Original Research Article

Umbilical and middle cerebral arteries Doppler velocimetry in early and late onset pre-eclampsia

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ABSTRACT

Background: Pre-eclampsia (PE) is a multisytemic disorder originating from the placenta with a high prevalence in sub-Saharan Africa. Early (<34 weeks) and late ($\geq$34 weeks) – onset PE have different maternal and perinatal outcomes with overlapping clinical features. Differences in Doppler velocimetry pattern in these subgroups appears unsettled.
Methods: In a prospective cohort study, 110 pregnant women with singleton pregnancy diagnosed with PE were recruited and had umbilical and middle cerebral arteries (MCA) Doppler velocimetry done. The pregnancies were followed up to delivery and outcome recorded and analysed using Microsoft excel 2013. Student t-test and Chi-squared test were used for continuous and categorical variables respectively. Level of significance was set at less than 0.05.
Results: There were 53 (49.1%) women with early – onset preeclampsia and 55 (50.9%) with late-onset PE. The mean age of women was 30.30±5.2 years. The mean umbilical artery, middle cerebral artery pulsatility indices (PI) and cerebroplacental ratio (CPR) were 1.3±0.5, 1.1±0.5 and 1.1±1.2 respectively. There was statistical significant difference between the umbilical artery PI (p<0.001), middle cerebral artery PI (p<0.05) and CPR (p<0.001) between early onset and late onset preeclamptic women. The resistance index and systolic diastolic ratio of both the umbilical and middle cerebral arteries were similar between the two groups (p>0.05).
Conclusions: This study showed that umbilical and middle cerebral artery PI and CPR may be the most important Doppler parameters to watch-out for in monitoring women with PE.

Keywords: Umbilical artery, MCA, Doppler, Early, Late onset preeclampsia

INTRODUCTION

Preeclampsia (PE), a pregnancy-related disorder is a major cause of maternal and new born morbidity and mortality especially in resource constraint environment.[1] It occurs in the second half of pregnancy and can affect all maternal systems and the fetus.[2] Some of the fetal manifestations include intrauterine growth restriction, preterm birth and small for gestation. It has been documented that fetuses with intrauterine growth restriction (IUGR) or preterm birth are at risk of life long sequelae like hypertension and

type 2 diabetes mellitus.[3] Global estimate revealed that PE affects 4.6% of all pregnancies.[4] In Nigeria, it contributes 20.5% and 29% of maternal death and near miss respectively.[5] PE affects 6.4% of pregnancy in our institution while a prevalence of up to 16% had been reported in Nigeria.[6,7]

Attention is now growing away from classifying PE as mild and severe PE.[8,9] The most recent is the classification into early-onset PE, preterm PE, late-onset PE and term PE.[9] This classification is based on time of delivery. Early

onset PE is one that develops before 34 weeks while late – onset PE is a one that develops at/after 34 weeks of gestation.[9-11] In both types of PE delivery is before and after 34 weeks respectively. Both are associated with different maternal and perinatal outcomes and with overlapping clinical features.

The pathophysiology of PE is centred on uteroplacental circulation. While early onset PE is linked to poor placentation and IUGR, the late onset PE is linked to maternal factors.[11] In early-onset PE, the placental dysfunction is said to be extrinsic to the placenta, due to incomplete spiral artery remodelling in early pregnancy while in late-onset PE, the cause is said to be intrinsic to the growing and ageing placenta, limiting intervillous perfusion.[11,12] Both pathologies lead to secondary syncytiotrophoblast stress and release of pro-inflammatory factors into the maternal circulation.[11,12]

It has been established that, the blood flow velocity of the uterine, umbilical and middle cerebral arteries and ductus venoses can be assessed using Doppler ultrasonography including the blood floor volume, direction and impedance.[13] Doppler tool can be applied to identify fetuses at risk of PE complication like IUGR or monitor those already affected. The features of the blood flow of the arteries can be assessed using various parameters like peak systolic velocity (PSV), end diastolic velocity (EDV), and various mathematical combinations of PSV and EDV like pulsatility index (PI), resistance index (RI) and systolic diastolic (S/D) ratio.[14] These are the most commonly used parameter in obstetrics and are highly correlated.[14,15] Pulsatility (Goslin) index is derived from maximum, minimum and mean Doppler frequency shift during a cardiac cycle.[16] Mathematically, it is represented as given below.[13]

$$PI = Peak\ systolic\ velocity - end\ diastolic\ velocity / mean\ velocity$$

It shows a linear correlation with vascular resistance and does not approach infinity when there are absent or reversed diastolic values.[14] PI is the most commonly used index in obstetrics.[14] Resistance (Pourcelot) index is derived from maximum and minimum velocity is given below.

$$RI = Peak\ systolic\ velocity - end\ diastolic\ velocity / peak\ systolic\ velocity$$

While SD ratio is peak systolic velocity by end diastolic velocity.[13] Both RI and SD ratio show a parabolic relationship with increasing vascular resistance.[14] Cerebroplacental ratio (CPR) has recently emerged as an important predictor of adverse pregnancy outcome and has been recommended to be considered in the assessment of fetuses in 3rd trimester irrespective of the values of the umbilical and middle cerebral arteries .[16] It is the ratio between the middle cerebral artery (MCA) PI to the uterine artery (UA) PI (MCA PI/UA PI). CPR represents the interaction of alteration in blood flow to the brain as manifest by increased diastolic flow as the result from hypoxia and increased placental resistance, resulting in a decreased diastolic flow of the umbilical artery.[17] A low CPR indicates redistribution of blood floor to the cerebral circulation and is associated with adverse outcome than Doppler indices of UA and MCA alone.[17] Various studies were conducted on preeclampsia/eclampsia in our sub-region with very few paying attention to early onset PE. Despite this, no available literature on Doppler velocimetry comparing early and late onset PE in the sub region could be found. This study was set out to compare the pattern of Doppler velocimetry indices as monitoring tools in the settings of early and late onset preeclampsia. Critical values of the indices beyond which a likely adverse fetal outcome may ensue are also documented for clinical use.

METHODS

This was a prospective comparative study involving 110 women. One hundred and eight women (108) eventually completed the study comprising 53 early–onset and 55 late–onset PE that was conducted at a Teaching Hospital in a suburb of Abuja, Nigeria over a two-year period (November 2018–October 2020). All women at the antenatal clinic or ward with a singleton pregnancy, blood pressure ≥140/90 mmHg with proteinuria or any feature of PE using ISSHP criteria at or greater than 20 weeks gestational age were included in the study.[18] Women with chronic hypertension, renal disease in pregnancy, congenital anomalies, multiple pregnancies, antepartum haemorrhage and anaemia in pregnancy were excluded from the study. The sample population was obtained using GPower software and a total of 98 at a ratio of 1:1 was obtained. With a 10% attrition rate, 110 women were recruited. Women were recruited using a random sampling method. The women were grouped into early–onset and late–onset PE based on the gestation age at diagnosis of PE. Basic scan was conducted to confirm the location and viability of the singleton pregnancy. An umbilical and middle cerebral arteries Doppler velocimetry were conducted using GE voluson P8 with a curvilinear transabdominal transducer (3.5 MHZ). A free loop of the umbilical cord was identified and the angle of insonation was set at <20⁰ with a gate size <2 mm during the Doppler interrogation. An axial section of the brain, including the thalami and the sphenoid bone wings was obtained and magnified. Colour flow mapping was used to identify the circle of Willis and the proximal MCA. The pulsed-wave Doppler gate was then placed at the proximal third of the MCA, close to its origin in the internal carotid. The angle between the ultrasound beam and the direction of blood flow was kept as close as possible to 0⁰. Doppler values were obtained three times using auto trace and the mean value was recorded. Parameters recorded were PI, RI, and SD ratio which were obtained automatically without fetal breath and/or movement. Then cerebrospinal ratio (CPR=MCAPI/UAPI) was calculated. The

ultrasonography was conducted by an obstetrician with specialisation in maternal–fetal medicine. The pregnancies were followed up to delivery and fetal outcomes were recorded. Data was recorded and analysed using Microsoft excel 2013.

Chi squared test and Student's t-test were used for categorical and continuous variables respectively. The level of significance was set at p value <0.05.

RESULTS

Only one hundred and eight (108) women completed the study. The women were grouped into early onset [53 (49.1%)] and late–onset [55 (50.9%)] PE. The mean age of all the participants was 30.30±5.2 years with no significant difference between the 2 groups (p=0.817). There were significant differences in booking status (p=0.000),

gestational age at diagnosis (p=0.000), and gestational age at delivery (p=0.000) between the 2 groups (Table 1).

The mean uterine artery PI in the early-onset PE (1.67±0.35) was significantly higher than that of late-onset PE (0.94±0.34), (p=0.000). MCA PI in early onset PE group (1.04±0.49) was statistically lower (p=0.049) than the MCA PI in the late onset group (1.21±0.45). The overall mean CPR was 1.1±1.2. The CPR in early onset PE (0.63±0.36) was lower than CPR in late onset PE (1.56±1.54). This was demonstrated to be statistically significant (p=0.000). Other Doppler parameters were similar between the 2 groups (Table 2).

Only 4 (3.7%) fetuses had IUGR in which 1 (0.9%) occurred in the late onset PE group. However, there was no statistical difference in the IUGR between the two groups. Mode of delivery (p=0.00) and live birth (p=0.018) were shown to be statistically significant (Table 3).

Table 1: Baseline characteristics.

Characteristics	Early onset Preeclampsia (mean, mode or frequency)	Late onset preeclampsia (mean, mode or frequency)	P value
Age	30.42±4.5	30.18±5.82	0.817
Parity	0	1	
Booking status			0.000
Booked	27	47	
Not booked	26	8	
Gestational age at diagnosis	29.42±2.4	36.20±2.3	0.000
Gestational age at delivery	31.58±2.9	36.20±2.3	0.000
Weight	74.31±16.9	75.07±14.706	0.804
Systolic BP	163.11±18.4	162.31±17.229	0.815
Diastolic BP	95.96±7.9	96.9±9.7	0.591

Table 2: Relationship between umbilical and middle cerebral artery velocimetry and the onset of preeclampsia.

Parameter	Early onset preeclampsia	Late onset preeclampsia	t-test	P value	95% CI
UA PI	1.67±0.35	0.94±0.34	10.519	0.000	0.608–0.890
UA RI	0.60±0.05	0.59±0.045	0.950	0.344	0.009–0.027
SD	2.58±0.312	2.56±0.28	0.307	0.760	0.095–0.130
MCA PI	1.04±0.49	1.21±0.45	-1.979	0.049	-0.363–0.000
MCA RI	0.62±0.15	0.59±0.049	1.273	0.206	- 0.015–0.071
MCA SD	2.58±0.31	2.56±0.28	0.307	0.760	-0.095–0.130
CPR	0.63±0.36	1.56±1.54	-4.257	0.000	-1.355–0.495

Table 3: Relationship between the onset of PE and fetal outcome.

Outcome	Early onset PE	Late onset PE	P-value
IUGR			
Present	3	1	0.291
Absent	50	54	
Mode of delivery			
Vaginal delivery	37	29	0.000
Caesarean section	6	26	
Abortion	8	0	
Live birth			0.018

Outcome	Early onset PE	Late onset PE	P-value
Alive	39	50	
Still birth	14	5	
NICU admission			
Yes	23	12	0.17
No	30	43	

DISCUSSION

In this study there were 53 (49.1%) and 55 (50.9%) cases of early and late onset PE respectively. The mean age of the women was 30.3±5.2 years and there was no statistical significant difference between the two groups. This is consistent with the observation in the Polish population.[8,19] There were more women that booked the pregnancy in the late–onset group compared to the early onset group. This was shown to be statistically significant. The booking and subsequent antenatal care especially in early pregnancy can influence the development and progression of PE disease. Regular monitoring and interventions like use of low dose aspirin had been proven to reduce the occurrence of preeclampsia.[9] The mean gestational age at diagnosis in the early and late onset PE group were 29.4 and 36.2 weeks respectively. The age of diagnosis in early onset group from our study is lower compared to the findings by Wojtowicz et al.[8] PE is found to be higher in our sub region when compared to Europe where there is improved socio-economic status and mostly an insurance coverage as early as 10 weeks for all pregnant women.[1,8] Therefore the low socio-economic status in this region may have posed a challenge of poor antenatal care in early pregnancy where women at risk of (early onset) PE can be identified and appropriate intervention instituted.

Our observation of UA PI, RI and SD ratio in this study were similar to finding by Adekanmi et al.[20] These may be explained by similarities in bio-demographic characteristics of the participants in both studies. It was however observed in our study that the UA PI is lower in the early onset group compared to the late onset group (p<0.001). This is in agreement with the observation by Kornacki and Skrzpczak in Europe.[19] The MCA PI in the early onset group was significantly lower than the late onset group (p<0.05). This observation was in contrast to findings from Poland.[19] The CPR in the late onset group was higher than the early onset group (p<0.001). The CPR in late onset group from our study was similar to that of Polish study while that of early onset group was in contrast. It is opined that from our study, the umbilical and middle cerebral artery PI and CPR may be the most important Doppler parameters to look for in monitoring fetuses in PE disease.

There were 4 (3.7%) cases of IUGR in this study of which 3 (2.8) of the fetuses were from the early onset group. This was found to be likely a chance occurrence and comparable to the observation by Kornacki and Skrzpczak where they found no statistical significant difference in IUGR between the two groups.[19]

The difference in mode of delivery between the two groups is statistically significant. More women had caesarean section in the late onset PE group when compared to the early onset group while abortion is only found in the early onset group. The latter may be because of the gestational age at diagnosis in the early onset group since termination of pregnancy before the age of viability is admissibly, an abortion. Only 5 (4.6%) perinatal mortalities were recorded in the late onset group. There was statistical significant difference in perinatal mortality between the two groups. Similar findings were earlier reported in the retrospective studies by Wojtowicz et al, in Poland and Ebeigbe and Aziken in Nigeria.[8,21]

It is however noted that there was no perinatal death in the late–onset group from the polish study while the Nigerian study used the older classification of the hypertension in pregnancy which makes it difficult to compare results.

CONCLUSION

Our study showed that the umbilical and middle cerebral artery PI and CPR may be the most important Doppler parameters to look for in monitoring fetuses in women with preeclampsia. Furthermore, women with late-onset PE had as expected, better perinatal outcome as compared with early-onset preeclampsia. It is clear that women who booked their pregnancy as noticed in the late-onset PE group had the chance for intake of low dose aspirin which has remained a valuable intervention in the prevention of PE and its overall outcome. There is need to carry out further studies with a larger sample size in our environment for evidence to be conclusive.

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