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Mbarak Nuru
Senior Resident, *Department of Radiology and Imaging, School of Medicine, Moi University, Kenya*

Abuya Joseph
Senior Lecturer, Department of Radiology and Imaging, School of Medicine, Moi University, Kenya

Kaaria Alice
Lecturer, Department of Reproductive Health, School of Medicine, Moi University, Kenya

Correspondence:
Dr Joseph Mochama Abuya
Senior Lecturer, Department of Radiology and Imaging, School of Medicine, Moi University, Kenya
Email: abuyajm@yahoo.com

Comparison of Biophysical Profile Score with Fetal Doppler Ultrasound in Patients with Pre-eclampsia at Moi Teaching and Referral Hospital, Kenya

Mbarak Nuru, Abuya Joseph, Kaaria Alice*

Abstract

Background: Pre-eclampsia is a major direct cause of maternal mortality second only to hemorrhage with 50,000-60,000 pre-eclampsia related deaths worldwide annually. Pregnancies complicated by preeclampsia require close fetal surveillance to guide management and improve outcomes. Poor Biophysical profile scores are associated with poor perinatal outcomes. Recent research has however shown that Doppler flow changes occur much earlier and can be used to time delivery with better perinatal outcomes. Objective: To compare Doppler indices of the umbilical and middle cerebral arteries with biophysical profile scores in the prediction of perinatal outcomes in patients with pre-eclampsia. Methods: This was a cross sectional study. Patients with preeclampsia above 28 weeks gestation were consecutively sampled, questionnaires administered, ultrasound done, followed up to delivery and outcomes documented. Statistical analysis was done using STATA/MP version 13.0. Results: One hundred and sixty-five patients whose ages ranged from 15-42 years with an average of 29 years were studied. Majority (72.7%) presented between 28-34 weeks and 66.06% had pre-eclampsia with severe features. An abnormal outcome was seen in 86.4% of those who had abnormal Biophysical Profile (BPP) scores and abnormal BPP increased the Odds of poor outcome 4.95 times ($p<0.001$). An abnormal outcome was seen in 80% of those who had abnormal Doppler findings and abnormal Doppler findings increased the Odds of poor perinatal outcome 11.5 times ($p<0.001$). Conclusion: Abnormal BPP and Doppler findings were significantly associated with poor perinatal outcomes with Doppler being a better predictor

Keywords: Preeclampsia, Biophysical profile, Fetal Doppler ultrasound.

INTRODUCTION

Although pregnancy and delivery is a naturally occurring process, pregnancies can be complicated by a number of factors that render them high-risk. Worldwide data from 2015 suggests that 303,000 women died as a result of pregnancy and childbirth. This is equivalent to 830 women per day[1]. Over 98% of all maternal mortality (MMR) occurs in the developing countries. Preeclampsia is a disorder of vascular endothelial malfunction that occurs after 20 weeks gestation and can occur up to 4-6 weeks postpartum. It is characterised by hypertension with or without proteinuria and organ damage.

Pregnancies complicated by preeclampsia require close monitoring of both fetal and maternal status to guide management and time delivery. Fetal surveillance is done using Non Stress Tests (NST), Contraction Stress tests (CST), biophysical profile (BPP) and Doppler ultrasonography. The traditional methods of fetal surveillance like non-stress test, fetal heart monitoring and fetal biophysical profile are no longer ideal tests because of their inability to detect early stages of fetal distress, significant number of false positive tests and low predictive value [2].

Doppler ultrasonography is done in the third trimester and it is a non-invasive way of evaluating fetal circulation through the umbilical vessels, middle cerebral artery, uterine artery and fetal venous circulation. The umbilical artery (UA) Doppler measurements do not provide information on how the foetus is coping with a compromised supply and therefore will not identify all the compromised foetuses in a population. For this reason, study of systemic vessels such as the middle cerebral artery (MCA) is also carried out [3].

Among the many available tests used for fetal surveillance, there is no single one that can give accurate fetal status. Several studies have demonstrated combination of BPP and Doppler to have higher predictive values as opposed to using them separately. BPP is the most requested test in our set up but Doppler changes have been shown to occur much earlier [4].

All over the world, major changes are taking place in the area of maternal and child health to achieve the goals set out in international declarations and country commitments. Maternal, infant and child mortality are considered the most sensitive indicators of a nation's health status and level of socio-economic development [5]. The Sustainable Development Goals aim to end preventable maternal mortality and has a target of reducing the global MMR to less than 70 per 100,000 live births by 2030[6].

Preeclampsia has been shown to have short and long-term adverse effects on both the mother and child. Women with preeclampsia have an increased risk of antenatal stroke, renal, hepatic, pulmonary, neurological and hematological dysfunction [7]. Furthermore, there is a 4-fold increase in cardiovascular and cerebrovascular disease in future [8]. Fetuses affected suffer from intra-uterine growth restriction (IUGR), preterm delivery and its attendant complications and later increased risk of cardiovascular, cerebrovascular, cognitive, and psychiatric disorders [7].

The etiology is not known but several factors have been shown to be associated with increased risk for preeclampsia and they include: nulliparity, maternal age >35years, black race, smoking, previous history of preeclampsia, family history of preeclampsia, obesity, diabetes mellitus, multiple gestation, chronic hypertension, chronic renal disease [9]. Some studies have also shown that there seems to be both a maternally and a paternally transmitted genetic predisposition to preeclampsia [10].

Pregnancies affected with preeclampsia require close antepartum surveillance. A central premise of antepartum surveillance is that identification and timely delivery of the hypoxic or acidotic fetus will prevent intrauterine death and decrease long-term neurologic damage [3]. The optimal method to identify fetal hypoxia-acidosis has not been determined but common tests include fetal movement assessment, non-stress tests (NST), contraction stress tests (CST), biophysical profile (BPP), modified BPP, and umbilical artery Doppler velocimetry.

Ultrasound provides a cheap, available, non-invasive method for fetal growth assessment and well-being. Addition of Doppler studies serves to detect fetal growth restriction, predict adverse perinatal outcome and determine the optimal time for delivery.

Placental studies have shown that > 60% of the placental vascular bed is obliterated once impedance is increased in the umbilical artery. When there is absent diastolic flow in the umbilical artery, the capillaries in placental terminal villi are decreased in number and they have fewer branches [11]. Blood gases obtained at cordocentesis have shown that 80% of fetuses with absent diastolic flow are hypoxic and 46% are acidemic [12]. Absent end-diastolic flow and reversed diastolic flow within the umbilical artery have an associated 40% and 70% perinatal mortality, respectively. Absent or reversed end diastolic flow patterns appear to be present 12-15 days preceeding fetal deteroriation [13].

In pregnancies with progressive deterioration of the fetal condition, abnormal umbilical cord blood flow patterns occur first. Subsequently, FHR variation is reduced, followed by loss of breathing movements, while general fetal movements and tone are the last parameters to demonstrate abnormal results. Thus BPP detects changes much later compared to UA doppler [4]. Incorporation of Doppler studies into antenatal care of patients with preeclampsia improves fetal surveillance with timely intervention to improve both maternal and perinatal outcome

MATERIALS AND METHODS

A cross-sectional study was carried out at the Moi Teaching and Referral Hospital in Eldoret, Kenya. The study compared Doppler ultrasound with Biophysical profile among pregnant mothers with preeclampsia who are attending MTRH for delivery. Consecutive sampling was used in this study. Patients diagnosed with preeclampsia were referred for ultrasound from the antenatal clinic or antenatal ward. All nurses in labour ward were formally trained on Appearance, Pulse, Grimace, Activity, Respiration (APGAR) scoring and they were further sensitized and updated on accurate APGAR scoring, weighing of new borns and proper recording in patients' files.

Obstetric and Doppler ultrasound of the umbilical artery (UA) and middle cerebral artery (MCA), calculation of the Cerebro-Placental Index (CPI), accurate biophysical profile scoring and archiving of images was done using a real time scanner with the trans-abdominal approach were done. A Mindray M7 machine 2016 model with 3.5-5 MHz curvilinear probe was used. The examination was done with the patient lying supine or semi-recumbent on the examination couch. The abdomen is exposed and paper towel used to protect the patient's clothes. Prewarmed coupling gel was applied to the abdomen then a standard third trimester obsteric ultrasound with biophysical profile and doppler studies of the UA and MCA conducted. Doppler protocols were adopted from the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines of 2013 [14].

Data was collected between 1st October, 2016 and 30th September, 2017 using a structured questionnaire. Data was imported into STATA/MP version 13, where coding, cleaning and analysis was done.

RESULTS

Majority of the patients were multiparous 57.58% with 7.8% being grand multiparous. Majority (61%) had personal previous history of hypertension in pregnancy.

On average the Gestation by Ultrasound was 31.1(SD 4.4) weeks with a range of 22 to 42 weeks. IUGR was present in 30.3% of the patients, 20.61% had oligohydramnios

25.7% of those had normal BPP ended up with overall abnormal pregnancy outcomes.

Table 1: Association between BPP and specific post-natal outcomes

		BPP total scores		
Post-natal outcome	**Category**	**Normal**	**Abnormal**	**P-value**
Gestation		37(SD 0.4)	32(SD 0.5)	<0.001*
Baby state at birth	Alive	94	38	<0.001
	Still birth	5	28	
Delivery mode	SVD	64	18	0.026
	CS	30	20	
CS reason	Others	19	4	0.003
	Fetal distress	11	16	
Apgar score	Normal (8-10)	90	17	<0.001
	Abnormal (<8)	4	21	
BWT	Normal (>2499g)	53	11	0.004
	Underweight (<2500g)	41	27	
BWT	ELBW (<1000g)	2	3	<0.001†
	VLBW (1000-1499g)	7	17	
	LBW (1500-2499g)	32	7	
	NBW (>2499g)	53	11	

†*Fishers Exact Test *t-test*

This table 1 demonstrates that there was a statistically significant association between abnormal BPP and poor perinatal outcomes in all the 5 categories.

Table 2: Association between post-natal outcome and specific Doppler findings

		Post-natal outcome		
Doppler findings	**Category**	**Normal**	**Abnormal**	**P-value**
UA-RI	Normal	49	49	<0.001
	Abnormal	3	64	
SD-Ratio	Normal	31	35	0.001
	Abnormal	21	78	
MCA-RI	Normal	45	93	**0.494**
	Abnormal	7	20	
CPI	Normal	41	35	<0.001
	Abnormal	11	78	
End diastolic flow	Normal	48	26	<0.001
	Abnormal	4	87	

Only MCA-RI was not statistically associated with post-natal outcomes (p=0.494).

Table 3: Association Apgar score and specific Doppler findings

		Apgar score		
Doppler findings	**Category**	**Normal**	**Abnormal**	**P-value**
UA-RI	Normal	91	4	<0.001
	Abnormal	16	21	
SD-Ratio	Normal	64	1	<0.001
	Abnormal	43	24	
MCA-RI	Normal	88	19	0.473
	Abnormal	19	6	
CPI	Normal	72	3	<0.001
	Abnormal	35	22	
End diastolic flow	Normal	73	0	<0.001
	Abnormal	34	25	

Only MCA RI was not significantly associated with APGAR score ≤ 7 at 5 minutes.

Table 4: Association gestational age at delivery and specific Doppler findings

		Gestational age at delivery			
Doppler findings	**Category**	**Mean**	**SD**	**[95% CI]**	**p-value**
UA-RI	Normal	37.23	4.17	[36.39, 38.07]	<0.001
	abnormal	32.25	3.90	[31.29, 33.21]	
UA-SD	Normal	37.06	4.22	[36.02, 38.09]	<0.001
	abnormal	34.00	4.68	[33.06, 34.93]	
MCA-RI	Normal	35.13	4.92	[34.29, 35.96]	0.543
	abnormal	35.74	3.70	[34.27, 37.20]	
CPI	Normal	37.52	4.09	[36.59, 38.46]	<0.001
	abnormal	33.25	4.36	[32.32, 34.17]	
End diastolic flow	Normal	37.77	4.09	[36.82, 38.72]	<0.001
	abnormal	33.14	4.19	[32.26, 34.02]	

t-test was used to compare mean gestational age at delivery among different categories of Doppler findings. The average gestational age among those who had normal and abnormal MCA-RI findings were statistically equal (p>0.05). All other Doppler parameters had statistically significant different mean gestational age (p<0.05), where all those with normal Doppler findings had a mean gestational age of 37 weeks compared to those who had abnormal Doppler findings which ranged between 32 to 34 weeks.

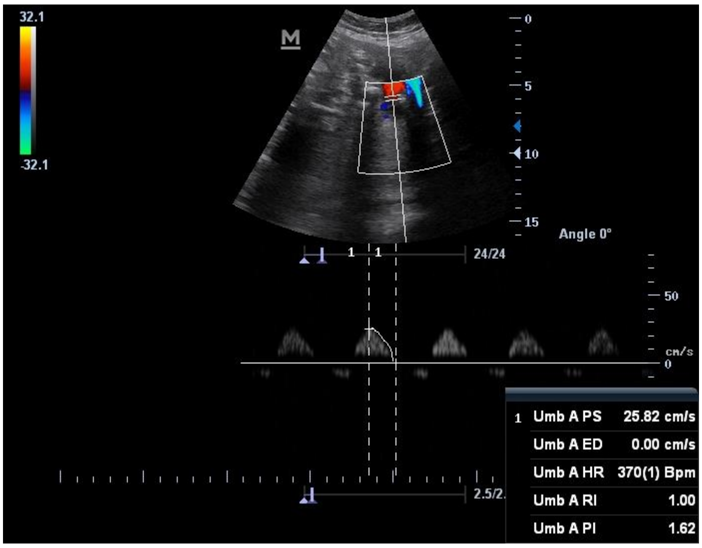

Figure 1: A31 year old with preeclampsia at 29 weeks. Reversed EDV. Had IUFD at 30 weeks.

DISCUSSION

There was a statistically significant association between abnormal BPP and poor perinatal outcomes. Middle Cerebral Artery Resistive Index (MCA RI) had no significant association with poor outcomes when used alone, except when used as Cerebro-Placental Index (CPI). All fetal Doppler parameters except MCA RI had a significant association with APGAR score ≤ 7 at 5 minutes. Poor perinatal outcomes included still birth, preterm birth, low birth weight and low APGAR score.

Biophysical profile was found to be abnormal in 40.61% of the patients and this compares well with Laxmi et al (40%) and Nisa et al (31%)[15,16].This figure is however much higher than what was found by Nguku et al (15%) although Nguku sub-classified BPP into normal, equivocal and abnormal [17].

The most common abnormal finding was fetal tone followed by amniotic fluid index (AFI). Manning and colleagues in 1980 described that fetal tone is the first parameter to be impaired in case of neurological suppression [18]. Amniotic Fluid Index was found to be the only parameter associated with disease chronicity/duration by Nguku in Nairobi [17]. Several studies have demonstrated an association between Oligohydramnios and adverse perinatal outcomes including fetal distress, IUGR, caesarean delivery, low APGAR scores and admission to neonatal intensive care unit (NICU) [19]. However, a study by Voxman only found an association between oligohydramnios and abnormal fetal heart rate tracing but no other outcome measures [20].

Overall, 78.79% of the patients had abnormal Doppler findings; UA RI (40.2%), UA S/D (59.76%), UA EDV (54.88%), MCA RI (83.64%), CPI (53.66%). Komuhangi in Uganda found 94% of patients with hypertension to have abnormal Doppler although he only studied the umbilical artery [21]. Devi in India found 44% of patients to have abnormal Doppler findings but this was a case-control study with only 50 patients with hypertensive disorders in pregnancy [2].

Abnormal UA flow patterns was present in 54.88%; reduced (16.46%), absent (35.98%) and reversed (2.44%). The rate of agreement between BPP and Doppler findings in this study was 61.8%. Laxmi in India found 74% which is similar to our study[15].This is in contrast to Yoon who found a rate of agreement of 91.4% but he classified patients into 4 groups based on BPP and Doppler findings and had the highest number in the group with normal BPP and Doppler [12]. Nguku in Nairobi found a low agreement of 40.1% but this study only looked at one Doppler parameter, the umbilical artery resistive index [17].

Majority (68.48%) of the patients had abnormal outcomes; preterm birth (53.05%), IUFD (20.16%), low birth weight (51.53%), CS for NRFS (16.46%), APGAR < 7 at 5 minutes (18.94%), admission to NBU (31.82%).

There was a statistically significant association between abnormal BPP and overall adverse perinatal outcomes with 86.4% of the patients having abnormal BPP scores also having abnormal outcomes (p<0.001). The association between BPP profile and specific perinatal outcomes was also significant. This is similar to other studies which found abnormal BPP to be associated with poor perinatal outcomes including still birth, low APGAR scores, NRFS and fetal acidosis [16, 22 &12].

A statistically significant association was demonstrated between Doppler findings and poor perinatal outcomes. This is similar to what was found by a study in India with a similar composition of outcomes [2]. All the specific abnormal Doppler findings were also associated with poor outcomes except MCA RI (P=0.494).

The biophysical profile was developed by Manning et al in 1980 and has been in use with relatively good sensitivity but is subjective and takes time [18]. Biophysical changes have also been shown to develop days to weeks after Doppler changes [4].

Having an abnormal BPP increased the odds of getting a poor outcome 4.95 times. BPP has been shown to be positively associated with fetal acidemia (adjusted OR 4.84; 95% CI 1.33–17.66) [22]. Another study found BPP to be associated with poor outcomes with an odds ratio of 2.93 at 95% confidence interval (CI) = 1.2 - 7.3, *P* = 0.021) [23].

There were some limitations in this study, including that some pre-eclampsia patients presented late for the evaluations. Doppler studies of both the Umbilical and Middle Cerebral Arteries including the Cerebro-Placental Index were not routinely requested for in the prenatal evaluation of pregnancies affected by preeclampsia. The department has not developed a management guideline incorporating both BPP and Doppler studies of UA and MCA in evaluation of patients with preeclampsia.

CONCLUSIONS

40.6% of patients had abnormal biophysical profile (BPP) while 78.7% had abnormal Doppler findings with 51.1% having abnormal umbilical artery spectral flow patterns. There was fair agreement between BPP and Doppler at 61.8%. Both abnormal BPP and Doppler were significantly associated with poor perinatal outcomes and increased odds of having a poor outcome with doppler showing a higher Odds Ratio.

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