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RESEARCH ARTICLE

PERINATAL OUTCOME PREDICTION IN PATIENTS WITH PREECLAMPSIA USING FETAL DOPPLER STUDIES AT MOI TEACHING AND REFERRAL HOSPITAL

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Abstract

Background: Preeclampsia is a major direct cause of maternal mortality second only to hemorrhage with 50,000-60,000 preeclampsia related deaths worldwide annually. In the fetus, it can lead to ischemic encephalopathy, growth restriction and the various sequelae of premature birth. Pregnancies complicated by preeclampsia require close fetal surveillance to guide management and improve outcomes.

Objective: To determine the fetal Doppler indices of the umbilical and middle cerebral arteries in the prediction of perinatal outcomes in patients with preeclampsia.

Methods: A cross sectional study done at the Moi Teaching and Referral Hospital. Consenting patients with preeclampsia above 28 weeks gestation were consecutively sampled. A total of 165 patients were studied. Descriptive statistics were carried out. Inferential statistics was also carried out.

Results: Majority (72.7%) presented between 28-34 weeks and 66.06% had preeclampsia. An abnormal outcome was seen in 80% of those who had abnormal Doppler findings which increased the Odds of poor outcome 11.5 times ($p < 0.001$). Poor perinatal outcomes included still birth, preterm birth, low birth weight and low APGAR score. MCA RI had no significant association with poor outcomes except when used as Cerebro-Placental Index (CPI).

Conclusion: Majority had abnormal Doppler findings. Abnormal Doppler findings were significantly associated with poor perinatal outcomes.

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Introduction:-

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. It has a global incidence of 5-14% and 4-18% in developing countries¹. The incidence of hypertensive disorders in pregnancy in Kenya is 19% but preeclampsia/eclampsia has an incidence of 2.7 %.² Geographic, social, economic and racial differences are thought to be responsible for the difference in incidence rates among populations³. It is the second most common obstetric cause of fetal and early neonatal death in developing countries⁴.

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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 fetus is coping with a compromised supply and therefore will not identify all the compromised fetuses in a population. For this reason, study of systemic vessels such as the middle cerebral artery (MCA) is also carried out⁵.

Although Doppler studies have been shown to improve outcome in high risk pregnancies, they are of no use in low risk pregnancies and should not be used in routine screening of such pregnancies⁶. In Kenya the maternal mortality due to preeclampsia is as high as 16% and preeclampsia has a four-fold increase in preterm births, perinatal mortality and admission to the new born unit⁷.

Umbilical Artery (UA) is the most widely studied vessel and its value well established in several studies. However, there is conflicting data on the value of Middle Cerebral Artery (MCA) doppler except in assessment of fetal anemia. Some studies have shown assessment of the MCA to have limited predictive accuracy of perinatal outcome⁸. Use of the Cerebro-placental Index (CPI) is more accurate than individual vessel indices in prediction of perinatal outcomes as it gives information on how the fetus is coping with the impaired blood flow^{9,10}.

The value of Doppler studies has been established the world over. However, this has not been done in our hospital setup and Biophysical Profile (BPP) is still the main ultrasound fetal surveillance tool. Only two studies have been done in Kenya regarding Doppler in obstetrics and both were done more than 10 years ago^{11,5}. None of these studied fetal vessels and both were in private hospitals. Thus, there is general paucity of data in our setup regarding utility of obstetric Doppler studies. Although a study by Nguku et al in Nairobi showed that umbilical artery Doppler is more sensitive than biophysical profile in prediction of perinatal outcome, this study did not evaluate systemic vessels like the MCA¹¹.

Doppler ultrasound provides important information to guide obstetricians in management and time delivery. International guidelines exist on use of Doppler in obstetrics and specifically in preeclampsia but there are no clear local guidelines.

The World Health Organization (WHO) estimated the maternal mortality rate (MMR) in 2015 to be 216 maternal deaths per 100,000 live births with developing regions accounting for 99% and Sub-Saharan Africa alone accounting for roughly 66%. The MMR in Kenya was estimated at 510/100,000 live births¹². Preeclampsia is second to hemorrhage as a cause of maternal mortality with an estimated 50,000-60,000 preeclampsia related deaths worldwide every year^{13,12}.

Preeclampsia is clinically defined as hypertension (BP > 140/90), proteinuria with or without pathological edema¹⁴. According to the new guideline by American College of Obstetricians and Gynaecologists (ACOG), diagnosis of preeclampsia no longer requires presence of proteinuria or edema for diagnosis¹⁵. Severity depends on cut-offs for hypertension and proteinuria and clinical or laboratory evidence of end organ damage. In the fetus, it can lead to ischemic encephalopathy, growth retardation and the various sequelae of premature birth.

The umbilical artery (UA) was the first vessel to be evaluated by Doppler velocimetry. Flow velocity waveforms from the umbilical cord have a characteristic saw-tooth appearance of arterial flow in one direction and continuous umbilical venous blood flow in the other. Indices used to assess umbilical artery abnormalities include Systolic/Diastolic (S/D) ratio, resistive index (RI) and pulsatility index. These can be used interchangeably with similar predictive values for perinatal outcome¹⁶.

The umbilical artery (UA) is a low resistance vessel, with preeclampsia increase in vascular resistance leads to reduction in end diastolic velocity. Placental insufficiency can be quantified based on the reduction of end-diastolic Doppler flow velocity into:

1. Reduced end diastolic flow velocity
2. Absent end-diastolic flow velocity
3. Reversed end-diastolic flow velocity

The risk of perinatal mortality increases up to 60%, with increasing severity from reduced to reversed end-diastolic flow velocity¹⁷.

Doppler assessment of the foetal middle cerebral artery (MCA) is an important part of assessing fetal cardiovascular distress, fetal anemia or fetal hypoxia. Examination of the MCA is used as an adjunct to UA doppler to monitor those fetuses at risk of perinatal morbidity or mortality due to placental insufficiency. The MCA is a high resistance vessel compared to the umbilical artery with minimal flow in fetal diastole. With mild hypoxia, the resistance in the UA is increased with no change in the resistance in the MCA. With progressive hypoxia, vasodilation occurs to protect the brain, heart and adrenals with reduced flow to the placental and peripheral circulations-brain sparing effect. With brain sparing the doppler waveform depicts increased diastolic flow and reduced pulsatility index. With worsening hypoxia, there is a paradoxical rise in resistance with 'normalisation' of the waveform and this is a poor prognostic sign¹⁸.

Use of the umbilical artery or the middle cerebral arteries in isolation to predict perinatal outcome has lower sensitivities and positive predictive values⁹. For this reason many studies have been conducted on the use of Cerebro-placental index (CPI) to predict perinatal outcome and it has been shown to be superior than individual vessels¹⁰. Use of the cerebro-placental index is a valuable predictor of outcome in preeclampsia irrespective of whether the fetus is small or appropriate for gestational age¹⁹.

Virginia Apgar was an anesthesiologist who invented the Apgar score in 1952 as a method to quickly summarize the health of newborn children. It uses five simple criteria on a scale from zero to two, then summing up the five values thus obtained. The resulting Apgar score ranges from zero to 10²⁰. The test is generally done at one and five minutes after birth, and may be repeated later if the score is and remains low. Scores 7 and above are generally normal, 4 to 6 fairly low, and 3 and below are generally regarded as critically low. A low score on the one-minute test may show that the neonate requires immediate medical attention. An Apgar score that remains below 3 at later times—such as 10, 15, or 30 minutes may indicate longer-term neurological damage, including a small but significant increase in the risk of cerebral palsy.

Methods:-

This was a cross-sectional study with prenatal data collected at one point and post-natal findings also recorded at a single point in time. The study was conducted in the Radiology and Imaging department and the antenatal, labour and neonatal wards in the Moi Teaching and Referral Hospital (MTRH), Eldoret, Kenya. The study population included pregnant women with preeclampsia referred for ultrasound. Only patients who planned to deliver in MTRH were recruited in this study so as to reduce loss to follow-up as postpartum results were also required. The study was conducted over a period of 12 months from October 2016 to September 2017. Patients in their third trimester (>28 weeks) of pregnancy with a clinical diagnosis of preeclampsia made by the attending clinicians in the reproductive health department were recruited. However, patients with multiple gestation, those in labour and those with fetal congenital malformations like neural tube defects, cardiac malformations, fetal hydrops were excluded.

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 reproductive health department of MTRH were formally trained on APGAR scoring and they were further sensitized and updated on accurate APGAR scoring, weighing of new borns and proper recording in patients' files.

A trans-abdominal approach using a Mindray M7 ultrasound 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 following ultrasound findings were considered abnormal:

1. UA RI ≥ 0.71 (S. Waa & S. Vinayak, 2010)
2. UA S/D ratio > 3 (Lalthantluanga et al., 2015)
3. Absent or reversed end diastolic velocity.
4. MCA RI ≤ 0.71 (S. Waa & S. Vinayak, 2010)
5. CPI < 1 (Lalthantluanga et al., 2015)

The outcomes of interest were whether live or still birth, mode of delivery, gestation at birth, APGAR score at 5 minutes and birth weight. Abnormal outcomes were:

1. Preterm delivery < 37 weeks.
2. Caesarean section for non-reassuring fetal status (NRFS).
3. Still birth/Intrauterine fetal demise.
4. Low birth weight < 2500 gm.

APGAR score ≤ 7 at 5 minutes

Data was collected using a structured questionnaire. Data was then imported into STATA/MP version 13, where coding, cleaning and analysis was done.

Results:-

The results are based on 165 patients whose age ranged from 15 to 42 years with an average of 29 (SD 6.3) years. The median age was 30 (IQR 24, 34) years. Majority (n=138, 83.6%) of patients were married and 63% had attained secondary level of education

Table 1:- Doppler findings.

Variable	Category	Frequency	Percent
UA-RI	Normal	98	59.39
	Abnormal	67	40.61
UA-SD	Normal	66	40.00
	Abnormal	99	60.00
MCA-RI	Normal	27	16.36
	Abnormal	138	83.64
CPI	Normal	76	46.06
	Abnormal	89	53.94
End diastolic flow	Normal	74	44.85
	Reduced	27	16.36
	Absent	60	36.36
	Reversed	4	2.42
End-diastolic flow summary	Normal	74	44.85
	Abnormal	91	55.15
Doppler findings summary	Normal	35	21.21
	Abnormal	130	78.79

Overall, 78.79% of the patients had abnormal Doppler findings with MCA RI being the most common abnormal parameter in 83.64% of the patients.

Table 2:- Pregnancy outcome.

Variable	Category	Frequency	Percent
Gestation at birth	Normal	77	46.67
	Preterm	88	53.33
State of baby at birth	Alive	132	80.0
	Intrauterine Fetal Demise	33	20.0
Delivery mode	Spontaneous Vertex Delivery	82	62.12
	Cesarean Section	50	37.88
Reasons for Caesarian Section (n=50)	Others	23	46
	Fetal distress	27	54
Apgar score at 5 minutes	Normal	107	81.06
	Abnormal	25	18.94
Birth weight categories	ELBW (<1000g)	5	3.79
	VLBW (1000-1499g)	24	18.18
	LBW (1500-2499g)	39	29.55
	NBW (>2499g)	64	48.48
Birth weight summary	Normal	64	48.48
	Abnormal	68	51.52
Post-natal outcome	Normal	52	31.52
	Abnormal	113	68.48

This table demonstrates the distribution of abnormal outcomes in the 5 categories. There was an abnormal outcome in 68.48% of the patients and perinatal mortality was present in 20%.

Table 3:- Association between Doppler findings and pregnancy outcome.

Doppler findings	Post natal outcome		Total
	Good n (%)	Poor n (%)	
Normal	26 (74.29)	9 (25.71)	35
Abnormal	26 (20.00)	104 (80.00)	130
Total	52	113	165

$$\chi^2 = 37.651, p < 0.001$$

There was a statistically significant association between Doppler findings and overall pregnancy outcome ($p < 0.001$), where majority (80%) who had abnormal Doppler findings were also found to have abnormal overall pregnancy outcome, 25.7% of those who had normal Doppler ended up with overall abnormal pregnancy outcomes. Those with abnormal Doppler findings were 11.5 times more likely to have poor post natal outcomes as compared to those with normal Doppler findings (OR=11.55, $p < 0.001$, 95% CI 4.83, 27.61)

Table 4:- Association between post natal outcome and specific Doppler findings.

Doppler findings	Category	Post natal outcome		P-value
		Normal	Abnormal	
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 5:- Association baby state at birth and specific Doppler findings.

Doppler findings	Category	Baby state at birth		P-value
		Alive	Still birth/IUFD	
UA-RI	Normal	94	4	<0.001
	Abnormal	37	20	
SD-Ratio	Normal	64	2	<0.001
	Abnormal	67	32	
MCA-RI	Normal	106	32	0.071
	Abnormal	25	2	
CPI	Normal	74	2	<0.001
	Abnormal	57	32	
End diastolic flow	Normal	73	1	<0.001
	Abnormal	58	33	

There was a statistically significant association between all abnormal Doppler findings and still birth/IUFD except MCA RI.

Table 6:- Association Apgar score and specific Doppler findings.

Doppler findings	Category	Apgar score		P-value
		Normal	Abnormal	
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.

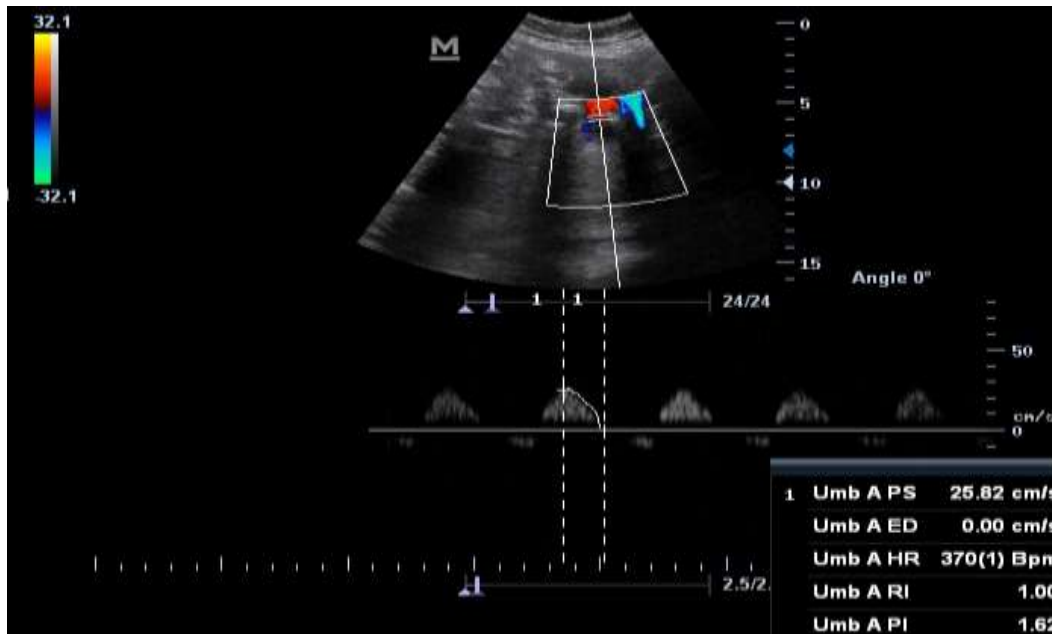


Fig. 1:- 31 year old with preeclampsia +severe features at 29 weeks.
Reversed EDV. Had IUFD at 30 weeks

Discussion:-

Ultrasound is the imaging modality of choice in obstetrics as it gives insight to the well-being of the fetus. In patients with preeclampsia, addition of Doppler studies evaluates how the foetus is coping and guides clinical management. Average gestation by ultrasound was 31 weeks with a range of 22-42 weeks. 16.97% of the patients were below 28 weeks by ultrasound.

Intrauterine Growth restriction (IUGR) was present in 30.3% of the patients and this is similar to what was found by Nguku et al in Nairobi who found IUGR in 30.5% of their pre-eclamptic patients¹¹. Similar results were demonstrated in a study done in Pennsylvania which showed 2-4 fold increase in odds of getting IUGR in preeclampsia and incidence increased with severity of preeclampsia²¹. IUGR in preeclampsia is explained by utero-placental insufficiency which leads to impaired fetal blood supply thus the fetus does not grow to its full genetic potential.

20.61% of the patients were found to have oligohydramnios as measured by the Amniotic Fluid Index (AFI). Oligohydramnios is a common finding in pregnancies complicated by IUGR and it is explained by decreased fetal blood volume, renal blood flow, and, subsequently, fetal urine output²².

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%). Komuhangiet al in Uganda found 94% of patients with hypertension to have abnormal Doppler although he only studied the umbilical artery²³. Deviet alin 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 pregnancy²⁴. Abnormal UA flow patterns was present in 54.88%; reduced (16.46%), absent (35.98%) and reversed (2.44%) Of note was that all the 66 patients who had abnormal BPP also had abnormal Doppler findings. Laxmi and Kotha found out of 40 patients who had abnormal BPP, 34 of them had abnormal Doppler²⁵. This further supports the fact that Doppler changes occur much earlier than BPP changes²⁶. Other studies have shown that BPP is associated with false positive results because of its subjective nature²⁷.

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 outcomes²⁴. All the specific abnormal Doppler findings were also associated with poor outcomes except MCA RI (P=0.494). A case control study done in Egypt showed no significant difference between individual Doppler indices except CPI in patients with preeclampsia and those without¹⁸. The same study demonstrated combination of UA and MCA indices as the CPI had better sensitivity, specificity and predictive values. Another study in India also demonstrated that CPI is a better predictor of perinatal outcome compared to UA S/D ratio²⁸.

Several studies have sought to validate different antenatal tests but no single test has been shown to accurately provide information on fetal status. Most clinical guidelines advocate combination of clinical findings, laboratory tests and ultrasound findings to make decisions on delivery in patients with preeclampsia²⁹. Moreover, poor postnatal outcomes are varied and cord blood pH is considered the most objective method of assessing post-natal outcome³⁰.

Having an abnormal Doppler increased odds of having an abnormal outcome 11.5 times. A study in Pennsylvania demonstrated an Odds ratio of 4.2 with CPI threshold of less than 1.08 with an odds ratio (95% confidence interval)³¹. The higher odds in our study can be explained by the use of several Doppler parameters as opposed to using only one (CPI).

Conclusions:-

Majority (78.7%) had abnormal Doppler findings with 51.1% having abnormal umbilical artery spectral flow patterns. Abnormal Doppler findings were significantly associated with poor perinatal outcomes.

Doppler studies of both the Umbilical and Middle Cerebral Arteries including the Cerebro-Placental Index should be included in the prenatal evaluation of pregnancies affected by preeclampsia.

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