may detect fetal compromise much before any other antepartum test [6,7].

The main principle underlying the use of Doppler indices is that Preeclampsia which is due to faulty placentation will lead to increased resistance to blood flow in the maternal-fetal vessels indicating compromised maternal-placental perfusion sequence [8]. The subsequent reduction of blood flow in the fetal umbilical arteries signifies compromised placenta-umbilical circulation. The fall in blood flow through the umbilical arteries triggers fetal compensation in the form of brain sparing; by this effect, there is preferential perfusion of the brain through the middle cerebral arteries, the so-called centralization [8]. Many Doppler velocimetry indices in current use are from studies done elsewhere, given that Doppler indices may be influenced by the patient's race coupled with the suboptimal performance of locally available fetal surveillance tools [3,4,10-12], makes a study of this nature imperative.

Despite the dangers of Preeclampsia, reliable tool(s) for fetal surveillance that can guarantee optimal outcomes remain an area of

research. This dearth of evidence is rampant in sub-Saharan Africa, where the burden of Preeclampsia is high, and a sizable portion of the population is of low socio-economic status with poor health-seeking behaviour. The hemodynamic derangements in Preeclampsia, which may lead to adverse effects, occur in or near term; some studies have shown the promise of Doppler investigation in identifying at-risk fetuses before damage is done [6,12-14].

Doppler indices are affected by race; Caucasian parameters, when superimposed on Africans, may be misleading. The ability to accurately identify parturients that will develop Preeclampsia and the successful development of effective prevention strategies will significantly reduce the morbidity and mortality associated with Preeclampsia. Though some studies in Nigeria have been reviewed on this practice, a local study will help to situate the practice at the centre and make the results more accessible to inform local policy changes.

Materials and method

Study design

This cross-sectional study involved pregnant women with Preeclampsia who were followed up from admission till delivery. This study lasted a period of seven months (June to December 2018)

Diagnosis of Preeclampsia

The Acuson® brand mercury sphygmomanometer was used for the blood pressure measurement with appropriate cuff size covering at least 2/3rd of the length of the patient's left arm. Blood pressure was measured with the patient in a reclined position. Before taking measurements, the patient is allowed 30 minutes of rest. In taking the measurement, the cuff was inflated while simultaneously palpating the radial pulse. Inflation was continued for a further 20mmHg beyond the point where the radial pulse became impalpable. The pressure was slowly released at a pace of 2mmHg until the radial pulse became palpable again, indicating systolic blood pressure. The cuff is then re-inflated, a stethoscope is applied to the cubital fossa, and the pressure is slowly released as in the previous fashion. The phase 1 Korotkoff sound is recorded as the systolic blood pressure (SBP), while the phase 5 Korotkoff sound was recorded as the diastolic blood pressure (DBP) measurement. Severe hypertension was diagnosed if the patient's blood pressure was recorded as systolic or diastolic blood pressure equal to or more than 160mmgHg or 110mmHg, respectively. Urinalysis was done by dipstick testing of clean catch midstream urine. The participants were given a wide-bore clean universal bottle and asked to collect a clean catch midstream urine specimen. Before taking the sample, the patients were asked to wash their perineum using clean water provided in the toilet. They were educated to stand astride, open the sample bottle, and collect a mid-stream urine specimen. After specimen collection, a urinalysis was performed to test for proteinuria. Proteinuria of 2+ or more was considered significant. Severe hypertension with significant proteinuria confirms a diagnosis of severe Preeclampsia.

Protocol for patient Doppler evaluation

Doppler interrogation of the umbilical and middle cerebral arteries was conducted, and the Pulsatility index (PI), resistive index (RI), systolic/diastolic ratio (SDR) and cerebro-placenta ratio (CPR) were documented. This investigation was accomplished using the SamsungMedison, AccuvixA30 ultrasound machine manufactured in South Korea in 2013. A 3.5-MHz trans-abdominal transducer was used. The sonologists trained for the study performed the investigation using the same instrument setting and technique. Each patient was investigated in the semi-recumbent position at an angle of about 300 with a 150 left lateral tilt.

The technique of Umbilical Doppler velocimetry

Power was set within the fetal study limit, and the pulsed wave Doppler cursor was positioned on the vessel of interest. The Doppler reading was obtained from a free-floating portion of the umbilical cord in the absence of uterine contraction, breathing or fetal movement using an insonation angle of 600 at a point 1cm from cord insertion on the placenta. The pulsed Doppler frequency was adjusted to suit the flow condition, and the Doppler indices were electronically read off. The PI, RI, and S/D ratio of the four waveforms were measured and averaged automatically by an in-built computer in the ultrasonography machine to ensure validity. Values of indices greater than the 95th percentile for the gestational age are abnormal.

The technique of MCA Doppler Velocimetry

An axial section of the fetal brain, including the thalami and the sphenoid bone, was located, and magnified to evaluate the MCA. The pulsed-wave Doppler gate was placed at the proximal third of the MCA, close to its origin on the internal carotid artery [15,16]. This was because the systolic velocity decreased with increasing distance from the point of origin of this vessel. Care was taken to avoid any undue pressure on the fetal head. The PI, RI, CPI and S/D ratio were noted. The abnormal recording was reported when the RI, PI and S/D ratio is <5th percentile [12] while a (CPR) of <1 was taken as abnormal [17].

Delivery

For those who had a vaginal delivery, their labour was managed using the departmental protocol for managing Preeclampsia. This entailed using a partograph and continuous electronic fetal monitor for monitoring labour events. Those delivered abdominally had the procedure performed by a senior registrar or consultant in the Obstetrics and Gynaecology department. The neonatology team attended all the deliveries.

Data collection

On recruitment of each participant, a structured proforma was used to collect data on the sociodemographic characteristics (age, marital status, education level, husband occupation, residence, parity, and gestational age, which was calculated from first and early second-trimester ultrasound scan or her last menstrual period if sure). Blood pressure, proteinuria, and Doppler velocimetry indices of umbilical and middle cerebral arteries (RI, PI, S/D ratio and CPR) were documented. The gestational age at delivery, significant intrapartum events, delivery route, APGAR scores, birth weight, newborn intensive care unit (NICU) admission, perinatal deaths, and maternal complications, if any, were also recorded. Recruited participants had severe Preeclampsia and planned for delivery. The adverse fetal outcome was low birth weight, birth asphyxia, NICU admission and perinatal death.

Primary outcome measure

Number of patients with abnormal Doppler velocimetry indices.

Secondary outcome measures: Number of patients with preterm delivery, birth asphyxia, low birth weight, NICU admission and women who suffered perinatal deaths and the number of patients who suffered maternal complications such as eclampsia, primary postpartum haemorrhage, abruption placentae, disseminated intravascular coagulation (DIC), intensive care unit (ICU) admission, maternal death.

Data entry and analysis

Data were entered into a personal computer using Microsoft Excel software and analyzed with Statistical Package for Social Sciences (IBM-SPSS, version 22, Chicago II, USA). This was represented in tables using means and standard deviation. Means were compared using the Z-test for continuous variables, while categorical variables were compared with Chi-square. Relationships were assessed using Pearson's correlation, with significance at $P< 0.05$. Doppler performance in terms of Sensitivity, specificity, positive predictive

value (PPV) and negative predictive value (NPV) was calculated using contingency tables.

Results

Eighty participants were enrolled for this study, but four signed against medical advice and left before they were delivered. The remaining 76 were analyzed. In this study, the sociodemographic characteristics showed that the modal age of the participants, 32(42.0%), fell within the age range of 20-29 years. The mean age of the study population was 29.0±7.0 years. Their mean parity was 2.0, but nulliparous and multiparous women had an equal number of participants, 32(42.1%). The mean diastolic, systolic, and diastolic blood pressures were respectively 113.4±13.3 mmHg and 172.3±15.7 mmHg.

Table 1 shows no statistically significant, $p>0.05$ association between Doppler indices and maternal complications. While in Table 2, there was a statistically significant association between fetuses with adverse outcomes and abnormal fetal middle cerebral artery Doppler, $p<0.05$. Abnormal PI of the fetal umbilical and middle cerebral arteries had a statistically significant association ($p<0.05$) with adverse fetal outcomes. Even though more babies with adverse outcomes had abnormal RI, this was not statistically significant, $p>0.05$ (**Table 3**).

In Table 4, the umbilical artery Doppler indices showed a higher sensitivity tool, while the middle cerebral artery indices had better specificity scores. The fetal umbilical artery, individually, the RI, PI and SDR had sensitivities of 92.0%, 68.0% and 8.0%, respectively. The specificities for the PI, and SDR, were, respectively 84.6%, and 84.6% and negative predictive value (NPV) was highest for RI 60.0%), while positive predictive value (PPV) was highest for PI (92.1%) and least for SDR (50.0%). The fetal middle cerebral artery indices, PI, RI and SDR individually showed specificities of 98.0%, 92.3% and 92.3%, respectively, for adverse fetal outcomes. Positive predictive values for PI were 100.0%, 91.7% for SDR and 80.0% for RI.

Table 1: Doppler results and maternal outcome

Maternal complication	Indices (either singly or a combination of pi,ri, SDR, CPR)			
	Normal Umbilical artery indices (%)	Abnormal (%)	Fisher's exact test	P-value
Eclampsia	0	4	4.978	0.290
Abruptio placentae	0	2		
Pph	2	4		
Icu admission	0	6		
Maternal death	0	2		
Total	2	18		
	Middle cerebral artery (normal)	Abnormal	8.996	0.109
Eclampsia	0	2		
Abruptio placentae	0	2		
Pph	2	4		
Icu admission	0	6		
Maternal death	0	2		
Total	2	18		

Table 2: Doppler results and neonatal outcome

Indices (pi,ri, SDR, CPR)	Normal doppler n(%)	Abnormal doppler n(%)	Chi-square (x^2)	P-value
Neonatal complications	Umbilical artery Doppler		4.978	0.290
Birth asphyxia	6(7.8)	16(21.1)		
Low birth weight	4(5.3)	14(18.4)		
Nicu admission	10(13.2)	30(39.5)		
Perinatal death	5(6.6)	9(11.8)		
	Middle cerebral artery Doppler			
Birth asphyxia	4(5.3)	18(23.7)	30.938	*0.000
Low birth weight	3(3.9)	15(19.7)		
Nicu admission	8(10.5)	32(42.1)		
Perinatal death	6(7.8)	8(10.5)		

**Significant*

Table 3: Relationship between abnormal Doppler indices and adverse fetal outcome (birth asphyxia, NICU admission and perinatal death)

Indices	Abnormal indices	Adverse fetal outcome	Good fetal outcome	Chi-square	P-value
Uma					
Pi	38	34	4	19.86	0.001*
Ri	66	46	20	4.978	0.290
Sdr	8	4	4	5.556	0.235
Mca					
Pi	12	12	0	13.2	0.010*
Ri	10	8	2	2.08	0.720
Sdr	24	22	2	21.64	0.000*
Cpr	40	38	2	35.10	0.000*

Table 4: Accuracy of Doppler indices

Variable	Sensitivity (%)	Specificity (%)	Negative predictive value (%)	Positive predictive value (%)
Umbilical artery				
Pi	68.0	84.6	57.9	92.1

Ri	92.0	23.1	60.0	69.7
Sdr	8.0	84.6	32.4	50.0
Middle cerebral artery				
Pi	24.0	100.0	40.6	100.0
Ri	16.0	92.3	36.4	80.0
Sdr	44.0	92.3	46.2	91.7
Cpr	78.0	76.0	81.0	58.0

Discussion

Doppler interrogation of fetal vessels could be helpful for early pick-up of signs that could identify fetuses at risk or in jeopardy even before deleterious harm is done [12,18]. Although maternal complications ranging from eclampsia at 5.3%, abruptio placentae at 2.6%, primary postpartum haemorrgae (PPH) at 7.9%, ICU admission at 6% to maternal death in 2.6% were recorded in this study, there was no statistically significant association between maternal complications and abnormal fetal velocimetry indices. This was not unexpected because the Doppler indices investigated were those of the fetus. This is like the findings reported in other studies [2,12,19,20]. In contrast, there was a significant association between fetal middle cerebral artery (MCA) velocimetry indices and adverse fetal outcomes. However, there was no significant association between abnormal umbilical artery Doppler and adverse fetal outcomes. Our findings contrast the reports of Veradju et al., wherein they found a significant association between adverse perinatal outcome and abnormal fetal umbilical artery (UmA) Doppler indices [12]. Padmini et al. also studied 80 preeclamptic patients using UmA and MCA Doppler velocimetry indices. They reported that of the 30 patients with abnormal Doppler indices, 25 had adverse outcomes ranging from low APGAR scores to perinatal deaths and NICU admission [16]. Alnakash et al. found a significant association between abnormal indices of UmA and MCA with the adverse fetal outcomes of low birth weight, low Apgar score and higher NICU admission [21]. Udo et al. working at the University of Benin Teaching Hospital [22], and Ayuba et al. at Aminu Kano Teaching Hospital [23], found a significant association between abnormal Doppler indices and adverse pregnancy outcomes. However, their study population was heterogeneous in population with patients with hypertensive disorders other than Preeclampsia included. Abnormal middle cerebral artery doppler is a late event when there is placental dysfunction due to fetal compensation, so-called centralization.

For the individual indices, we found that abnormal PI of the fetal umbilical and middle cerebral arteries had a statistically significant association ($p<0.05$) with adverse fetal outcomes. Also, the SDR of the fetal MCA and the CPR showed similar associations. In contrast to our observation, Rani et al., performed a randomized controlled trial, found a significant association between adverse pregnancy outcomes and all the indices of Doppler velocimetry [24]. Ours was not a randomized controlled trial. Padmini et al. found a significant association for only CPR, although more than half of the patients in his study had mild Preeclampsia [18]. Other studies [25,26] also found similar associations. Omtzigt did not find any significant association [27], while Agrawal et al. found that only the SDR of the umbilical artery had the highest correlation with adverse outcomes [28].

The MCA indices had low sensitivities, 24.0% for PI, while PI, RI and SDR individually showed specificities of 100.0%, 92.3% and 92.3%, respectively. Positive predictive values for PI were 100.0%, 91.7% for SDR and 80.0% for RI. The negative predictive values for all the indices were less than 50%. Our study shows that the umbilical artery indices are more sensitive; abnormal values indicate fetuses likely in jeopardy and require further evaluation and intervention. In contrast, high specificity for the middle cerebral artery indices implies that typical values are a reassuring sign of fetal well-being. These findings compare with Padmini et al.'s, where specificity was higher for UmA PI than Sensitivity (98.3%v75%), while the RI was most sensitive with 95.2% [18]. The PPV was equally high for the PI and RI of the UmA and the PI of MCA. Our findings differ from Rani et al.'s, where specificity was higher than Sensitivity for the UmA than MCA indices [24]. The specificities were>90% for MCA PI, UmA PI and RI, but MCA RI was 37.5%. Lopez-Mendez et al., in their study, found that individually and in combination, the indices of UmA and MCA had high specificities and high PPV values (80-90%). However, their sensitivities were at most 50% [2].

We found that the CPR had the best accuracy scores across the board (76-81%). Just like we reported, a systematic review by Vollgraff et al. concluded that CPR outperformed other parameters of fetal Doppler velocimetry to identify at-risk fetuses [29]. This is more because the CPR represents the events at the umbilical (downstream) artery and middle cerebral artery (upstream); by the time the CPR becomes abnormal, centralization would have occurred, implying that the fetus is already in the compensatory phase of the pathology [29]. Hence measuring the CPR when assessing fetal Doppler indices is indispensable for fetal prognostication [24,28-30].

Conclusion

This study found an association between fetal Doppler velocimetry indices of the umbilical and middle cerebral arteries with adverse fetal outcomes. Abnormal fetal umbilical artery velocimetry indices imply fetal jeopardy, which requires further evaluation or intervention. In contrast, normal middle cerebral artery velocimetry indices are a reassuring sign which indicates the fetus was coping fine. An abnormal cerebroplacental ratio signifies a decompensated fetus; further deterioration will lead to fetal compromise.

Ethical considerations

Approval for this study was obtained from the Research and Ethics Committee of the Federal Teaching Hospital Abakaliki. Patients signed written and informed consent forms after carefully explaining the objectives, procedure, and full implications of participation in the study. This study was conducted in compliance with the ethical standards of our institution on human subjects and with the Helsinki Declaration.

List of abbreviations

mmHg: Milimeter of mercury
CPR: Cerebro-placenatal ration
DBP: Diastolic blood pressure
DIC: Disseminated intravascular coagulation
ICU: Intensive care unit
MCA: Middle cerebral artery
NICU: Newborn intensive care unit
NPV: Negative predictive value
PI: Pulsatility index
PPH: Postpartum haemorrage
PPV: Positive predictive value
RI: Resistive index
SBP: Systolic blood pressure
SDR: Systolic diastolic ration
UmA: Umbilical artery
WHO: World health organization

Conflict of interest

None

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Authors' Contributions

Johnbosco E. MAMAH conceived the study. Johnbosco E. MAMAH, Darlington-Peter C. UGOJI, and Chichetaram R. OTU collected the data and performed literature review. Robinson ONOH, Michael ORJI and Odidika U. J. UMEORA supervised the work. All the authors wrote the final draft and approved the final manuscript.

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Data availability

Data would be available upon reasonable request.

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