COMPARISON OF DOPPLER STUDIES WITH BIOPHYSICAL PROFILE IN PREDICTION OF PERINATAL OUTCOME IN PATIENTS WITH PREECLAMPSIA AT MOI TEACHING AND REFERRAL HOSPITAL

BY

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This thesis is submitted to the School of Medicine, College of Health Sciences, Moi University in partial fulfilment of the requirement for the award of the degree of Masters of Medicine in Radiology and Imaging

DECLARATION

I declare that this is my original work, it has not been presented for a degree in any other university and no part may be reproduced without prior permission from the author or the university.

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DEDICATION

To my amazing husband Anwar Khan for his unconditional support. To my daughters Jamilah, Junaina and Janaan whose innocent smiles keep me going. To my parents and siblings for their tremendous encouragement and motivation.

I am truly grateful.

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LIST OF ABBREVIATIONS

APGAR	Appearance, Pulse, Grimace, Activity, Respiration
BPP	Biophysical Profile
CPI	Cerebro-Placental Index
CS	Caesarean Section
EDD	Expected Date of Delivery
FHR	Fetal Heart Rate
GBD	Gestation by Date
IREC	Institutional Research and Ethics Committee
IUFD	Intrauterine Fetal Death
IUGR	Intrauterine Growth Restriction
KMTC	Kenya Medical Training College
LNMP	Last Normal Menstrual Period
MCA	Middle Cerebral Artery
NBU	New Born Unit
MTRH	Moi Teaching and Referral Hospital
NRFS	Non-Reassuring Fetal Status
PI	Pulsatility Index
RI	Resistive Index
RMBH	Riley Mother and Baby Hospital
S/D RATIO	Systolic/Diastolic ratio
UA	Umbilical Artery
US	Ultrasound

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OPERATIONAL DEFINITIONS

- **Preeclampsia**- Complication of pregnancy occurring after 20 weeks gestation characterised by hypertension-Blood Pressure more than 140/90 with or without proteinuria and damage to an organ system (ACOG, 2015).
- Preeclampsia with severe features
    - BP >160/110
    - Impaired hepatic function
    - Progressive renal insufficiency
    - Cerebral or visual disturbances
    - Pulmonary edema
    - Thrombocytopenia
- **Biophysical profile**- Ultrasound assessment of fetal physiological status (breathing, tone, activity and AFI). A score ≤6 is abnormal.
- **Doppler ultrasound**- Vessels studied were the umbilical artery and middle cerebral artery.
- **Oligohydramnios**- Diminished amniotic fluid volume as measured by the 4-pocket method. AFI ≤5cm is considered Oligohydramnios.
- **IUGR**- Estimated fetal weight <10th percentile for gestational age as estimated by the Hadlock et al growth curve (Gardosi, 2006).
- **Perinatal period**-The perinatal period commences at 22-28 weeks completed weeks (154 days) of gestation and ends seven completed days after birth (Walsh, Feifer, Measham, & Gertler, 1993).
- **Abnormal perinatal outcomes**
    - Preterm delivery (<37 weeks)
    - Low birth weight <2500gm
    - APGAR score <7 at 5 minutes
    - Caesarean Section for NRFS
    - Still birth/IUFD

COMPARISON OF DOPPLER STUDIES WITH BIOPHYSICAL PROFILE IN PREDICTION OF PERINATAL OUTCOME IN PATIENTS WITH PREECLAMPSIA AT MOI TEACHING AND REFERRAL HOSPITAL.

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. Preeclampsia has a global incidence of 5-14% with an incidence of 4-18% in developing countries. Incidence in Africa is 2-8% but has increased in recent years due to increase in risk factors. Preeclampsia is associated with several adverse maternal and fetal outcomes. 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. 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 including reduced rates of perinatal admissions, induction of labor, caesarean delivery and the odds of perinatal death.

Objective: To determine and compare Doppler indices of the umbilical and middle cerebral arteries with biophysical profile scores in the prediction of perinatal outcomes in patients with preeclampsia at Moi Teaching and Referral Hospital.

Methods: This was a hospital based cross sectional study conducted at the Radiology and Imaging and Reproductive Health departments at Moi Teaching and Referral Hospital from October 2016 to September 2017. Consenting patients with preeclampsia above 28 weeks gestation were consecutively sampled, questionnaires administered, scanned, followed up to delivery and outcomes documented. The ultrasounds were done by the principal investigator or a trained research assistant and later discussed with two consultant radiologists. Statistical analysis was done using STATA/MP version 13.0. Descriptive statistics were carried out for continuous variables using mean, median, standard deviation and interquartile range. Inferential statistics was carried out using Chi square test and data was presented in form of tables, graphs and pie charts.

Results: One hundred and sixty five patients whose ages ranged from 15-42 years with an average of 29 years were included into the study. Majority (72.7%) presented between 28-34 weeks and 66.06% had preeclampsia with severe features. An abnormal outcome was seen in 86.4% of those who had abnormal 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 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: Abnormal BPP and Doppler findings were significantly associated with poor outcomes with Doppler being a better predictor.

Recommendation: Doppler studies of both the UA and MCA including the CPI should be included in the prenatal ultrasound evaluation of pregnancies affected by preeclampsia.

CHAPTER ONE

INTRODUCTION

1.1 Background

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 (Say et al., 2014). Over 98% of all maternal mortality 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.

It has a global incidence of 5-14% and 4-18% in developing countries (Villar, Betran, & Gulmezoglu, 2001). Rates from African countries such as South Africa, Egypt, Tanzania, and Ethiopia vary from 1.8% to 7.1% (Osungbade & Ige, 2011). The incidence of hypertensive disorders in pregnancy in Kenya is 19% but preeclampsia/eclampsia has an incidence of 2.7 % (Ota, Ganchimeg, Mori, & Souza, 2014). A study done in Kibera in 2010 found the prevalence in that area to be 6% (OTIENO, 2012). Geographic, social, economic and racial differences are thought to be responsible for the difference in incidence rates among populations (López-Jaramillo, Pradilla, Castillo, & Lahera, 2007). It is the second most common obstetric cause of fetal and early neonatal death in developing countries (Ngoc et al., 2006).

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 (Devi, Kumar, Shukla, & Jain, 2017).

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 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 (S. Waa & S. Vinayak, 2010). According to the Cochrane database of 2000, meta-analysis of randomized clinical trials have shown Doppler ultrasonography to reduce the number of perinatal admissions (44%), induction of labour (20%), caesarean delivery (52%) and the odds of perinatal death (38%) (Zarkok Alfirevic & Neilson, 1995).

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 pregnancies (Zarko Alfirevic, Stampalija, & Gyte, 2010)

1.2 Problem Statement

Hypertension in pregnancy complicates 5-10% of pregnancies and it has a strong effect on maternal and fetal morbidity and mortality (Lalthantluanga et al., 2015). 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 unit (Say et al., 2014). Many challenges exist in the prediction, prevention,

and management of preeclampsia while treatment remains prenatal care, timely diagnosis, proper management and timely delivery (Osungbade & Ige, 2011). In 2016, a total of 651 patients were seen in MTRH with the specrum of gestational hypertension and 500 of them had preeeclampsia with severe features (Records department, MTRH).

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 **(**Deka 2013)

UA is the most widely studied vessel and its value well established in several studies. However, there is conflicting data on the the value of MCA doppler except in assessment of fetal anemia. Some studies have shown assessment of the MCA to have limited predictive accuracy of perinatal out come (Morris, Say, Robson, Kleijnen, & Khan, 2012). 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 (Yalti, Oral, Gürbüz, Özden, & Atar, 2004) (DeVore 2015).

The value of Doppler studies has been established the world over. However, this has not been done in our hospital and BPP is still the main US fetal surveillance tool. This study therefore will form a basis to include Doppler studies in the prenatal evaluation of patients with preeclampsia.

In MTRH more than 500 patients are seen with preeclampsia per year yet only 32 obstetric Doppler scans were done in 2016.

1.3 Justification

As alluded to earlier, preeclampsia is a dreaded complication of pregnancy with increased risk to both the mother and fetus. It is therefore paramount to identify the fetus at risk and deliver at a time when maternal condition is not compromised and fetal outcomes are acceptable.

Ultrasound provides an affordable, readily available, safe and non-invasive way of assessing fetal well-being. Despite having trained personnel and facilities, obstetric Doppler studies are rarely performed in our set-up. This shows that this service is greatly underutilised in our hospital.

MTRH is the second national referral hospital in Kenya serving a large population west of Nairobi with more than 13,000 deliveries (13,252 in 2015). It is well equipped with state of the art equipment, a large number of consultant obstetricians and radiologists and competent sonographers.

Although ultrasound is operator and technique dependent adequate training and clear protocols ensures that both the Doppler studies and BPP are done to standard.

Only two studies have been done in Kenya regarding Doppler in obstetrics and both were done more than 10 years ago (Nguku, Wanyoike-Gichuhi, & Aywak, 2006; Sheila Waa & S Vinayak, 2010). 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 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 MCA (Nguku et al., 2006).

Furthermore, fetal-maternal medicine is an emerging sub-speciality requiring close collaboration between obstetricians, radiologists and neonatologists in the management of high risk pregnancies. The radiologist therefore plays a key role in this management.

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.

This study aims to assess the significance of ultrasound in relation to perinatal outcomes and to assist in the development of guidelines for the management of preeclampsia. It will further assist in policy making decisions, resource and personnel allocation.

1.4 Research Questions

What is the comparison between use of Doppler findings of the umbilical and middle cerebral arteries and biophysical profile in the prediction of perinatal outcomes in patients with preeclampsia?

1.5 Objectives

1.5.1 Broad Objective

To determine Doppler findings of the umbilical and middle cerebral arteries and compare with biophysical profile scores in the prediction of perinatal outcomes in patients with preeclampsia at MTRH.

1.5.2 Specific Objectives

1. To describe the biophysical profiles and Doppler findings in the UA and MCA in patients with preeclampsia at MTRH.
2. To analyse the rate of agreement between Doppler findings and biophysical profile scores in patients with preeclampsia at MTRH.
3. To compare prediction of perinatal outcomes using biophysical profile and Doppler findings of the umbilical and middle cerebral arteries in patients with preeclampsia at MTRH.

CHAPTER TWO

LITERATURE REVIEW

2.1 Background

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 (Ikamari, 2013). 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 (WHO, 2015).

The WHO estimated the 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 births (WHO, 2015). Preeclampsia is second to hemorrhage as a cause of maternal mortality with an estimated 50,000-60,000 preeclampsia related deaths worldwide every year (Organization, 2005; WHO, 2015).

2.2 Preeclampsia

Preeclampsia is a disorder of widespread endothelial malformation and vasospasm occurring after 20 weeks gestation to as late as 4-6 weeks postpartum. It is clinically defined as hypertension (BP> 140/90), proteinuria with or without pathological edema (Laganà, Favilli, Triolo, Granese, & Gerli, 2015). According to the new guideline by American College of Obstetricians and Gynaecologists, diagnosis of preeclampsia no longer requires presence of proteinuria or edema for diagnosis (ACOG, 2015). 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 incidence of preeclampsia varies with location and ethnicity; in the United States it is estimated to be 2-6% in healthy nulliparous women while the global incidence ranges from 5-14% (Sibai, 2003). In developing countries the incidence is 4-18% and it is the second most common cause of still births and early neonatal deaths in these countries (Ngoc et al., 2006). In Sub-Saharan Africa it is one of the major causes of direct maternal death together with haemorrhage, infections, unsafe abortions and obstructed labour. In sub-Saharan Africa, hypertension in pregnancy accounts for 19% of maternal mortality, 15% of antenatal hospitalisations and 18% of fetal deaths (Lalthantluanga et al., 2015). There is concern that the incidence and prevalence of preeclampsia are rising in society with the increase in some of the known risk factors including teenage pregnancies, increased maternal age and BMI >30 (Hakim, Senterman, & Hakim, 2013). In developed countries the incidence has increased by upto 25% in the past two decades (Wallis, Saftlas, Hsia, & Atrash, 2008).

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 (Hakim et al., 2013). Furthermore, there is a 4-fold increase in cardiovascular and cerebrovascular disease in future (Davis et al., 2012). Fetuses affected suffer from IUGR, preterm delivery and its attendant complications and later increased risk of cardiovascular, cerebrovascular, cognitive, and psychiatric disorders (Hakim et al., 2013).

2.3 Risk Factors and Pathophysiology

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 (Obstetricians & Gynecologists, 2013). Some studies have also shown that there seems to be both a maternally and a paternally transmitted genetic predisposition to preeclampsia (Pipkin, 2001)

The mechanisms by which preeclampsia occurs is not certain, and numerous maternal, paternal, and fetal factors have been implicated in its development. The factors currently considered to be the most important include the following (Cunningham et al., 2010):

- Maternal immunologic intolerance
- Abnormal placental implantation
- Genetic, nutritional, and environmental factors
- Cardiovascular and inflammatory changes

The increased incidence of perinatal morbidity and mortality seen in pregnancies complicated by pre-eclampsia is primarily due to uteroplacental insufficiency resulting in a compromised blood flow to the fetus and the need for premature delivery. The primary adoptive response of the fetus to placental insufficiency is a decrease in growth. Persistent placental insufficiency will result in decreased fetal movement to conserve energy, hemodynamic redistribution to favor the oxygenation of critical organs such as the brain, heart, adrenal glands and attempt to improve the

efficiency of the placental gas exchange by increasing the heart rate and the synthesis of red cells. This is known as the brain sparing effect.

Progressive decompensation will lead to a metabolic and respiratory acidosis, increased impedance to fetoplacental circulation, renal insufficiency with decreased amniotic fluid volume; myocardial compromise, absent or reversed atrial flow in ductus venosus, late deceleration in the fetal heart rate (FHR) tracing and fetal death (CHAKRABORTY et al., 2013).

2.4 Diagnosis

Preeclampsia is defined as the presence of:

(1) A systolic blood pressure (SBP) greater than or equal to 140 mm Hg or a diastolic blood pressure (DBP) greater than or equal to 90 mm Hg or higher, on two occasions at least 4 hours apart in a previously normotensive patient,

OR

(2) A SBP greater than or equal to 160 mm Hg or a DBP greater than or equal to 110 mm Hg or higher (In this case, hypertension can be confirmed within minutes to facilitate timely antihypertensive therapy.)

Proteinuria of greater than or equal to 0.3 grams in a 24-hour urine specimen, a protein (mg/dL)/creatinine (mg/dL) ratio of 0.3 or higher, or a urine dipstick protein of 1+ (if a quantitative measurement is unavailable) is required to diagnose preeclampsia

Preeclampsia with severe features

- SBP of 160 mm Hg or higher or DBP of 110 mm Hg or higher, on two occasions at least 4 hours apart
- Impaired hepatic function-elevated liver enzymes or persistent epigastric/right upper quadrant pain
- Progressive renal insufficiency
- New onset visual or cerebral disturbances
- Pulmonary edema
- Thrombocytopenia
- HELLP syndrome-Haemolysis, Elevated Liver enzymes, Low platelets
- Eclampsia-seizures

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 (S. Waa & S. Vinayak, 2010). 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.

2.5 Ultrasound Findings

2.5.1 Intrauterine Growth Restriction (IUGR)

IUGR is defined as estimated fetal weight less than the 5^{th} or 10^{th} percentile of estimated gestational age. Preeclampsia has a two to four-fold increase in IUGR (Bujold et al., 2010; Srinivas et al., 2009). In a study by Nguku et al, Intrauterine Growth Restriction was shown to affect about 30% of preeclamptic pregnancies (Nguku et al., 2006).

IUGR results from placental insufficiency and has adverse perinatal complications including necrotizing enterocolitis, respiratory distress syndrome, thrombocytopenia, temperature instability and renal failure. Complications of IUGR that last well into adulthood include metabolic syndrome, impaired kidney function, mental health problems and learning impairment. Specifically, Tideman found that impaired fetal circulation as demonstrated by Doppler studies in association with IUGR results in worsened cognitive function in adulthood (Tideman, Maršál, & Ley, 2007).

BPP scores and Doppler studies help to differentiate the constitutionally small fetus (SGA) from the pathologically small fetus and management based on these will reduce perinatal morbidity and mortality (Baschat, 2003).

2.5.2 Biophysical profile

A biophysical profile (BPP) is a prenatal ultrasound evaluation of fetal well-being involving a scoring system, with the score being termed Manning's score (Manning, Platt, & Sipos, 1980). Poor scores indicate fetal hypoxemia and acidosis. It combines ultrasound assessment and a Non-Stress Test done using a cardiotocograph.

Table 1.0: Biophysical Profile Scoring

Biophysical Variable	Normal (Score = 2)	Abnormal (Score = 0)
Fetal breathing movements	1 or more episodes of ≥20 s within 30 min	Absent or no episode of ≥20 s within 30 min
Gross body movements	2 or more discrete body/ limb movements within 30 min (episodes of active continuous movement considered as a single movement)	<2 episodes of body/limb movements within 30 min
Fetal tone	1 or more episodes of active extension with return to flexion of fetal limb(s) or trunk (opening and closing of hand considered normal tone)	Slow extension with return to partial flexion, movement of limb in full extension, absent fetal movement, or partially open fetal hand
Reactive FHR	2 or more episodes of acceleration of ≥15 bmp* and of >15 s associated with fetal movement within 20 min	1 or more episodes of acceleration of fetal heart rate or acceleration of <15 bmp within 20 min
Qualitative AFV	1 or more pockets of fluid measuring ≥2 cm in vertical axis	Either no pockets or largest pocket <2 cm in vertical axis

Each component is assigned 2 points, resulting in a score ranging from 0 to 10, with scores from 8 to 10 considered normal, 6 considered borderline/equivocal and below 6 considered problematic.

We only used ultrasound parameters for biophysical profile assessment in our study giving a total score of 8 with similar interpretation as outlined above.

The BPP is a reliable method of predicting fetal survival with a false negative mortality rate of 0.77/1000 tests. There is also an association between poor biophysical scores and fetal acidosis although the sensitivity is lower than that of doppler studies (B. H. Yoon et al., 1993). Fetal biophysiscal changes occur later than doppler changes and BPP scores < 6 are an indication for delivery. Several studies

have also demonstrated association between poor BPP scores and poor perinatal outcomes incuding low 5-minute APGAR score (Nisa, Hamid, Nasreen, & Khanum, 2014). Nguku in Nairobi found that the was no significant association between BPP score and severity of preeclampsia (Nguku et al., 2006)

A Cochrane review on BPP for fetal assessment in high-risk pregnancies (Lalor et al, 2008) concluded that there is currently insufficient evidence from randomized trials to support the use of BPP as a test of fetal wellbeing in high-risk pregnancies.

2.6 Doppler Ultrasound

The doppler effect was first described by an Austrian physicist, Christian Doppler in 1880 but doppler ultrasound has been in use since the 1950s. Doppler ultrasound velocimetry uses the Doppler principle to analyse the properties of the blood flow in a vessel of interest. This physical principle explains the observed change in wave frequency relative to the speed of a moving object. In case of Doppler ultrasound, the emitted ultrasound frequency will change when ultrasound beam encounters moving blood. The principle can be applied using different ultrasound modalities such as continuous-wave Doppler, pulsed-wave Doppler, colour and power Doppler wave. Colour doppler is used to map the vessels to be examined while spectral doppler provides a more detailed analysis and allows calculation of the various indices. In addition to these indices, the flow waveform may be described or categorized by the presence or absence of a particular feature, for example the absence of end-diastolic flow and the presence of a post-systolic notch.

Doppler ultrasound provides a noninvasive technique to asses both th uteroplacental and fetoplacental circulations.

2.7 Umbilical Artery Doppler

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 asses UA abnormalities include Systolic/Diastolic ratio, resistive index and pulastility index. These can be used interchanagably with similar predictive values for perinatal outcome (Trudinger, Giles, & Cook, 1985).

The 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 velocity (Montenegro et al., 1998).

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 (Kingdom, Burrell, & Kaufmann, 1997). Blood gases obtained at cordocentesis have shown that 80% of fetuses with absent diastolic flow are hypoxic and 46% are acidemic (B. Yoon, Syn, & Kim, 1992). 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 (Mone, McAuliffe, & Ong, 2015)

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 (Deka, 2013). Incorporation of Doppler studies into antenatal care of patients with preeclampsia improves fetal surveillance with timely intervention to improve both maternal and perinatal outcome.

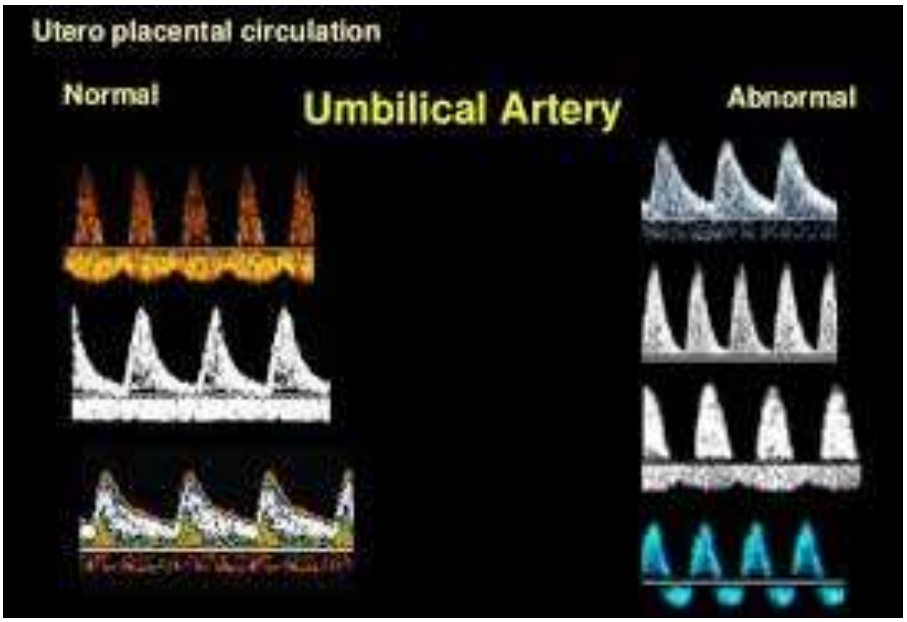


Figure 1.0: Normal and abnormal Umbilical Artery waveforms in each trimester

EDFV-end diastolic flow velocity

2.8 Middle cerebral artery Doppler

Doppler asesment of the fetal midddle cerebral artery (MCA) is an important part of asssessing 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 brainsparing 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 sign (Yakasai, Tabari, Rabiu, & Ismail, 2013).

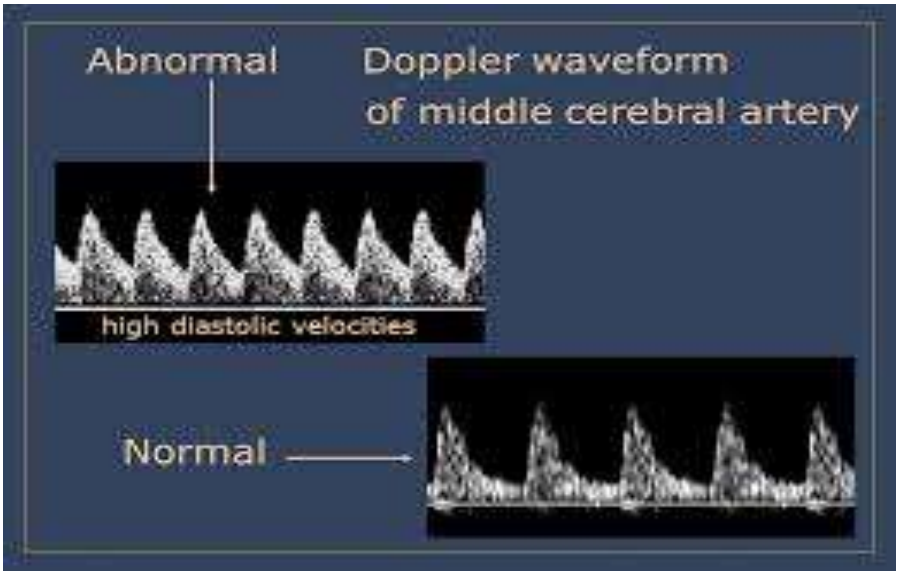


Fig 1.1 Middle cerebral artery waveforms

2.9 Cerebro-placental index (CPI)

Use of the umbilical artery or the middle cerebral arteries in isolation to predict perinatal outcome has lower sensitivities and positive predictive values (Yalti et al., 2004). For this reason many studies have been conducted on the use of CPI to predict perinatal outcome and it has been shown to be superior than individual vessels (DeVore, 2015). 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 age (Ebrashy, Ibrahim, Waly, Azmy, & Edris, 2005).

Apgar scoring

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 10 (Ogba, 2015).

The five criteria are summarized using words chosen to form an acronym (**A**ppearance, **P**ulse, **G**rimace, **A**ctivity, **R**espiration).

	Score of 0	**Score of 1**	**Score of 2**	**Component of acronym**
Complexion	blue or pale all over	blue at extremities body pink (acrocyanosis)	no cyanosis body and extremities pink	**A**ppearance
Pulse rate	Absent	< 100 beats per minute	> 100 beats per minute	**P**ulse
Reflex irritability grimace	no response to stimulation	grimace on suction or aggressive stimulation	cry on stimulation	**G**rimace
Activity	None	some flexion	flexed arms and legs that resist extension	**A**ctivity
Respiratory effort	Absent	weak, irregular, gasping	strong, lusty cry	**R**espiration

Interpretation

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.

CHAPTER THREE

METHODOLOGY

3.1 Study Design

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.

3.2 Study Site

The study was conducted at the ultrasound room in the Radiology and Imaging department and the antenatal, labour and neonatal wards in the Riley Mother and Baby wing of Moi Teaching and Referral Hospital.

The Hospital is located in Eldoret town, which is 310 Kilometers Northwest of the Capital Nairobi. MTRH is a tertiary (level 6) health facility serving as a teaching hospital for Moi University School of Medicine, Public health and Dentistry. Others include Kenya Medical Training Center (KMTC), Eldoret and University of Eastern Africa Baraton School of Nursing. MTRH is also a training center for medical, clinical and nursing officer interns. It is the referral hospital for the Western part of Kenya and North rift and has a catchment population of approximately 13 million people.

The reproductive health department is in the Riley Mother and Baby hospital. This site is ideal for my study as it serves a large population with a high number of deliveries per year (13,252 in 2015). It also has high end radiological and obstetric facilities with more than 10 radiologists and upto 20 obstetricians thus providing standard healthcare.

3.3 Study Population

The study population included pregnant women with preeclampsia referred for ultrasound. Only patients who planned to deliver in RMBH were considered in this study to reduce loss to follow-up as postpartum results were also required. The study was conducted over a period of 12 months from 1st October, 2016 to 30th September 2017.

3.4 Eligibility Criteria

3.4.1Inclusion Criteria

1. Patients with a clinical diagnosis of preeclampsia made by residents or consultants in the reproductive health department.
2. Patients in their third trimester >28weeks of pregnancy.
3. Patients who consented to the study.

3.4.2 Exclusion Criteria

1. Patients with multiple gestation.
2. Fetal congenital malformations e.g neural tube defects, cardiac malformations, fetal hydrops.
3. Patients in labor.
4. Patients who declined to give consent.

3.5 Sampling Techniques

3.5.1 Sample size.

The main objective of the study is to compare Doppler ultrasound with Biophysical profile among pregnant mothers with preeclampsia who are attending MTRH for delivery. That is, the study is seeking to establish the level of agreement of the two methods in the diagnosis of the likelihood of a bad perinatal outcome. A study

conducted in India showed that both Doppler ultrasound and Biophysical profile were able to correctly classify 6% and 68% of the subjects as likely to have normal and abnormal perinatal outcomes respectively (Laxmi & Kotha, 2015). This gives an absolute level of agreement for the two diagnostic methods as 74%. For our sample size estimation we shall round this off to 70% and determine the sample size that will be sufficient to detect this rate. Thus in order to be 95% confident with 80% power that we shall be able to demonstrate a 70% agreement within plus or minus 10% we determine the required sample size using the following formula (Hulley et al, 2007).

$$n = \left(\frac{Z_{1-\alpha/2} + Z_{\beta}}{d} \right)^2 \times P_0(1-P_0)$$

$$= \left(\frac{Z_{1-0.05/2} + Z_{0.8}}{0.10} \right)^2 \times 0.7(1-0.7)$$

$$= \left(\frac{1.96+0.84}{0.10} \right)^2 \times 0.7(1-0.7)$$

$$=165$$

Where P_0 is the anticipated rate of agreement between the two diagnostic methods, and d is effect size, $\beta - Type\ II\ error, Power = 1-\beta,\ \alpha - Type\ I\ error.$

We estimated the sample size assuming the smallest possible effect size based on the likelihood of the two diagnostic methods to disagree. That is, if the women present at an early stage the biophysical profile would fail to capture any abnormality hence disagreeing with the Doppler ultrasound that is known to be highly effective at an early stage of the condition. Therefore our effect size is this anticipated rate that is likely to cause the agreement rate to be different from 70%.

3.5.2 Sampling method

Consecutive sampling was used in this study. This was settled on due to the frequent interruptions by industrial action during the study period. Furthermore, some studies have suggested seasonal variation in the frequency of preeclampsia in the tropics being more common in the colder months (Melo, Amorim, Katz, Coutinho, & Figueiroa, 2014). Therefore, randomized sampling would not have achieved the target sample size.

Patients diagnosed with preeclampsia were referred for ultrasound from the antenatal clinic or antenatal ward. The first patient with preeclampsia referred for ultrasound on the day the study began (30th October, 2016) was the first one to be enrolled into the study. Patients who met the criteria and consented to the study were consecutively enrolled until the desired sample size was reached.

3.5.3 Study procedure

Reproductive health consultants and residents were sensitized prior to the study and requested to refer patients with preeclampsia for ultrasound. All nurses in RMBH are 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.

Consent was sought to do the ultrasound from all potential study participants referred for ultrasound. Informed consent and assent was then sought from patients who met the eligibility criteria who were then enrolled into the study. A semi-structured questionnaire was then administered by the principal investigator and/or a trained research assistant (sonographer) and postnatal information gotten from patient records.

The obstetric ultrasound and Doppler was conducted by the principal investigator or a trained sonographer. The sonographer was well trained in doing Doppler ultrasound of the UA and MCA, accurate biophysical profile scoring and archiving of images.

This was done using a real time scanner with the trans-abdominal approach. 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 is applied to the abdomen then a standard third trimester obsteric ultrasound with biophysical profile and doppler studies of the UA and MCA conducted. Details of the ultrasound protocols are in the appendix. Doppler protocols were adopted from the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines of 2013 (Bhide et al., 2013). Biophysical profile was conducted as initially described by Manning and colleagues in 1980 excluding the NST and a score given out of 8 (Manning, Platt, & Sipos, 1980).

The following ultrasound findings were considered abnormal:

- BPP ≤ 6 (Manning et al., 1980)
- UA RI ≥ 0.71 (S. Waa & S. Vinayak, 2010)
- UA S/D ratio > 3 (Lalthantluanga et al., 2015)
- Absent or reversed end diastolic velocity.
- MCA RI ≤ 0.71 (S. Waa & S. Vinayak, 2010)
- CPI < 1 (Lalthantluanga et al., 2015)

Categorical cut-offs for the doppler indices were used in this study as studies have shown that there is no significant difference between using age specific reference

levels and categorical cut-offs in doppler indices (Odibo, Riddick, Pare, Stamilio, & Macones, 2005)

The images were archived and later reviewed by the principal investigator and two consultant radiologists and a consensus of the findings recorded. The patients were given a hard copy of their results.

For patients who had more than 1 ultrasound study done during the study period the last ultrasound findings before delivery were considered for analysis. The final ultrasound was selected as this provided the status of the fetus just before delivery and would thus correlate better with postnatal findings.

Delivery was awaited and postnatal outcomes documented from patient files by the principal investigator. 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:

- Preterm delivery <37 weeks.
- Caesarean section for non-reassuring fetal status (NRFS).
- Still birth/IUFD.
- Low birth weight <2500gm.
- APGAR score ≤ 7 at 5 minutes.

These outcomes were documented from patient files on a standard data collection form. All information was kept confidential in a secure cabinet by the principal investigator.

3.6 Data Collection and Management

3.6.1 Data Collection

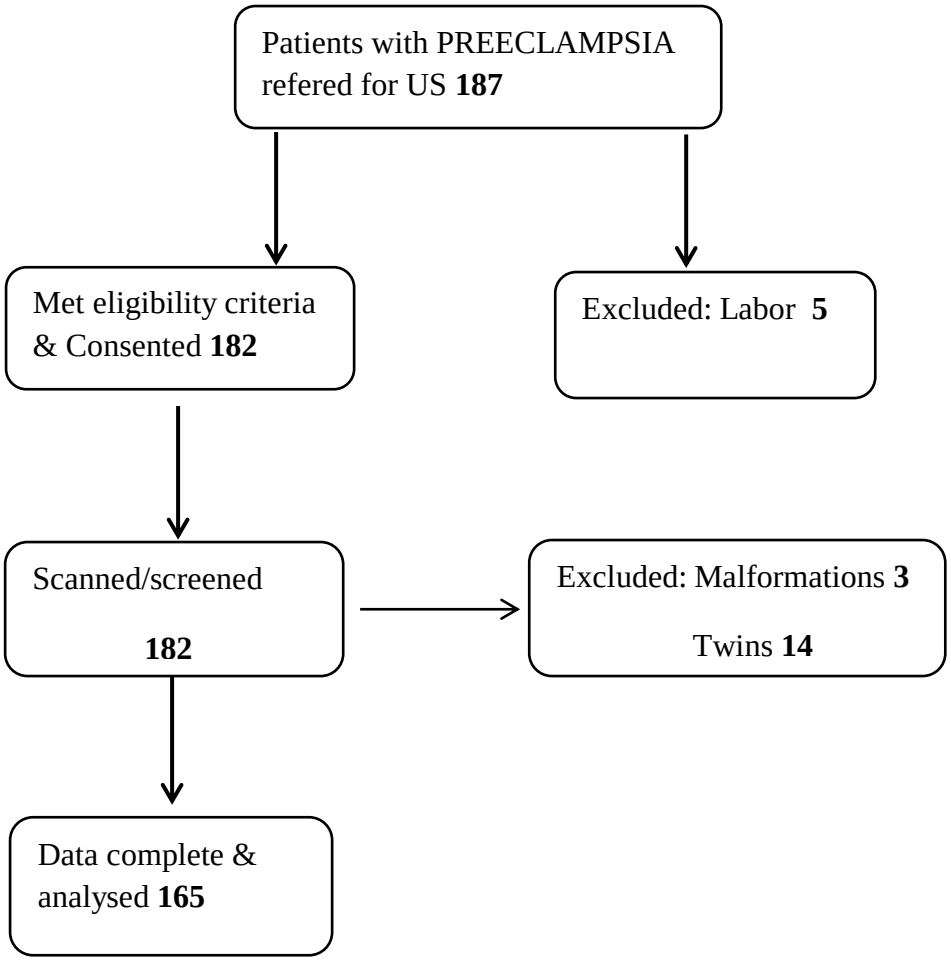
Data was collected between 1st October, 2016 and 30th September, 2017 using a structured questionnaire. The gathered data was de-identified and entered into an electronic database.

The database was encrypted to ensure confidentiality of the data, and the password was made available to the principal investigator and statistician alone. The data was backed-up to cushion against loss. Once the raw data was completely converted into the electronic database, the questionnaires were kept in a safe cabinet under lock and key, and access allowed to the principal investigator alone. They will be shredded after five years. Patients have a copy of their results and have autonomy over who else it can be disclosed to. Serial numbers were used in the digital data in order to protect patients' identity.

3.6.2 Quality Control

The ultrasound was conducted at the MTRH ultrasound unit using the same machine and following the standard protocol. The images were then reviewed by the principal investigator and two consultant radiologists and a consensus of the findings recorded. Information on outcomes was sought from the patients' files. Quality of the post natal data is ensured from the pre-study sensitization, countinous training of nurses in the repoductive health department and good record keeping. Weighing scales in the reproductive health department are regularly calibrated to ensure accuracy.

1.7 Study Recruitment Schema



1.8 Data Analysis and Presentation

Data was imported into STATA/MP version 13, where coding, cleaning and analysis was done.

Descriptive statistics was done to explore and summarize the variables; for categorical variables such as marital status, education level, obstetric history; frequencies and proportions were reported in tables. For numeric variabes (continuous/discrete) such as age, measures of central tendency (mean/median) and dispersion (standard

deviations/IQR) were computed and presented in tables for variables. Histograms were used to present the distribution pictoricaly.

Bivariate analysis (Chi Square test/Fisher's Exact test/Unadjusted logistic regression) was done to determine associations between BPP and doppler findings with perinatal outcomes. The test statistic was chosen based on type and distribution of data. Total raw agreement between BPP and doppler findings was calculated. At multivariable level, multiple logistic regression was done. All statistical tests were done at α level of significance of 0.05 and test statistics and corresponding p-values reported.

3.8.1 Study Limitations

- Lack of control over the events occuring during labor and delivery which could have also affected post natal outcomes.
- Selecion bias is another limitation as only patients reffered for ultrasound were included into the study.

3.9 Ethical considerations

- Ethical approval to carry out the study was sought and granted from the Institutional Research and Ethics Committee (IREC).
- Permision to conduct the study at MTRH was sought and granted from the CEO of Moi Teaching and Referral Hospital.
- All patients/guardians were informed about the study and the procedures involved in the study and the possible benefits and harm to them and that the procedure is generally safe with no potential risks.
- A consent form was used to seek informed consent from potential study participants. Informed consent to participate in the study was obtained from all

adult patients, while assent was obtained from minors (less than 18 years) and the consent form signed by their parents or guardians.

- Interviews and examination of patients was done in a confidential room.
- All patients received medical attention as necessary regardless of their willingness/unwillingness to participate in the study. Participation in the study was on a voluntary basis, the participants were at liberty to withdraw from the study at any stage without being penalized. No incentives or inducements were used to convince patients to participate in the study.
- Patients were informed of their results and appropriate standard treatment given. Confidentiality was maintained throughout the study.
- The data collection forms used were kept confidential and access limited to the principal investigator and biostatistician only. Data collection tools were kept in a locked cabinet during the study period.
- The results of the research will be presented to the Moi University, School of Medicine and the Hospital's management. It will also be availed to radiology & imaging and reproductive health departments for use as necessary. It will be available for academic reference in the College of Health Sciences Resource Centre. The results of this research shall be published in a reputable journal of medicine for use by the wider population in the general improvement of patient management and as a reference for future studies.

CHAPTER FOUR

FINDINGS

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 as depicted in the table below.

Table 4.0: Demographic characteristics

Variable	Category	Frequency	Percentage
**Age	29(SD 6.3)	Min 15	Max 42
Marital status	Single	27	16.36
	Married	138	83.64
Education level	Primary	11	13.33
	Secondary	104	63.03
	Tertiary	39	23.64

*** Variable summary reported in Mean (SD) and minimum and maximum*

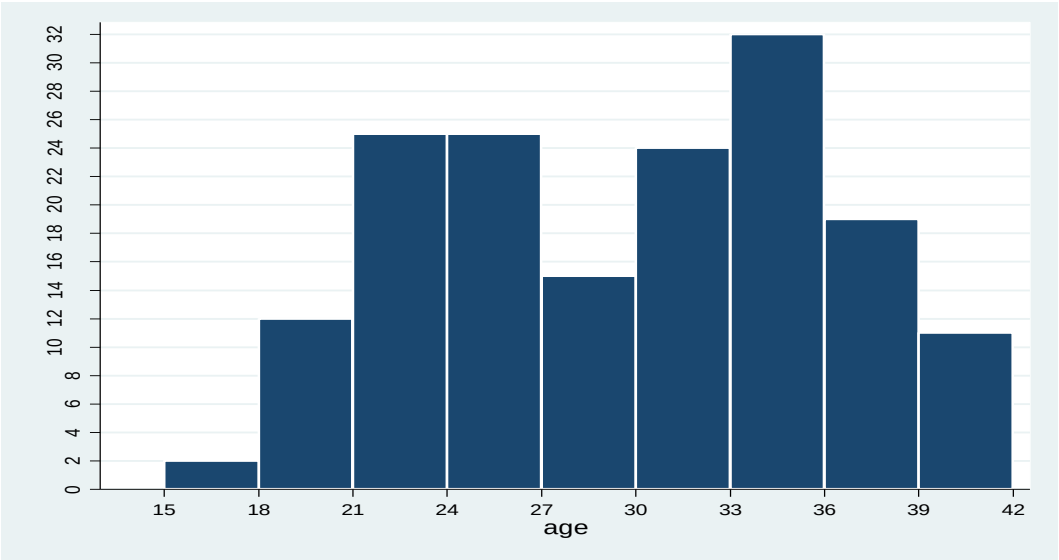


Figure 4.0: Age distribution

Obstetric history

Majority of the patients were multiparous 57.58% with 7.8% being grand multiparous. Majority (61%) had personal previous history of hypertension in pregnancy. The rest of the obstetric history is summarized in the table below.

Table 4.1: Obstetric history

Variable	Category	Frequency	Percent
Parity	0	57	34.55
	1-4	95	57.58
	>4	13	7.88
Personal history of hypertension in pregnancy	No	64	38.79
	Yes	101	61.21
Family history of hypertension in pregnancy	No	137	83.03
	Yes	28	16.97
History of caesarian delivery	No	116	70.3
	Yes	49	29.7
History of preterm delivery	No	106	64.24
	Yes	59	35.76
History of miscarriage	No	100	60.61
	Yes	65	39.39

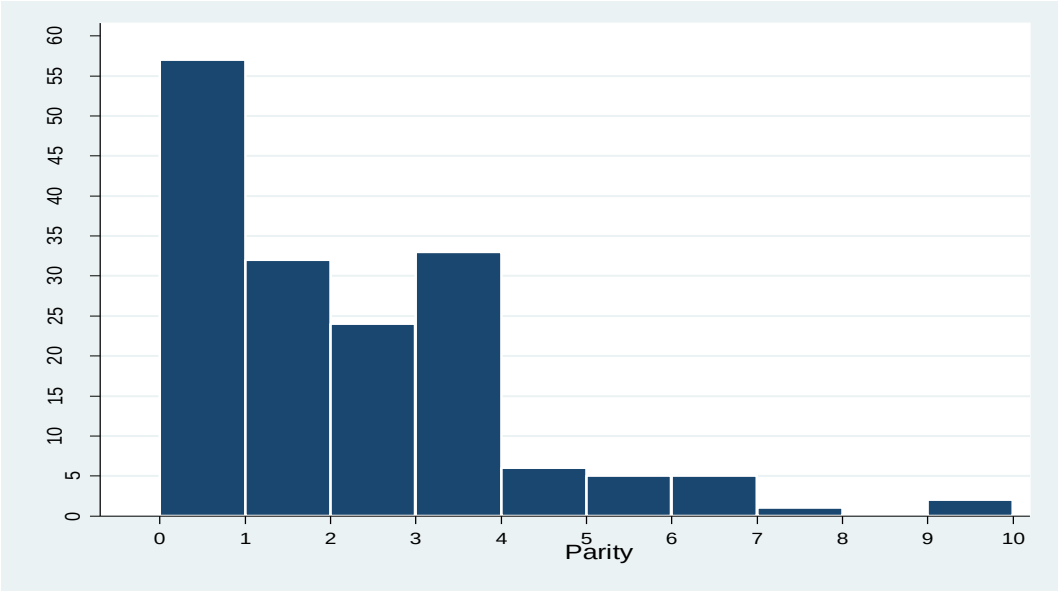


Figure 4.1: Parity

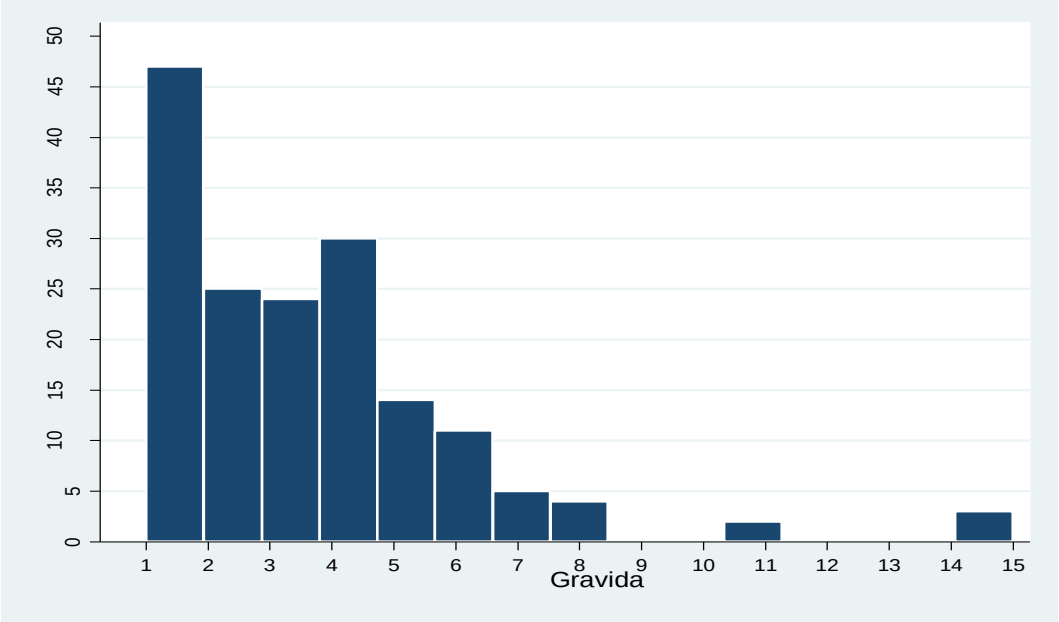


Figure 4.2: Gravidity

Table 4.2: Current pregnancy

Variable	Category	Frequency	Percent
GBD at contact	28-34 weeks (Early onset)	120	72.73
	>34-37 weeks (Late onset)	24	14.55
	>37 weeks	21	12.73
Pre-eclampsia	Mild	56	33.94
	Severe	109	66.06

The Gestation by Dates (GBD) based on last normal menstrual period ranged between 28 and 42 weeks with a mean of 32.36 (SD 3.6) weeks.

Majority (72.73%) had early-onset preeclampsia presenting before 34 weeks gestation and 66.06% of the patients had preeclampsia with severe features.

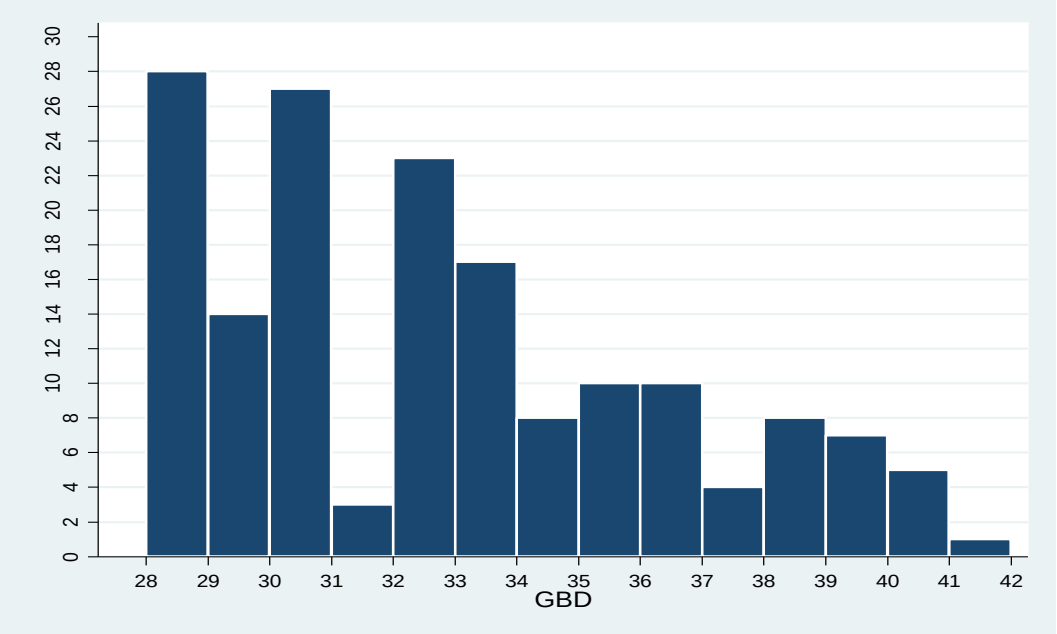


Figure 4.3: Gestation by dates (GBD)

Table 4.3: Ultrasound findings

Variable	Category	Frequency	Percent
Gestation by Ultrasound	<28 weeks	28	16.97
	28-34 weeks	99	60.00
	35-37 weeks	24	14.55
	>37 weeks	14	8.48
IUGR	No	115	69.70
	Yes	50	30.30
Oligohydramnios	No	131	79.39
	Yes	34	20.61
US BPP	Normal	98	59.39
	Abnormal	67	40.61

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 and 40.61% had abnormal BPP.

Table 4.4 Abnormal BPP parameters

Variable	Category	Frequency	Percent
Amniotic fluid index	Normal	131	79.39
	Abnormal	34	20.61
Fetal breathing	Normal	149	90.3
	Abnormal	16	9.70
Fetal tone	Normal	106	64.24
	Abnormal	59	35.76
Fetal heart rate	Normal	158	95.76
	Abnormal	7	4.24

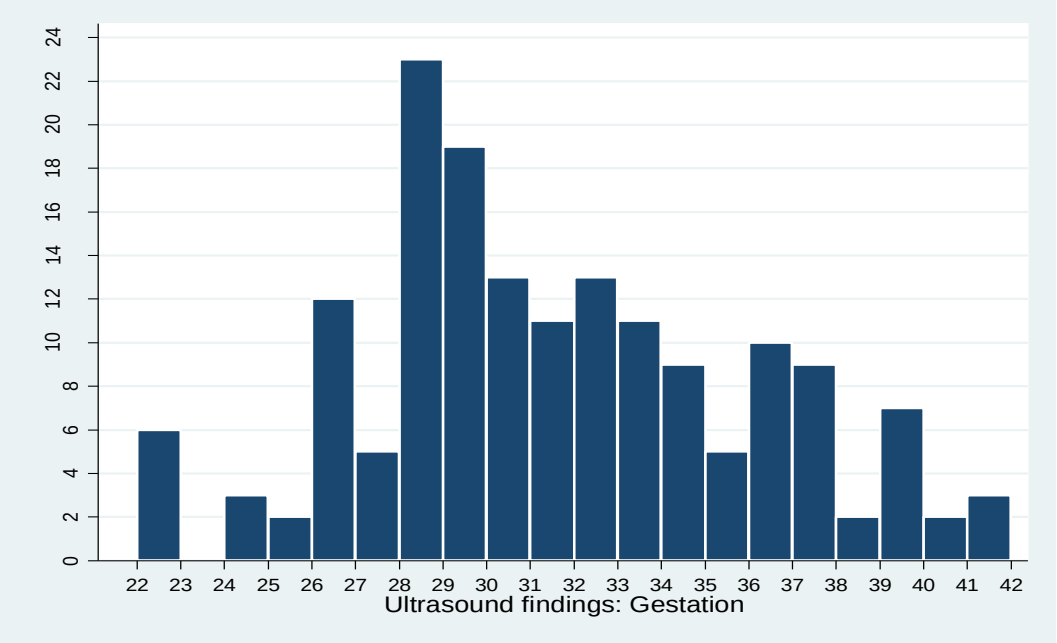


Figure 4.4: Gestation by ultrasound

Table 4.5: 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 4.6: 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
	IUFD	33	20.0
Delivery mode	SVD	82	62.12
	CS	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 Summary	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 4.7: Association between BPP and Doppler findings

BPP total scores	Doppler findings		Total
	Normal	Abnormal	
Normal	**35**	63	98
Abnormal	0	**67**	67
Total	35	129	**165**

$$raw\ agreement = \frac{35 + 67}{165}$$

=61.81

Out of 67 patients who were found to have abnormal BPP none was found to have normal Doppler findings. Total row agreement between BPP and Doppler findings was 61.8%

Table 4.8: Association between BPP and pregnancy outcome

BPP total scores	Post natal outcome		Total
	Good n (%)	Poor n (%)	
Normal	43(43.88)	55(56.12)	98
Abnormal	9(13.43)	58(86.57)	67
Total	52	113	165

$\chi^2 = 16.656, p < 0.001$

There was a statistically significant association between BPP profile and overall pregnancy outcome (p<0.001), where majority (86.4%) who had abnormal BPP scores also were found to have abnormal overall pregnancy outcome, 56.1% of those had normal BPP ended up with overall abnormal pregnancy outcomes. Those with

abnormal BPP score were 4.9 times more likely to have poor post natal outcomes as compared to those with normal BPP (OR=4.95, p<0.001, 95% CI 2.20, 11.11)

Table 4.9: Association between Doppler findings and pregnancy outcome

	Post natal outcome		
Doppler findings	**Good n (%)**	**Poor n (%)**	**Total**
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 4.10: Association between combined BPP & Doppler findings and pregnancy outcome

	Post natal outcome		
Combined BPP & Doppler	**Good n (%)**	**Poor n (%)**	**Total**
Normal	26 (74.29)	9 (25.71)	35
Abnormal	26 (20)	104 (80)	130
Total	52	113	165

$\chi^2(1) = 37.651, p < 0.001$

There was a statistically significant association between combined BPP & Doppler findings and overall pregnancy outcome (p<0.001), where majority (80%) who had abnormal BPP scores also were found to have abnormal overall pregnancy outcome, 25.7% of those had normal BPP ended up with overall abnormal pregnancy outcomes.

Table 4.11: Association between BPP and specific post natal outcomes

Post natal outcome	Category	BPP total scores		P-value
		Normal	Abnormal	
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 demonstrates that there was a statistically significant association between abnormal BPP and poor perinatal outcomes in all the 5 categories.

Table 4.12: 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 4.13: 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 4.14: Association between reason for Caesarian Section and specific Doppler findings

Doppler findings	Category	Reason for CS n-50		P-value
		Others	Fetal distress	
UA-RI	Normal	17	11	0.019
	Abnormal	6	16	
SD-Ratio	Normal	13	6	0.013
	Abnormal	10	21	
MCA-RI	Normal	14	24	0.021
	Abnormal	9	3	
CPI	Normal	14	4	0.001
	Abnormal	9	23	
End diastolic flow	Normal	16	1	<0.001
	Abnormal	7	26	

All Doppler findings were significantly associated with caesarian section due to non-reassuring fetal status.

Table 4.15: 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.

Table 4.16: Association birth weight and specific Doppler findings

Doppler findings	Category	Birth weight		p-value
		Normal	Abnormal	
UA-RI	Normal	57	38	<0.001
	Abnormal	7	30	
SD-Ratio	Normal	36	29	0.118
	Abnormal	28	39	
MCA-RI	Normal	57	50	0.023
	Abnormal	7	18	
CPI	Normal	44	31	0.007
	Abnormal	20	37	
End diastolic flow	Normal	50	23	<0.001
	Abnormal	14	45	

There was no significant association between UA SD ratio and low birth weight (<2500gm).

Table 4.17: Association gestational age at delivery and specific Doppler findings

Doppler findings	Category	Gestational age at delivery			p-value
		Mean	SD	[95% CI]	
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.

SAMPLE IMAGES

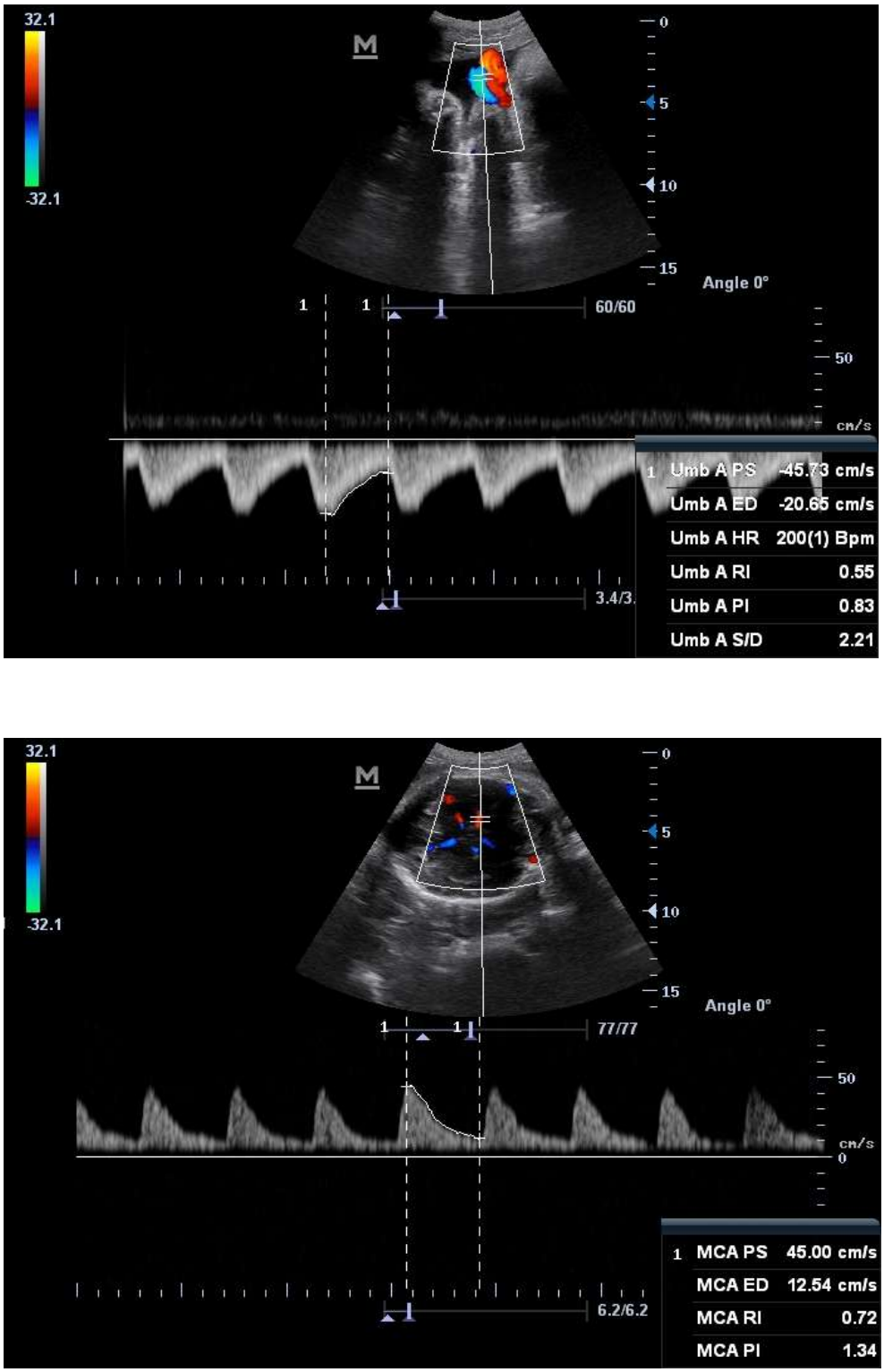


Figure 4.5: 27 year old with preeclampsia at 36 weeks gestation. Normal UA and MCA Doppler

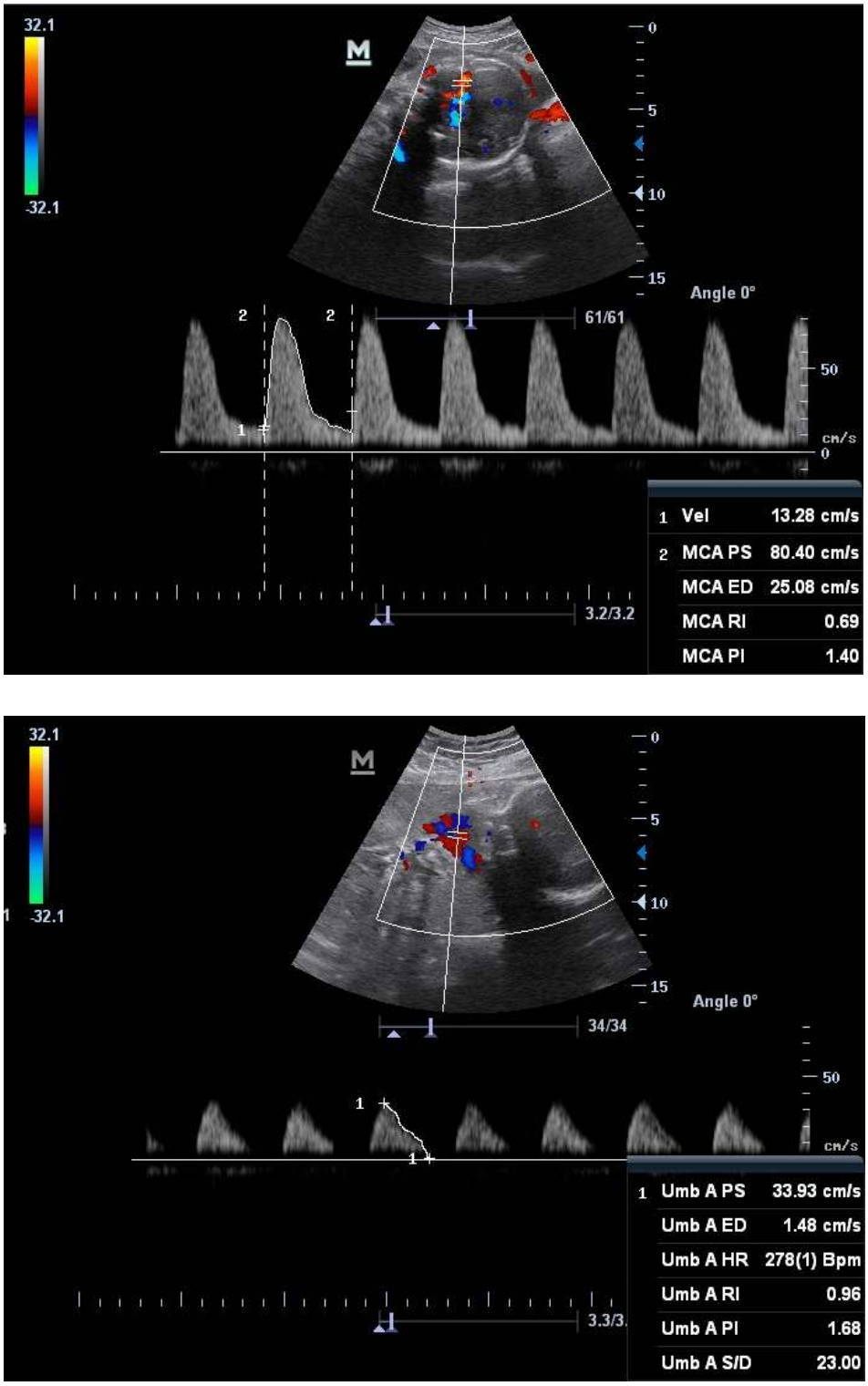


Figure 4.5: 34 year old with preeclampsia +severe features at 29 weeks. Absent EDV with brain sparing

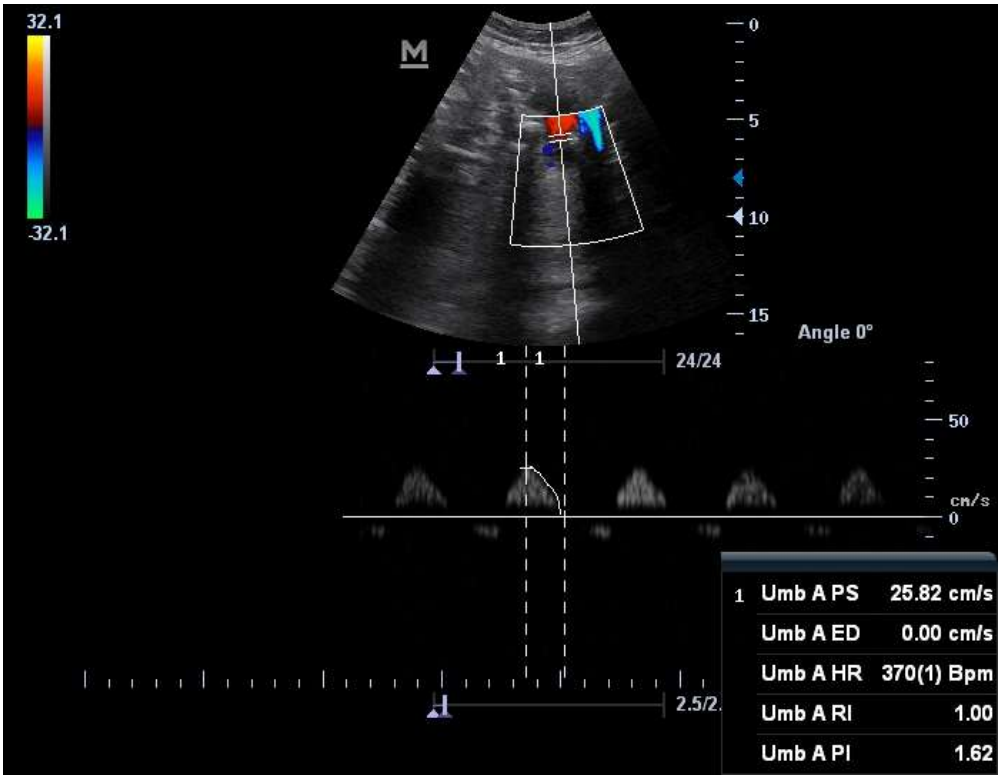


Figure 4.6: 31 year old with preeclampsia +severe features at 29 weeks. Reversed EDV. Had IUFD at 30 weeks.

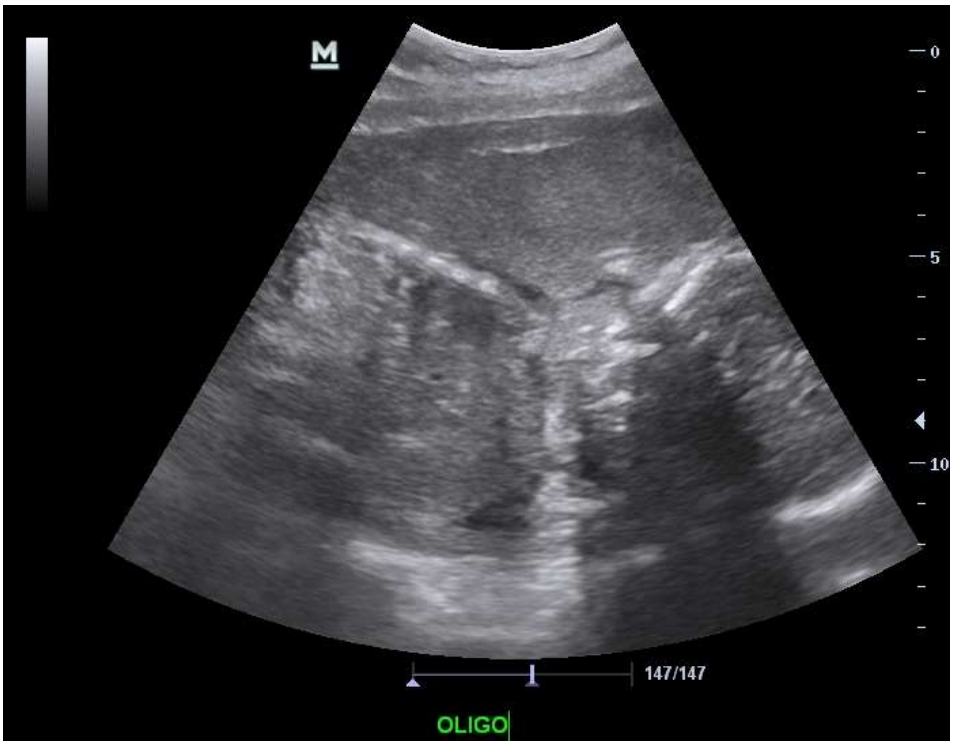


Figure 4.7: Severe Oligohydramnios in a 37year old with preeclampsia + severe features with IUGR

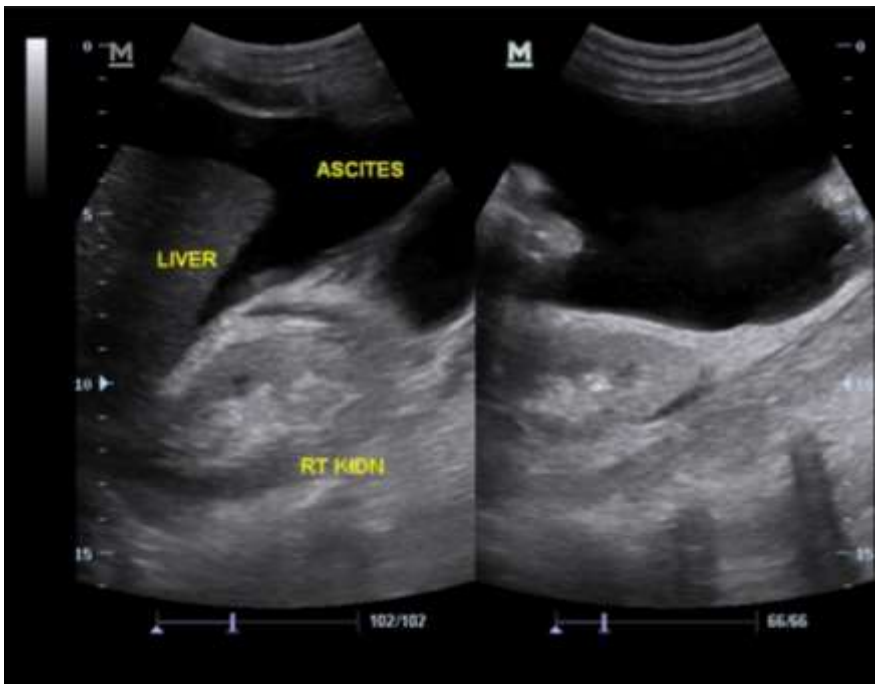


Figure 4.8: Severe maternal ascites in a patient with preeclampsia with severe features

CHAPTER FIVE

DISCUSSION

5.1 Introduction

The purpose of this study was to compare the predictability of perinatal outcomes using biophysical profile scores and fetal Doppler studies in patients with preeclampsia. 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 fetus is coping and guides clinical management.

5.2 Demographic Characteristics

The age of patients in this study ranged from 15-42 years which falls within the reproductive age-group of 12-49 as defined by the Farlex medical dictionary (Reproductive age. (n.d.) *Medical Dictionary*. (2009). Majority of the women were aged between 33-36 years which can be explained by increased education levels, increased contraceptive use and changing gender roles.

Majority were multiparous (65.46%) even though preeclampsia is 1.5-2 times more common in nulliparous women (Ananth, Keyes, & Wapner, 2013). This can be explained by the fact that most patients (61.21%) also reported previous history of preeclampsia and might have been nulliparous then.

Only 16% reported family history of hypertension in pregnancy and this is contrary to other studies which have shown up to 5 times increased risk of preeclampsia if there is family history (Ananth et al., 2013). Recall bias or lack of information or knowledge on family history could have contributed to this.

72.73% of the patients presented between 28-34 weeks gestation and are classified as having early onset preeclampsia. This is much higher compared to other studies which

have shown an incidence of 10% (Raymond & Peterson, 2011). 66.06% presented with preeclampsia with severe features. Other studies have shown preeclampsia with severe features to account for up to 25% of all cases (Sibai, 2003). The higher figures in our study can be explained by higher number of patients with early onset preeclampsia which is associated with severe features and the fact that this is a referral hospital.

5.3 Ultrasound Findings

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 due to IUGR.

Intrauterine Growth restriction 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 patients (Nguku et al., 2006). 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 preeclampsia (Srinivas et al., 2009). 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 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 output (Hakim et al., 2013)

Objective 1: Description of Biophysical profile and Doppler findings

Biophysical profile was found to be abnormal in 40.61% of the patients and this compares well with Laxmi et al (40%) and Mehr et al (31%) (Laxmi & Kotha, 2015; Nisa et al., 2014). 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.

The most common abnormal finding was fetal tone followed by AFI. Manning and colleagues in 1980 described that fetal tone is the first parameter to be impaired in case of neurological suppression (Manning et al., 1980). Amniotic Fluid Index was found to be the only parameter associated with disease chronicity/duration by Nguku in Nairobi (Nguku et al., 2006). Several studies have demonstrated an association between Oligohydramnios and adverse perinatal outcomes including fetal distress, IUGR, caesarean delivery, low APGAR scores and admission to NICU (Chauhan, Magann, Perry, & Morrison, 1997). However, a study by Voxman only found an association between oligohydramnios and abnormal fetal heart rate tracing but no other outcome measures (Voxman, Tran, & Wing, 2002).

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 (Komuhangi, Byanyima, Kiguli-Malwadde, & Nakisige, 2013). 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 (Devi et al., 2017).

Abnormal UA flow patterns was present in 54.88%; reduced (16.46%), absent (35.98%) and reversed (2.44%)

Of note is that all the 66 patients who had abnormal BPP also had abnormal Doppler findings. Laxmi found out of 40 patients who had abnormal BPP 34 of them had abnormal Doppler (Laxmi & Kotha, 2015). This further supports the fact that Doppler changes occur much earlier than BPP changes (Deka, 2013). Other studies have shown that BPP is associated with false positive results because of its subjective nature (B. Yoon et al., 1992).

Objective 2: Rate of agreement between BPP and Doppler findings

The row 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 (Laxmi & Kotha, 2015). 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 (B. H. Yoon et al., 1993). Nguku in Nairobi found a low agreement of 40.1% but this study only looked at one Doppler parameter, the umbilical artery resistive index.

Objective 3: Comparison of prediction of outcomes using BPP and Doppler

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 (Nisa et al., 2014; Payne et al., 2013; B. H. Yoon et al., 1993)

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 (Devi et al., 2017). 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 without (Ebrashy, Azmy, Ibrahim, Waly, & Edris, 2005). 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 ratio (Lalthantluanga et al., 2015).

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 preeclampsia (von Dadelszen et al., 2007). Moreover, poor postnatal outcomes are varied and cord blood pH is considered the most objective method of assessing post natal outcome (B. H. Yoon et al., 1993)

The biophysical profile was developed by Manning et al in 1980 and has been in use the longest with relatively good sensitivity but is subjective and takes time (Manning et al., 1980). Biophysical changes have also been shown to develop days to weeks after Doppler changes (Deka, 2013).

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)(Payne et al., 2013). Another study found BPP to be associated with poor outcomes wiht an odds ratio of 2.93 at 95% confidence interval (CI) = 1.2 - 7.3, *P* = 0.021)],(Lopez-Mendez et al., 2013).

Having an abnormal Doppler increased odds of having and 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)(Odibo et al., 2005). The higher odds in our study can be explained by the use of several Doppler parameters as opposed to using only one (CPI).

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1Conclusions

1. 40.6% of patients had abnormal biophysical profile (BPP) while 78.7% had abnormal Doppler findings with 51.1% having abnormal UA spectral flow patterns.
2. There was fair agreement between BPP and Doppler at 61.8%.
3. 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.

6.2Recommendations

1. 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.
2. Development of a management guideline incorporating both BPP and Doppler studies of UA and MCA in evaluation of patients with preeclampsia.
3. Futher study using both BPP and doppler to time delivery in preeclampsia and assess effect on outcomes.

REFERENCES

Alfirevic, Z., & Neilson, J. P. (1995). Doppler ultrasonography in high-risk pregnancies: systematic review with meta-analysis. *American journal of obstetrics and gynecology, 172*(5), 1379-1387.

Alfirevic, Z., Stampalija, T., & Gyte, G. (2010). Fetal and umbilical Doppler ultrasound in normal pregnancy. *Cochrane Database Syst Rev, 8*(8).

Ananth, C. V., Keyes, K. M., & Wapner, R. J. (2013). Pre-eclampsia rates in the United States, 1980-2010: age-period-cohort analysis. *Bmj, 347*, f6564.

Bangal, V. B., Giri, P. A., & Sali, B. M. (2011). Incidence of oligohydramnios during pregnancy and its effects on maternal and perinatal outcome. *Journal of Pharmaceutical and Biomedical Sciences (JPBMS), 12*(5), 1-4.

Baschat, A. (2003). Integrated fetal testing in growth restriction: combining multivessel Doppler and biophysical parameters. *Ultrasound in Obstetrics & Gynecology, 21*(1), 1-8.

Bhide, A., Acharya, G., Bilardo, C., Brezinka, C., Cafici, D., Hernandez-Andrade, E., . . . Lee, W. (2013). ISUOG practice guidelines: use of Doppler ultrasonography in obstetrics. *Ultrasound in obstetrics & gynecology: the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 41*(2), 233.

Bujold, E., Roberge, S., Lacasse, Y., Bureau, M., Audibert, F., Marcoux, S., . . . Giguère, Y. (2010). Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis. *Obstetrics & Gynecology, 116*(2, Part 1), 402-414.

CHAKRABORTY, B., MONDAL, T. K., BARMAN, S. C., RUDRA, B. P., SAHANA, R., & MONDAL, P. C. (2013). Evaluation of Perinatal Outcome by Antenatal CTG and Umbilical Artery Doppler in Pre-eclamptic Mothers. *Indian Journal of Clinical Practice, 24*(6).

Chauhan, S. P., Magann, E. F., Perry, J. K., & Morrison, J. C. (1997). Intrapartum amniotic fluid index and two-diameter pocket are poor predictors of adverse neonatal outcome. *Journal of perinatology: official journal of the California Perinatal Association, 17*(3), 221-224.

Chen, K., Chen, L., & Lee, Y. (2011). Exploring the relationship between preterm placental calcification and adverse maternal and fetal outcome. *Ultrasound in Obstetrics & Gynecology, 37*(3), 328-334.

Cunningham, F., Leveno, K., Bloom, S. L., Hauth, J., Rouse, D., & Spong, C. (2010). Pregnancy hypertension. *Williams obstetrics, 23*, 706-749.

Davis, E. F., Lazdam, M., Lewandowski, A. J., Worton, S. A., Kelly, B., Kenworthy, Y., . . . Sargent, I. (2012). Cardiovascular risk factors in children and young adults born to preeclamptic pregnancies: a systematic review. *Pediatrics*, peds. 2011-3093.

Deka, D. (2013). P02. 10: Comparison of umbilical artery Doppler velocimetry with biophysical profile in monitoring high risk pregnancies. *Ultrasound in Obstetrics & Gynecology*, *42*(s1), 117-117.

Devi, J., Kumar, D., Shukla, M., & Jain, P. (2017). Doppler interrogation of fetoplacental circulation in hypertensive disorder of pregnancy and their perinatal outcomes. *International Journal of Research in Medical Sciences*, *5*(6), 2687-2693.

DeVore, G. R. (2015). The importance of the cerebroplacental ratio in the evaluation of fetal well-being in SGA and AGA fetuses. *American Journal of Obstetrics & Gynecology*, *213*(1), 5-15.

Ebrashy, A., Azmy, O., Ibrahim, M., Waly, M., & Edris, A. (2005). Middle cerebral/umbilical artery resistance index ratio as sensitive parameter for fetal well-being and neonatal outcome in patients with preeclampsia: case-control study. *Croatian medical journal*, *46*(5).

Ebrashy, A., Ibrahim, M., Waly, M., Azmy, O., & Edris, A. (2005). Middle Cerebral/Umbllical Artery Resistance Index Ratio as Sensitive Parameter for Fetal Well-being and Neonatal Outcome in Patients with Preeclampsla: Case-control Study. *Croatian medical journal*, *46*(5), 821.

Gardosi, J. (2006). New definition of small for gestational age based on fetal growth potential. *Hormone Research in Paediatrics*, *65*(Suppl. 3), 15-18.

Grannum, P. A., Berkowitz, R. L., & Hobbins, J. C. (1979). The ultrasonic changes in the maturing placenta and their relation to fetal pulmonic maturity. *American journal of obstetrics and gynecology*, *133*(8), 915-922.

Hakim, J., Senterman, M. K., & Hakim, A. M. (2013). Preeclampsia is a biomarker for vascular disease in both mother and child: the need for a medical alert system. *International journal of pediatrics*, *2013*.

Ikamari, L. D. (2013). Regional variation in neonatal and post-neonatal mortality in Kenya. *Etude de la Population Africaine*, *27*(1).

Kingdom, J., Burrell, S., & Kaufmann, P. (1997). Pathology and clinical implications of abnormal umbilical artery Doppler waveforms. *Ultrasound in Obstetrics & Gynecology*, *9*(4), 271-286.

Komuhangi, P., Byanyima, R., Kiguli-Malwadde, E., & Nakisige, C. (2013). Umbilical artery doppler flow patterns in high-risk pregnancy and foetal outcome in Mulago hospital. *Case Reports in Clinical Medicine*, *2*(09), 554.

Laganà, A. S., Favilli, A., Triolo, O., Granese, R., & Gerli, S. (2015). Early serum markers of pre-eclampsia: are we stepping forward? *The Journal of Maternal-Fetal & Neonatal Medicine*, 1-5.

Lalthantluanga, C., Devi, N. R., Singh, N. J., Shugeta, N. D., Khuman, V., & Keishing, S. (2015). Study on role of obstetrical Doppler in pregnancies with hypertensive disorders of pregnancy. *Journal of Medical Society*, *29*(2), 79.

Laxmi, G., & Kotha, S. (2015). Comparison of Biophysical Profile and Doppler Ultrasound in Predicting the Perinatal Outcome in High Risk Pregnancies at or over 34 Weeks Gestation. *International Journal of Innovative Research and Development, 4*(10).

López-Jaramillo, P., Pradilla, L. P., Castillo, V. R., & Lahera, V. (2007). Socioeconomic pathology as a cause of regional differences in the prevalence of metabolic syndrome and pregnancy-induced hypertension. *Revista Española de Cardiología (English Edition), 60*(2), 168-178.

Lopez-Mendez, M. A., Martinez-Gaytan, V., Cortes-Flores, R., Ramos-Gonzalez, R. M., Ochoa-Torres, M. A., Garza-Veloz, I., . . . Martinez-Fierro, M. L. (2013). Doppler ultrasound evaluation in preeclampsia. *BMC research notes, 6*(1), 477.

Manning, F. A., Platt, L. D., & Sipos, L. (1980). Antepartum fetal evaluation: development of a fetal biophysical profile. *American journal of obstetrics and gynecology, 136*(6), 787-795.

Melo, B., Amorim, M., Katz, L., Coutinho, I., & Figueiroa, J. N. (2014). Hypertension, pregnancy and weather: is seasonality involved? *Revista da Associação Médica Brasileira, 60*(2), 105-110.

Mone, F., McAuliffe, F. M., & Ong, S. (2015). The clinical application of Doppler ultrasound in obstetrics. *The Obstetrician & Gynaecologist, 17*(1), 13-19.

Montenegro, N., Santos, F., Tavares, E., Matias, A., Barros, H., & Leite, L. s. P. (1998). Outcome of 88 pregnancies with absent or reversed end-diastolic blood flow (ARED flow) in the umbilical arteries. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 79*(1), 43-46.

Morris, R., Say, R., Robson, S., Kleijnen, J., & Khan, K. (2012). Systematic review and meta-analysis of middle cerebral artery Doppler to predict perinatal wellbeing. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 165*(2), 141-155.

Nabhan, A. F., & Abdelmoula, Y. A. (2009). Amniotic fluid index versus single deepest vertical pocket: a meta-analysis of randomized controlled trials. *International Journal of Gynecology & Obstetrics, 104*(3), 184-188.

Ngoc, N. T. N., Merialdi, M., Abdel-Aleem, H., Carroli, G., Purwar, M., Zavaleta, N., . . . Mathai, M. (2006). Causes of stillbirths and early neonatal deaths: data from 7993 pregnancies in six developing countries. *Bulletin of the World Health Organization, 84*(9), 699-705.

Nguku, S., Wanyoike-Gichuhi, J., & Aywak, A. (2006). Biophysical profile scores and resistance indices of the umbilical artery as seen in patients with pregnancy induced hypertension. *East African medical journal, 83*(3), 96.

Nisa, M. U., Hamid, N., Nasreen, F., & Khanum, F. (2014). Co-relation of biophysical profile with apgar score. *Cell, 92*, 321-9001662.

Obstetricians, A. C. o., & Gynecologists. (2013). Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' task force on hypertension in pregnancy. *Obstetrics and gynecology, 122*(5), 1122.

Odibo, A. O., Riddick, C., Pare, E., Stamilio, D. M., & Macones, G. A. (2005). Cerebroplacental Doppler ratio and adverse perinatal outcomes in intrauterine growth restriction: evaluating the impact of using gestational age–specific reference values. *Journal of ultrasound in medicine, 24*(9), 1223-1228.

Ogba, U. C. (2015). The Development of a Clinical Prediction Tool to Support Clinicians in the Assessment of the Risks of Fetal Asphyxia and Failure to Progress in Term Pregnancies.

Organization, W. H. (2005). *The World Health Report 2005: Make every mother and child count*: World Health Organization.

Osungbade, K. O., & Ige, O. K. (2011). Public health perspectives of preeclampsia in developing countries: implication for health system strengthening. *Journal of pregnancy, 2011*.

Ota, E., Ganchimeg, T., Mori, R., & Souza, J. P. (2014). Risk factors of pre-eclampsia/eclampsia and its adverse outcomes in low-and middle-income countries: a WHO secondary analysis. *PloS one, 9*(3), e91198.

Otieno, d. A. N. (2012). Factors contibuting to adverse outcomes of pre-eclampsia among pregnant women attending antenatal clinics in kibera slums, nairobi.

Payne, B. A., Kyle, P. M., Lim, K., Lisonkova, S., Magee, L. A., Pullar, B., . . . von Dadelszen, P. (2013). An assessment of predictive value of the biophysical profile in women with preeclampsia using data from the fullPIERS database. *Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health, 3*(3), 166-171.

Pipkin, F. B. (2001). Risk factors for preeclampsia: Mass Medical Soc.

Raymond, D., & Peterson, E. (2011). A critical review of early-onset and late-onset preeclampsia. *Obstetrical & gynecological survey, 66*(8), 497-506.

Say, L., Chou, D., Gemmill, A., Tunçalp, Ö., Moller, A.-B., Daniels, J., . . . Alkema, L. (2014). Global causes of maternal death: a WHO systematic analysis. *The Lancet Global Health, 2*(6), e323-e333.

Sibai, B. M. (2003). Diagnosis and management of gestational hypertension and preeclampsia. *Obstetrics and gynecology, 102*(1), 181-192.

Srinivas, S., Edlow, A., Neff, P., Sammel, M., Andrela, C., & Elovitz, M. (2009). Rethinking IUGR in preeclampsia: dependent or independent of maternal hypertension? *Journal of Perinatology, 29*(10), 680.

Tideman, E., Maršál, K., & Ley, D. (2007). Cognitive function in young adults following intrauterine growth restriction with abnormal fetal aortic blood flow. *Ultrasound in Obstetrics & Gynecology, 29*(6), 614-618.

Trudinger, B. J., Giles, W. B., & Cook, C. M. (1985). Flow velocity waveforms in the maternal uteroplacental and fetal umbilical placental circulations. *American journal of obstetrics and gynecology, 152*(2), 155-163.

Villar, J., Betran, A., & Gulmezoglu, M. (2001). Epidemiological basis for the planning of maternal health services. *WHO/RHR, 111*, 298-202.

von Dadelszen, P., Menzies, J., Gilgoff, S., Xie, F., Douglas, M. J., Sawchuck, D., & Magee, L. A. (2007). Evidence-based management for preeclampsia. *Front Biosci, 12*(5), 2876-2889.

Voxman, E. G., Tran, S., & Wing, D. A. (2002). Low amniotic fluid index as a predictor of adverse perinatal outcome. *Journal of Perinatology, 22*(4), 282.

Waa, S., & Vinayak, S. (2010). Comparision of doppler studies in obstetrics with foetal outcome. *East African medical journal, 87*(12), 502-508.

Waa, S., & Vinayak, S. (2010). Comparison of Doppler studies in obstetrics with foetal outcome. *East Afr Med J, 87*(12), 502-508.

Wallis, A. B., Saftlas, A. F., Hsia, J., & Atrash, H. K. (2008). Secular trends in the rates of preeclampsia, eclampsia, and gestational hypertension, United States, 1987–2004. *American journal of hypertension, 21*(5), 521-526.

Walsh, J. A., Feifer, C. M., Measham, A. R., & Gertler, P. J. (1993). Maternal and perinatal health.

WHO, U. (2015). Trends in Maternal Mortality: 1990 to 2015. Estimates by WHO, UNICEF: UNFPA, the World Bank and the United Nations Population Division.

Yakasai, I. A., Tabari, M. A., Rabiu, A., & Ismail, A. M. (2013). Pattern of fetal arterial blood flow in selected vessels in patients with pregnancy induced hypertension in Aminu Kano Teaching Hospital Kano, Nigeria. *West African Journal of Radiology, 20*(1), 9.

Yalti, S., Oral, Ö., Gürbüz, B., Özden, S., & Atar, F. (2004). Ratio of middle cerebral to umbilical artery blood velocity in preeclamptic & hypertensive women in the prediction of poor perinatal outcome. *Indian Journal of Medical Research, 120*(1), 44.

Yoon, B., Syn, H., & Kim, S. W. (1992). The efficacy of Doppler umbilical artery velocimetry in identifying fetal acidosis. A comparison with fetal biophysical profile. *Journal of ultrasound in medicine, 11*(1), 1-6.

Yoon, B. H., Romero, R., Roh, C. R., Kim, S. H., Ager, J. W., Syn, H. C., . . . Kim, S. W. (1993). Relationship between the fetal biophysical profile score, umbilical artery Doppler velocimetry, and fetal blood acid-base status determined by cordocentesis. *American journal of obstetrics and gynecology, 169*(6), 1586-1594.

APPENDICES

APPENDIX I: CONSENT FORM

English Version

Investigator: My name is Dr. Mbarak Chebet Nuru. I am a qualified doctor, registered with the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a Masters degree in Radiology and Imaging at Moi University. I would like to request you to participate in my research which is to study the use of ultrasound findings to predict perinatal outcome in patients with preeclampsia at Moi teaching and referral hospital.

Purpose: This study will seek to describe the ultrasound findings in pregnancies complicated by preeclampsia and their outcomes in MTRH.

Procedure: Women presenting with preeclampsia will be recruited into the study after consent is sought. They will undergo an obstetric ultrasound, proper history taking and physical examination. Data collection will be done by interviewing and filing of questionnaires. Data collecting material will be kept in a locked cabinet in the office of the principal investigator during the study period.

Benefits: There will be no direct benefits of participating in this study. Study subjects will be accorded same quality of management as non-study subjects. This study is aimed at improving management of preeclampsia.

Risks: There are no anticipated risks to the participants attributable to this study.

Confidentiality: All information obtained in this study will be treated with utmost confidentiality and shall not be divulged to any unauthorized person

Rights to Refuse: Participation in this study is voluntary, there is freedom to refuse to take part or withdraw at any time. This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

Sign or make a mark if you agree to take part in the study

Patient: …… Investigator: …….. Date…….

(For patients under 18 years)

Name of Guardian/ Parent giving consent……

Signature/*Sahihi*…….. Or/*Ama* Thumb print *(Left)/Alama ya kidole*

Gumba (kushoto)

Date/*Tarehe*……

Name of the person taking consent……

(Jina la anayetoa idhini

Signature/*Sahihi* …..**.....** Date/*Tarehe* ……

Swahili Version

Mpelelezi: Jina langu ni Dr Mbarak Chebet Nuru. Mimi ni daktari aliyehitimu na kusajiliwa na bodi ya Kenya ya Madaktari na Madaktari wa meno. Mimi sasa natafuta shahada ya uzamili katika Radiology na Imaging katika Chuo Kikuu cha Moi. Ningependakukusajili katika utafiti wangu ambao ni wa kujifunza majibu ya ultrasound ambayo yanaweza kutabiri matokeo ya ujauzito wenye hatari kwa sababu ya presha ya damu katika hospitali ya mafundisho na ya rufaa ya Moi.

Kusudi: Utafiti huu itajaribu kueleza uhusiano wa picha ya ultrasound na matokeo ya ujauzito wenye hatari kwa sababu ya presha ya damu.

Utaratibu: Wamama wenye shida ya ujauzito wenye hatari hii wataelezwa na kuombwa wafanyiwe uchunguzi na baadaye utafiti. Picha ya ultrasound itafanywa, historia na physical examination pia. Baada ya shida hii kujulikana kikamilifu daktari wa wamama atamwona na kufuatiliwa hadi kujifungua na matokeo yao kuandikwa .

Data zitakusanywa kwenye fomu za ukusanyaji data. Hifadhi zitakazo tumika katika ukusanyaji wa data zitawekwa katika kabati iliyofungwa katika nyumba ya mpelelezi mkuu katika kipindi cha utafiti.

Faida: Kutakuwa hakuna faida moja kwa moja ya kushiriki katika utafiti huu. Wanaofanyiwa utafiti watakuwa nahaki nakupewa ubora sawa na wale ambao hawatofanyiwa utafiti huo.

Hatari: Hakuna hatari kwa washiriki kutokana na utafiti huu.

Usiri: Habari zote zilizopatikana katika utafiti huu wa kutibiwa zitawekwa kwa usiri mkubwa na wala haitaolewa kwa mtu yeyote asiye husika na utafiti.

Haki ya kukataa: Kushiriki katika utafiti huu ni hiari yako, kuna uhuru wa kukataa kushiriki au kutoka wakati wowote. Utafiti huu imepitishwa na Utafiti wa Taasisi na Kamati ya Maadili (IREC) ya Chuo Kikuu cha Moi na Hospitali ya Rufaa ya Moi.

Kusaini au kufanya alama kama unakubali kushiriki katika utafiti

Mgonjwa: ..... Mpelelezi: .....

Tarehe: .....

Walio chini ya Miaka 18

Jina la Mzazi au mlezi

Sahihi ……Tarehe…….

Jina la anayechukua idhini

Sahihi ….....Tarehe ……

APPENDIX II :DATA COLLECTION TOOL

DEMOGRAPHICS

Date: ……. Serial Number

Age: ……

County of residence..... County of birth.....

LMP: …….. Parity…… Last delivery.....

Marital status: single ☐ married ☐ divorced ☐ widowed ☐

level of education

primary ☐

secondary ☐

tertiary ☐

Obstetric history

Personal history of hypertension in pregnancy? Yes ..... No.....

Family history of hypertension in pregnancy? Yes..... No.....

Is there any history of caeserian delivery? Yes…… No……..

History of preterm delivery?yes..... No.....

Have you ever had an abortion? Yes……..No…….

Current pregnancy

LNMP..... EDD..... GBD.....

ANC PROFILE: HB VDRL HIV U/A

BP FUNDAL HEIGHT FETAL HEART RATE

ULTRASOUND FINDINGS

Gestation by US
EFW
Placenta

Normal ☐

Grade I ☐

Grade II ☐

Grade III ☐

BPP score:

Amniotic fluid index	
Fetal breathing movements	
Fetal tone	
Fetal heart rate	
Total score	

DOPPLER STUDIES

Umbilical artery

- Resistive Index
- Pulsatility Index
- S/D ratio

Middle Cerebral Artery

- Resistive Index
- Pulsatility Index
- S/D ratio

Cerebro-placental index

End diastolic flow

- Reduced
- Absent
- Reversed

PREGNANCY OUTCOME

GESTATION AT DELIVERY.....

IUFD/Still birth ☐

Induction of labour yes ☐ no ☐

Mode of delivery SVD ☐ CS ☐

Baby alive

APGAR score .....

Birth weight .....

APPENDIX III: OBSTETRIC ULTRASOUND PROTOCOL

The examination will be conducted using either of the two ultrasound machines in the radiology department.

Patient lies supine on the examination couch, the abdomen is exposed and paper towel used to protect patient's clothes.

Pre-warmed coupling gel is applied to the 3.5-7 MHz curvilinear transducer and an obstetric ultrasound conducted.

The fetal presentation, fetal gestation, EFW, placental position and biophysical profile are evaluated and images taken.

Parameter	**Normal - 2**	**Abnormal – 0**
Fetal breathing movements	1 episode of FBM of at least 30s duration in 30 minutes	Absent FBM or no FBM >30s in 30 mins
Fetal movements	3 discreet body/limb movements	2 or fewer body/limb movements in 30 mins
Fetal tone	1 episode of active extension with return to flexion	Movements are either slow, incomplete or absent
Amniotic fluid index	AFI > 5cm (4 pockets)	AFI < 5cm

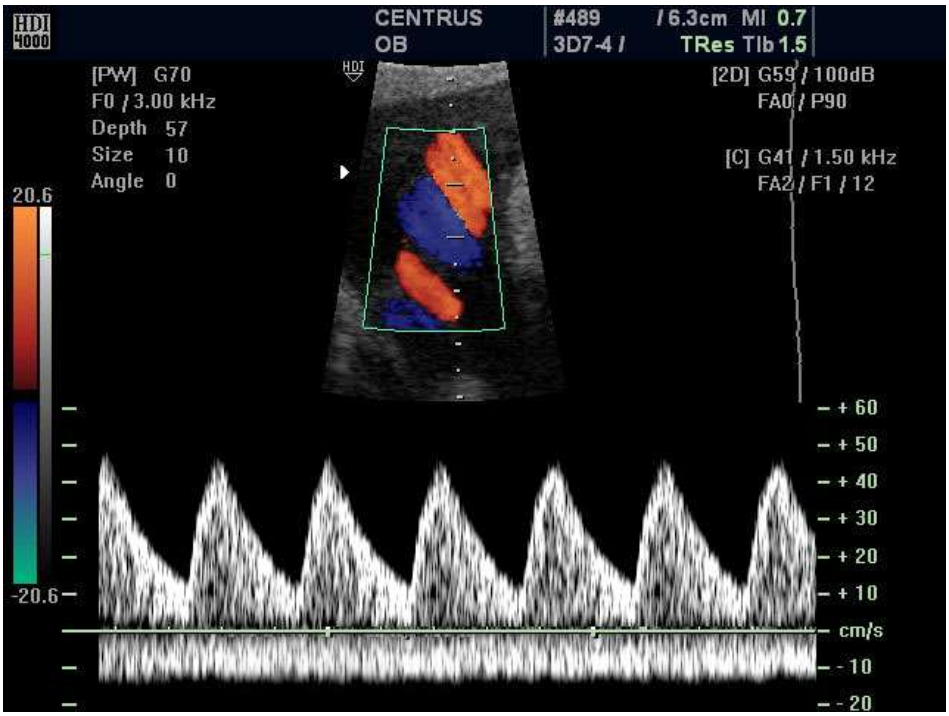
Umbilical artery Doppler

With a pulsed wave Doppler system, a free-floating portion of the cord is identified and the Doppler sample volume is placed over the artery and the vein.

The image is frozen once at least 5 equal pulsatile arterial waveforms are obtained.

The RI, PI and S/D ratio are calculated during absence of fetal breathing and movement.

The waveform is evaluated for presence or absence of reduced, absent or reversed end diastolic flow.



Middle cerebral artery

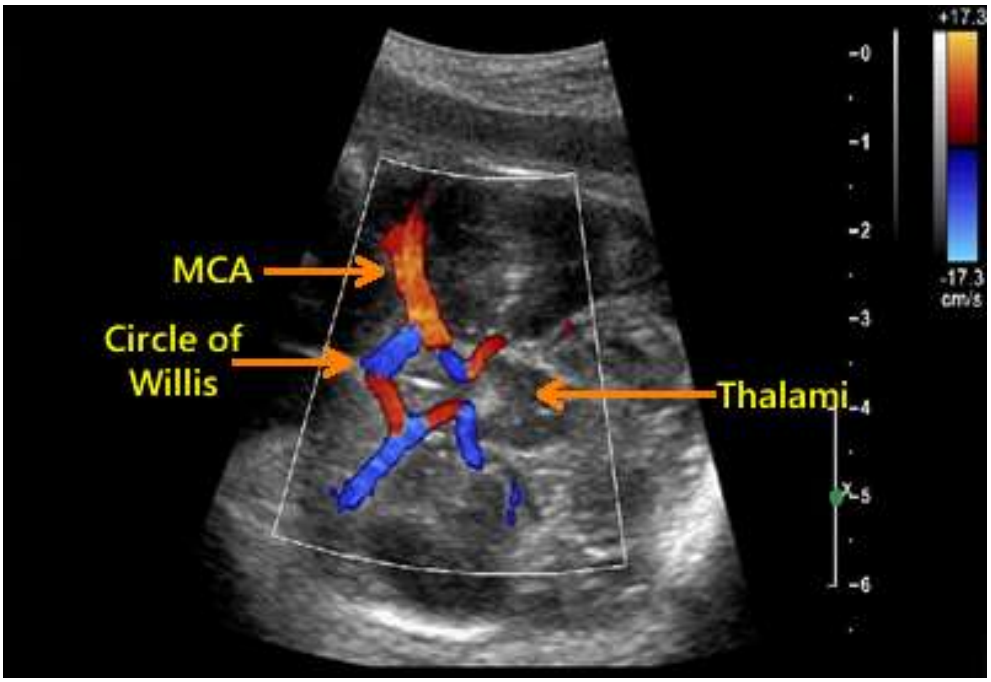
A transverse view of the fetal brain is obtained at the level of the thalami/biparietal diameter.

The transducer is then moved towards the base of the skull at the level of the lesser wing of the sphenoid bone.

Using color flow imaging, the middle cerebral artery can be seen as a major lateral branch of the circle of Willis, running anterolaterally at the borderline between the anterior and the middle cerebral fossae.

The pulsed Doppler sample gate is then placed on the middle portion of this vessel to obtain flow velocity waveforms.

During the studies, care should be taken to apply minimal pressure to the maternal abdomen with the transducer, as fetal head compression is associated with alterations of intracranial arterial waveforms.



APPENDIX IV: IREC APPROVAL

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2016/124
Approval Number: 0001752

26th September, 2016

Dr. Mbarak Chebet Nuru,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
26 SEP 2016
APPROVED
P. O. Box 4606-30100 ELDORET

Dear Dr. Nuru,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Comparison of Fetal Doppler Studies with Biophysical Profile in Prediction of Perinatal Outcome in Patients with Preeclampsia at MTRH".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1752*** on 26th September, 2016. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 25th September, 2017. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

APPENDIX V:HOSPITAL APPROVAL

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke
P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2008

30th September, 2016

Dr. Mbarak Chebet Nuru,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Comparison of Fetal Doppler Studies with Biophysical Profile in Prediction of Perinatal Outcome in Patients with Preeclampsia at MTRH".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

30/09/2016

DR. WILSON ARUASA
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD, HRISM