Original Article

Association Between Foetal Umbilical Artery Waveforms and Foetal outcomes in patients with Pre-eclampsia: An analytical Cross-sectional Study at Federal Teaching Hospital, Gombe, North-eastern Nigeria

Mohammed Garba Buwa[1], Aliyu Usman Elnafaty[2], Aminu Umar Usman[3], Shuaibu Saidu Musa[4], Muktar Musa Shallangwa[5], Usman Abubakar Haruna[6], Usman Rahman Yahaya[7], Muazu Shuaibu Ishaqa[8], Adamu Sa'idu Adamu[9], Ahmed A Jajere[10]

[1]Department of Obstetrics and Gynaecology, State Specialist Hospital, Gombe, Nigeria. [2]College of Medicine, Gombe State University, Gombe, Nigeria. [3] Federal Teaching Hospital Gombe, Gombe, Nigeria [4]Department of Nursing Science, Ahmadu Bello University, Zaria, Nigeria. [5]ART Unit, General Hospital Biu, Borno, Nigeria. [6]Department of Biomedical Sciences, Nazarbayev University School of Medicine, Astana, Kazakhstan [7]Department of Obstetrics and Gynaecology, Modibbo Adama University Teaching Hospital, Yola, Nigeria [8]Department of Family Medicine, State Specialist Hospital, Gombe, Nigeria [9]Department of Paediatrics, Abubakar Tafawa Balewa University, Bauchi, Nigeria [10]Department of Geography, Federal University of Kashere, Kashere, Nigeria

Correspondence: Mohammed Garba Buwa. Department of Obstetrics and Gynaecology, State Specialist Hospital, Gombe Nigeria. mbgarba18@gmail.com. +2348066529131

ABSTRACT

Background: Globally, pre-eclampsia is a major cause of maternal and perinatal morbidity and mortality. In Nigeria, it is identified as the primary cause of maternal complications. The objective of this study is to examine the association between foetal outcomes in patients with pre-eclampsia and the Doppler waveform of the umbilical artery at Federal Teaching Hospital Gombe (FTHG). Studies have shown umbilical artery Doppler can predict adverse foetal outcome early than the other methods before delivery of the foetus by a means difference of 9.2 days plus or minus 4days

Materials and methods: A cross-sectional study carried out at the antenatal clinic and gynecological emergency unit of Federal Teaching Hospital Gombe (FTHG), involving 96 patients who were diagnosed with pre-eclampsia. The samples were selected using convenience sampling techniques. The umbilical artery Doppler waveform was tested at the laboratory while the fetal outcome and maternal information/socio-economic information of the sampled women were collected from labor ward and semi-structured interviewer-administered questionnaire. Chi-square test was employed in analyzing the data collected with a significance level set at a p-value of less than 0.05.

Results: Of the 96 respondents studied, almost $^{1}/_{3}$ of the studied patients exhibited abnormal umbilical artery waveforms, which varied in severity. These abnormalities included reduced end diastolic flow in 27 accounting for about quarter of the studied cases, reversed end diastolic flow was observed in only 2 (2.1%) cases, and absent end diastolic flow in 1 (1.0%) case. It was observed that those with abnormal umbilical artery Doppler waveforms were seven times more likely to give birth to low-birth-weight babies (OR=7.09, p-value=0.008, 95% CI=1.494 – 14.041) and five times more likely to require admission to a special care baby unit (SCBU) (OR=5.06, p-value=0.024, 95% CI=0.088 – 0.846).

Conclusion: This study established a strong association between abnormal umbilical artery Doppler waveforms in women with pre-eclampsia and the likelihood of their babies being born with low birth weight and admission to SCBU. Therefore, the findings can serve as a guide in the timing of delivery for patients with pre-eclampsia. In addition, they can be used as an indication for referrals by facilities without SCBU and which cannot manage low birth weight babies in their hospital.

KEYWORDS: Foetal Umbilical Artery; Pre-Eclampsia; Foetal Outcome; Federal Teaching Hospital, Gombe

INTRODUCTION

Pre-eclampsia is a pregnancy complication characterized by high blood pressure and signs of damage to other organ systems, mostly the liver and kidneys, after the 20th week of gestation. It affects 2-10% of pregnancies worldwide and contributes significantly to maternal and perinatal morbidity and mortality, especially in low-resource settings[1, 2] In Nigeria, eclampsia complicated pre-eclampsia causes maternal mortality of about 27% [3], higher than obstetric hemorrhages and sepsis, which have a rate of 12.4% in southern Nigeria[4], and as high as 46.4% in northern Nigeria[5]. One of the main consequences of pre-eclampsia is impaired placental function and reduced uteroplacental blood flow, which can negatively impact foetal growth and well-being[6].

Doppler ultrasonography is a non-invasive tool that can assess foetal well-being by measuring blood flow through the umbilical artery[7]. The umbilical artery waveform is affected by downstream placental vascular resistance and reflects placental perfusion. In a normal pregnancy, the umbilical artery waveform has high diastolic flow with low resistance. In pre-eclampsia, placental abnormalities lead to increased resistance in the umbilical artery, causing abnormal waveforms. Several studies have demonstrated that abnormal umbilical artery Doppler findings, including increased systolic/diastolic (S/D) ratio, and absent or reversed end-diastolic flow, are associated with adverse foetal outcomes in pre-eclampsia[8-10]. It was found that an umbilical artery S/D ratio >95th percentile was associated with a higher risk of foetal growth restriction, low APGAR scores, neonatal intensive care unit admission, and perinatal mortality compared to normal S/D ratios[3]. The risks increased progressively from absent end-diastolic flow to reverse end-diastolic flow.

Similar findings were noted in a Nigerian study by Adeyekun et al.[11], where umbilical artery Doppler abnormalities were significantly associated with intrauterine growth restriction, intrauterine foetal death, low birth weight, and neonatal death. In a South African study, abnormal umbilical artery Doppler correctly identified 90% of growth-restricted fetuses in 149 pre-eclampsia patients[12]. The role of umbilical artery Doppler in predicting adverse outcomes has also been confirmed in systematic reviews and meta-analyses. A meta-analysis of 18 studies found that abnormal umbilical artery Doppler in high-risk pregnancies increased the risk of perinatal mortality 5-fold [13]. Another review reported that umbilical artery Doppler had high sensitivity (89%) and specificity (92%) for predicting adverse perinatal outcomes[14]. Therefore, it's against this backdrop that this study assesses the association between foetal umbilical artery waveforms and foetal outcomes in Pre-eclampsia Patients at Federal Teaching Hospital, Gombe.

MATERIALS AND METHODS

Study Design

A cross-sectional study was carried out within a hospital setting to investigate the association between foetal outcomes and umbilical artery Doppler waveform in patients diagnosed with pre-eclampsia. To be eligible for participation, pregnant women needed to provide consent and have a singleton pregnancy of 28 weeks' gestation or more, while also presenting with pre-eclampsia at either the antenatal clinic or Obstetrics and Gynecological Emergency Unit of FTHG.

Sample Size Determination

The sample size was calculated using the formula:

$$\mathbf{n} = \frac{Z^2 P(1-P)}{D^2}$$

A previous study done in Nigeria found the prevalence rate of pre-eclampsia among women who attended antenatal clinics to be 6%. Using this prevalence, the sample size was calculated as follows:

Where n = sample size,
Z=Constant =1.96 using a confidence limit of 95%,
P = prevalence value of 6%,
D= the absolute precision of the study, which is 0.05,

The sample size calculated was approximately 87 patients. It was increased to 96 patients after accounting for a 10% non response rate.

Sampling Methods

A convenience sampling method was used to recruit patients for the study. Pregnant women diagnosed with pre-eclampsia and who met the inclusion criteria were recruited as they presented at the gynaecological emergency unit and antenatal clinic until the required sample size of 96 was obtained.

Data Collection Methods

Biodata and clinical information of the patients, such as age, gravidity, parity, last menstrual period, gestational age, socio-demographic characteristics, and clinical features of pre-eclampsia, admitted blood pressure, and urinalysis was recorded in a data form. An umbilical artery Doppler ultrasound scan (USS) study was subsequently done and recorded, and the foetal outcome was observed and documented after delivery.

Blood pressure was taken when the patients were sitting, with arms exposed and supported at the level of the heart and the feet on the floor. They were allowed to rest for two to three minutes. An appropriately sized cuff was used for each patient. To ensure accurate measurements, the arm was encircled with a cuff that covered a minimum of 80% of its circumference. Systolic blood pressure was determined by palpating the brachial artery, and the cuff was inflated to 20 mmHg above this level. The inflation of the cuff was done gradually, at a rate of approximately 2 mmHg per second. A mercury sphygmomanometer was used to record the blood pressure readings. Both systolic and diastolic blood pressures were documented. The fifth Korotkoff sound (disappearance) was used to determine diastolic blood pressure, and only when the fifth sound was absent, the fourth Korotkoff sound (muffling) was considered.

A urine sample was also collected and analyzed using a dipstick for significant proteinuria. A trace was considered insignificant proteinuria, while 1+ and above was considered significant proteinuria. Gestational age (GA) was estimated by the last menstrual period (LMP) or an early ultrasound scan if it was done before the study; otherwise, the GA was determined by an ultrasound scan done at the presentation.

Foetal umbilical artery Doppler ultrasound scan was conducted as follows: an obstetric ultrasound scan examination of the abdomen was performed using a high-resolution real-time Doppler ultrasound scanner, the Philips HD-9, equipped with a 3.5–8.0 MHz sector array transducer with Doppler capability. A transducer of this frequency generally provides excellent resolution when examining the gravid uterus and foetus. The patients were examined in a semi-recumbent position, ultrasound gel was applied to the abdomen to serve as an acoustic coupling agent, and trans-abdominal scanning of the foetus was conducted in both transverse and longitudinal planes as appropriate.

A real-time B-mode ultrasound scan was used to exclude multiple gestations and gross fetal anomalies and to visualize the normal 3-vessel umbilical cord. The Doppler sample gate was placed over a free loop of the cord to include both the umbilical artery and vein. Colour Doppler interrogation was carried out to identify the artery which typically has a pulsatile spectrum. The accuracy of Doppler velocity readings at increased angles decreased and was unreliable at angles above 600. To increase the sensitivity of velocity readings the angle of insulation was maintained at $\leq$450 for all the Doppler scans. Pulse wave Doppler was then applied with the cord vessels visualized in the longitudinal section and in the absence of significant foetal movements to obtain the arterial waveform. The vessel wall filter was adjusted to 50Hz, low enough to eliminate noise from the movement of the vessel walls. However, it was high enough to record slow blood flow, especially in diastole. The pulse repetition frequency (PRF) was adjusted to ensure that the waveform fills at least 75% of the height of the Doppler scale and is free from substantial noise above or below the baseline. The recording of the waveform was initiated only when a stable and consistent state was achieved, requiring at least five consecutive pulsatile arterial waveforms. These waveforms encompassed various patterns, such as normal end diastolic flow, reduced end diastolic flow, absent end diastolic flow, and reversed end diastolic flow. The scanning machine automatically computed the Doppler indices using the peak systolic velocity (PSV), end-diastolic velocity (EDV), and time-average velocity (TAV) according to the following formulae:

1. Systolic/diastolic ratio = PSV/EDV
2. Pulsatility index = (PSV – EDV)/TAV
3. Resistivity index = (PSV – EDV)/PSV

For patients who did not deliver within seven days of the Doppler study, another umbilical artery Doppler study was done for them, and the previous ones were disregarded. The foetal outcome of each patient recruited was recorded on the recording paper. The foetal outcomes were:

1. Live birth
2. Stillbirth (that is, death of a foetus after the age of viability (28 weeks) and before delivery which could be macerated (foetal death more than 12 hours) or fresh stillbirth (foetal death lss than 12 hours)
3. Birth weight (low birth weight of less than 2.5kilograms and normal 2.5 to 3.9 Kg)
4. Birth asphyxia (fifth minute APGAR score)
5. Meconium-stained liquor (which could be thin or thick)

Data Analysis

Data was analyzed using the statistical package for social sciences (SPSS version 20). Mean and standard deviation were used to present quantitative variables such as age and blood pressure while categorical variables, such socio-demographic characteristics gravidity, parity waveforms, and foetal outcome, were presented in terms of frequencies and percentages. The association between umbilical artery Doppler waveform and foetal outcome was evaluated using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

Ethical Consideration

Ethical clearance for the study (NHREC/25/10/2013) was obtained from the Research and Ethics Committee of the FTHG. Participation in this study was voluntary,

withdrawal at any point in the study was allowed, and the care of the non-consenting patients was not overtly affected. Confidentiality was assured by the non-use of personal identification, and the data were used solely for research purposes. Bioethics principles were adhered to during the study.

RESULTS

The greater proportion of the respondents fall within the age category of 21-30 years, with only 2% were above 40 years. Almost $^{2}/_{3}$ of the respondent are house wives that doesn't engage in any economic activities outside their household. Majority of the respondents are Fulani and Hausa by tribe and almost all have a basic literacy skill. Almost half of the respondents were primigravidae, while about $^{1}/_{4}$ and exactly $^{1}/_{4}$ were grand-multigravidae and multigravidae respectively. (Table 1)

Table 1: Socio-demographic Characteristics of the Respondents

Characteristics	Frequency
Age group(years)	
≤ 20	26 (27.1%)
21-30	40 (41.7%)
31-40	28 (29.2%)
≥ 41	2 (2.1%)
Occupation	
Housewife	62 (64.6%)
Applicant	5 (5.2%)
Civil servant	20 (20.8%)
Students	1 (1.0%)
Others	8 (8.3%)
Educational status	
None	12 (12.5%)
Primary	9 (9.4%)
Secondary	43 (44.8)
Tertiary	32 (33.3%)
Ethnicity	
Fulanis	40 (41.7%)
Hausas	21 (21.9%)
Tera	7 (7.3%)
Tangale	3 (3.1%)
Others	25 (26%)

The mean gestational age of the participants was 35.90±3.26 weeks, and the majority 71 (74%) of them had late onset pre-eclampsia (that is occurrence at ≥34 weeks' gestation). The mean systolic blood pressure was 159.77±19.57 mmHg and the mean diastolic blood pressure was 107.0±13.41mmHg. Proteinuria of two pluses and above constitutes the majority. It was also found that 68 (70.8%) of the participants had severe pre-eclampsia (Table 2)

Table 2: Clinical Profile of the Respondents

Proteinuria (Dipstick urine test)	**Frequency**
One plus (+) of protein	36 (37.5 %)
Two plusses (++) of protein	37 (38.5%)
Three plus (+++) of protein	22 (22.9%)
Four plus (++++) of protein	1 (1.0%)
Total	**96 (100.0%)**
Degree of pre-eclampsia	
Mild	28 (29.2%)
Severe	68 (70.8%)
Total	**96 (100.0%)**

Table 3: Foetal Umbilical Artery Doppler Waveform of the Participants

UA Artery Doppler Waveform	Frequency
Normal end-diastolic flow	66 (68.8%)
Reduced end-diastolic flow	27 (28.1%)
Absent end-diastolic flow	1 (1.0%)
Reversed end-diastolic flow	2 (2.1%)
Total	**96 (100.0%)**

Table 4: Foetal Outcome Among the Participants

Outcome	Frequency
Live	94 (97.9%)
Fresh stillbirth	2 (2.1%)
Total	**96 (100%)**
Asphyxiated (APGAR score < 7)	2 (2.1%)
No asphyxia (APGAR score ≥7)	92 (97.9%)
Total	**96 (100.0%)**
Low birth weight (< 2.50 Kg)	47 (49.0%)
Normal birth weight (≥ 2.50 Kg)	49 (51.0%)
Total	**96 (100.0%)**
Admitted into special care baby unit (SCBU)	23 (24%)
Not admitted into SCBU	73 (76%)
Total	**96 (100.0%)**
Clear Liquor	88 (91.7%)
Thin Meconium-stained liquor	5 (5.2%)
Thick Meconium-stained liquor	3 (3.1%)
Total	**96 (100.0%)**

Normal end-diastolic flow was observed in almost $^{2}/_{3}$ participants, while end-diastolic flow was observed in only about ¼. The reversed end-diastolic flow and absent end-diastolic flow was found in only 2% and 1% respectively. Therefore, there were 29 abnormal waveforms and 67 were found to be normal, accounting for about 1/3 and 2/3 respectively. (Table 3)

Foetal outcomes included 94 live births (97.9%) and two fresh stillbirths (2.1%), following abruptio

Table 5: Association Between Umbilical Artery Doppler Waveforms and Foetal Outcome

Fetal outcomes 95% CI	Normal UA Doppler wave	Abnormal UA Doppler wave	Total	(X^2)	(P-value)
Birth status				0.334	**0.530***
Live birth	65(%)	29 (%)	94(100)		
Fresh stillbirth	1 (%)	1 (%)	2 (100)		
APGAR SCORE				3.719	**0.089***
Asphyxiated	1	3	4		
Not Asphyxiated	65	27	92		
Birth weight				16.826	**0.001**
Low birth weight	23	24	47		
Normal birth weight	43	6	49		
Meconium liquor status				2.049	**0.359**
Clear liquor	62	26	88		
Thin meconium-stained liquor	3	2	5		
Thick meconium-stained liquor	1	2	3		
SCBU Admission				16.243	**0.001**
Yes	58	15	73		
No	8	15	23		
Total					

placentas in two patients. Babies with APGAR Scores of < 7, at the fifth minute, were 4 (4.2%). Babies with low birth weight were 47 (49.0%). Twenty-three babies (24%) were admitted to the special care baby unit. Liquor status ranged from clear in 88 (91.7%) of the participants to thin Meconium-stained liquor in 5 (5.2%) and thick Meconium-stained liquor in 3 (3.1%). (Table 4)

Table 6: Relationship between SCBU Admission and low birth weight

	Odd Ratio	P-Value	95% CI
Admitted to SCBU	5.06	0.024	0.088 - 0.846
Low birth weight	7.09	0.008	1.494 - 14.041

This study found that patients with abnormal umbilical artery Doppler waveforms had babies with low birth weights (<2.50Kg) and were admitted to special care baby units (SCBU) at a p-value of <0.0001, which was statistically significant. The association between abnormal umbilical artery Doppler waveform with stillbirth (P-value of 0.531), birth asphyxia (P-value of 0.89), and Meconium-stained liquor (p-value of 0.359) was not statistically significant (Table 5).

DISCUSSION

This study found that abnormal umbilical artery Doppler waveforms, including reduced end-diastolic flow, reversed end-diastolic flow, and absent end-diastolic flow were significantly associated with adverse foetal outcomes like low birth weight and admission to the special care baby unit in women with pre-eclampsia. This is consistent with previous studies that have demonstrated associations between abnormal umbilical artery Doppler findings and higher risks of adverse perinatal outcomes [15-19].

The use of Doppler ultrasound of the umbilical artery is an innovation in foetal testing. This can indicate the state of the foeto-placental vascular bed, which can be relevant to fetal conditions. The age range of the participants was 16–44 years, which is not unusual as pre-eclampsia is a complication of pregnancy that occurs primarily among women of reproductive age. The mean age of the participants was 26.93 ± 7.08, which is similar to a finding among women with pre-eclampsia, with a mean age of 26.3 ± 2.3 years[20, 21]. The mean age from this study is however lower than the findings of Ayuba et al at Kano AKTH in Nigeria (31.33 ±5.92)[16]. This disparity may be due to differences in sociocultural influence, the lower level of education, and a higher level of poverty in Gombe. These factors predispose many women to early marriages, given the age at the onset of childbearing,

which is also lower than the study of Kirsten et al[22, 23]. Pre-eclampsia was also found to be more common in the 21–30 age groups, which is similar to findings by Singh et al in Sokoto, Nigeria[21].

The majority of patients had formal education (87.5%), and most are housewives (64.6%) who are less economically empowered. These put together may reflect the low level of patronage with only 36.5% booked for antenatal care. The study also found that, the incidence of pre-eclampsia was highest among primigravidae (45.8%). This is a common finding, as pre-eclampsia is more commonly associated with primigravidae [21, 24, 25, 26]. This could be due to the immunological theory which explains why pre-eclampsia is more common among women carrying pregnancy into the second trimester for the first time[1]. The mean gestational age of the patients in this study was 35.90±3.262 weeks, with the modal gestational age being 37 weeks. These findings are similar to those of previous studies[24].

The mean systolic and diastolic blood pressures are similar to those found in a previous study by Kooffreh et al[1]. The finding of proteinuria in all the patients is in line with the diagnostic criteria for pre-eclampsia, which is the occurrence of hypertension, after the gestational age of 20 weeks with significant proteinuria in a previously normotensive patient[1]. In this, foetuses with abnormal Doppler findings had more adverse fetal outcomes, i.e., low birth weight and admission to SCBU, compared to those with normal Doppler findings, with a P-value of <0.0001, which was statistically significant, and this agrees with the findings of Rocca et al. in Egypt[20].

The significant admission of infants with abnormal Doppler waveforms to the Special Care Baby Unit (SCBU) highlights a strong association. The assessment of haemodynamic in the foeto-placental circulation can further aid in determining the critical intervention point before fetal adaptive responses deteriorate. Conversely, the lack of statistical significance concerning Meconium-stained liquor implies that certain acute or chronic events might have impacted the fetus. It is crucial to recognize that adequate placental function, as assessed by umbilical artery Doppler, does not guarantee fetal well-being. Doppler results solely reflect the chronic condition of the fetoplacental circulation and cannot identify fetal compromise resulting from acute incidents such as acute cord trauma and placental abruption. This is particularly relevant for patients who experienced placental abruption leading to intrauterine fetal demise (IUFD).

The utility of umbilical artery Doppler in identifying fetuses at risk of adverse outcomes was also demonstrated in the TRUFFLE study, a multicenter randomized controlled trial that showed that incorporating Doppler ultrasound findings into clinical management of early-onset fetal growth restriction reduced perinatal mortality and morbidity.

This study however, has some limitations. The study was only conducted in an urban setting, without representation from rural areas. In terms of foetal outcomes, the situation may have been worse than what this study found in Gombe. This is because many women in Africa live in rural areas without access to adequate health facilities and equipment such as SCBUs.

CONCLUSION

The study findings demonstrated a significant relationship between abnormal umbilical artery Doppler waveforms and unfavourable foetal outcomes in pre-eclamptic patients. These outcomes show that there is need for admission of babies born by pre-eclamptic patients to a special care baby unit. The odds ratios indicated that infants with abnormal umbilical artery Doppler waveforms were seven times more likely to have low birth weight and five times more likely to require admission to the special care baby unit. Additionally, the study observed a higher prevalence of pre-eclampsia among primigravidae.

The existence of a significant association between abnormal umbilical artery Doppler waveforms and adverse foetal outcomes in pre-eclamptic patients suggests a potential predictive role. Therefore, the inclusion of festal umbilical artery Doppler studies in the management of patients with pre-eclampsia is recommended. This approach will enable effective surveillance and appropriate interventions to improve foetal outcomes.

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