CORRELATION OF UTERINE ARTERY DOPPLER VELOCIMETRY WITH LABORATORY FINDINGS IN PATIENTS WITH SEVERE PREECLAMPSIA PRESENTING TO KENYATTA NATIONAL HOSPITAL

Martha Ndanu Kitili

H58/6862/2017

A THESIS SUBMITTED

IN PARTIAL FULFILLMENT FOR THE AWARD OF THE DEGREE OF

MASTERS OF MEDICINE IN DIAGNOSTIC RADIOLOGY

IN THE DEPARTMENT OF DIAGNOSTIC IMAGING AND RADIATION MEDICINE,

UNIVERSITY OF NAIROBI

Date:

DECLARATION

This thesis is my original work, and to the best of my knowledge, has not been presented for a degree in any other University.

Signature…….. Date…03 November 2021……

Dr. Kitili Martha Ndanu
University of Nairobi

This thesis has been submitted for examination with our approval/knowledge as university supervisors.

Dr. Angeline Aywak; MBChB, M.Med (Diagnostic Radiology)
Senior lecturer,
Department of Diagnostic Imaging and Radiation Medicine,
School of Medicine, University of Nairobi

Signature…… Date……27/06/2021…….

Dr. Timothy Musila Mutala; MBChB, M.Med (Diagnostic Radiology)
Lecturer,
Department of Diagnostic Imaging and Radiation Medicine,
School of Medicine, University of Nairobi

Signature…… Date……27/06/2021……

Dr. Diana Kerubo Ondieki; MBChB, M.Med (Obstetrics & Gynecology), MSc Epidemiology (LSHTM)
Lecturer,
Department of Obstetrics & Gynecology,
School of Medicine, University of Nairobi

Signature…… Date……27/06/2021……

Table of Contents

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS AND ACRONYMS

ACOG – The American College of Obstetricians and Gynaecologists

APL – Antiphospholipid syndrome

ARDS – Acute Respiratory Distress Syndrome

BMI – body mass index

BP – Blood pressure

BPP- Biophysical Profile

CVS – Cardiovascular system

CNS – Central nervous system

DIC- Disseminated Intravascular Coagulopathy

FGR – Foetal growth restriction.

HELLP- Haemolysis, elevated liver enzymes, low platelet count

IUFD –Intrauterine fetal death

IUGR – Intrauterine growth restriction

ISUOG- the International Society of Ultrasound in Obstetrics and Gynaecology

KNH – Kenyatta National Hospital

LFTS – Liver function tests

NCPD - National Council for Population and Development.

NICU- Neonatal intensive care unit

PE – Preeclampsia

PET- Preeclampsia toxaemia

PI – Pulsatility index

RDS- Respiratory distress syndrome

RI- Resistive index

SLE – Systemic lupus erythematosus

UAS- Uterine Artery Score

UECs- Urea, electrolytes and creatinine

UtA- Uterine artery

WHO- World Health Organization

OPERATIONAL DEFINITIONS

Preeclampsia: - a pregnancy-related hypertensive disorder that occurs after 20 weeks' gestation. Clinically, it is characterized by new onset hypertension with a systolic blood pressure of 140mmHg or greater, or a diastolic blood pressure of 90mmHg or greater. New onset proteinuria greater than or equal to 0.3 grams in a 24-hour urine specimen or urine dipstick protein of 1+ is also required for diagnosis. In the absence of proteinuria, it is also defined as pregnancy related hypertension occurring in the presence of thrombocytopenia, impaired liver function, new onset renal dysfunction, pulmonary oedema or newly occurring cerebral or visual disturbances.

The symptoms of severe preeclampsia are headaches, visual disturbances and blindness, epigastric or right upper quadrant pain, and rapid increase of oedema or development of facial oedema.

Early onset preeclampsia: preeclampsia diagnosed prior to 34 weeks of gestation

Late onset preeclampsia: preeclampsia diagnosed at, or after, 34 weeks of gestation

Eclampsia: the occurrence of convulsions in a woman with preeclampsia after excluding all other possible aetiologies

Thrombocytopenia: platelet count less than 100,000 per microliter

Renal insufficiency: absolute serum creatinine level greater than 1.1 mg/dL (110mmol/L) or a doubling of the serum creatinine concentration in the absence of other renal disease

Impaired liver function: an abnormal elevation of the serum liver transaminases to twice the normal concentration or higher

ABSTRACT

Background

Preeclampsia complicates 2-8% of pregnancies worldwide and it is a recognized cause of maternal morbidity and mortality. Uterine artery Doppler velocimetry is a non-invasive method that is utilized in pregnancy to monitor both the foetus and the mother. Uterine artery Doppler studies are currently performed in patients with preeclampsia and they can, therefore be used to predict the presence or absence of abnormal laboratory findings in these patients, and therefore, expedite referral and management.

Objective

The purpose of this study was to correlate the uterine artery Doppler waveforms and indices with laboratory findings in consenting obstetric patients presenting to Kenyatta National Hospital, with severe preeclampsia

Methodology

A prospective cross-sectional study of patients presenting to Kenyatta National Hospital maternity ward with severe preeclampsia was conducted between November 2020 and April 2021. We recruited 80 pregnant women with singleton pregnancies above 20 weeks' gestation, however 3 were later excluded, leaving a total of 77 patients. A structured questionnaire was used for demographic, clinical and radiological data. An obstetric ultrasound, including bilateral uterine artery Doppler studies was performed. Laboratory values of Aspartate transaminase (AST) & alanine aminotransferase (ALT), creatinine levels and platelet counts obtained soon after admission were recorded into the data abstraction form. The data was then entered into and analysed on R Studio software using R version 4.0.2 and was presented on tables and graphs.

Results

Out of 77 patients, abnormal uterine artery Doppler findings were seen in 64 (83.1%) patients. Liver dysfunction, renal impairment or thrombocytopenia was found present in 26 (33.8%) patients. Abnormally elevated ALT levels were recorded in 13 (16.0%) compared to 8 (10.4%) patients with abnormally elevated AST levels. There was an association between uterine artery notching, abnormal uterine artery resistive indices and elevated ALT [OR = 74.85, 95% (CI 8.07 – 2035.35)] and [OR = 16.24, 95% (CI 2.52 – 335.80)] respectively. Elevated creatinine levels were seen in 14 (18.2%) patients and there was a significant association between uterine artery notching and elevated creatinine [OR = 6.15, 95% (CI 1.56 –

32.44)]. Thrombocytopenia was present in 7 (9.1%) patients. However, there was no significant association between thrombocytopenia and abnormal uterine artery Doppler waveforms and indices.

Severe preeclampsia diagnosed at a gestation earlier than 34 weeks was seen in 51 (66.2%) of patients while that diagnosed before 34 weeks was seen in 26 (33.8%) patients. Abnormal uterine artery notching was seen in 24 (47.1%) cases of early onset preeclampsia compared to 10 (36.5%) of late onset preeclampsia. All cases of thrombocytopenia (7) were seen in patients with early onset preeclampsia. Higher mean AST, ALT and creatinine levels were also seen in early onset preeclampsia.

Conclusion

The presence of a persistent uterine artery notch or elevated uterine artery resistive index above the 95th percentile in patients with severe preeclampsia is associated with multiple organ dysfunction, specifically liver and renal impairment. These findings are especially significant in patients presenting with early onset preeclampsia. These findings underscore the need for uterine artery Doppler assessment as part of routine obstetric ultrasound imaging in pregnant patients from 20 weeks' gestation.

CHAPTER 1. INTRODUCTION

Preeclampsia (PE) is a pregnancy-related hypertensive disorder that complicates 2-8% of pregnancies worldwide (1). It occurs after the 20th week of gestation in a previously normotensive patient(2). Previously considered essential to diagnosis, a urinary proteinuria dipstick value of at least +2, or 300 mg/dL of protein or more in a 24-hour urine specimen is no longer required (3). It is classified as mild preeclampsia (BP: 140-159mmHg systolic or 90-109mmHg diastolic) and severe preeclampsia (BP: ≥160mmHg systolic or ≥110mmHg diastolic) on two instances at least 4 hours apart (2). A sub-classification also exists where preeclampsia is described as early onset PE or late onset PE, in relation to diagnosis either before or after 34 completed gestational weeks respectively(4).

The incidence of preeclampsia varies in different populations, with that in developing countries being seven times higher than that in the developed countries (5). This is attributed to lack of timely access to health care, either due to delays in making the decision to seek healthcare, delays in reaching health facilities or delays in health care provision upon arrival at the health facilities(6). The prevalence of preeclampsia at Kenyatta National Hospital (KNH), one of the national referral hospitals, is estimated at 3.6%, (7) while the national prevalence ranges between 5.6 to 6.5 percent(8). The prevalence of severe preeclampsia characterized by haemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome, and pulmonary oedema at KNH is 2.8% and 2.9% respectively(7). Maternal, foetal and neonatal morbidity and mortality are recognized complications of preeclampsia which occur in approximately 3% of pregnancies (9). Together, preeclampsia and eclampsia are the second most common direct cause of maternal deaths worldwide(10), contributing to 9-15% of maternal mortality in Africa(11). Preeclampsia is responsible for 13.9% of maternal mortality cases seen at KNH (7). Globally, preeclampsia and eclampsia are the principal obstetrical cause of perinatal mortality(12).

Second trimester uterine artery Doppler studies have been incorporated by the International Society of Ultrasound in Obstetrics & Gynecology (ISUOG) for the screening of preeclampsia(13). Studies have also demonstrated the important role that uterine artery Doppler studies play in predicting foetal and neonatal complications of severe preeclampsia(14). Fewer studies that have been done have demonstrated a

relationship between abnormal uterine artery Doppler studies and maternal features of severe eclampsia and complications such as eclampsia, abruptio placenta, acute renal failure and eclampsia.

Preeclampsia is a significant cause of maternal mortality and morbidity in Kenya(15). This study, therefore, aimed to demonstrate a relationship between uterine artery Doppler studies and laboratory findings of renal insufficiency, thrombocytopenia and impaired liver function in severe preeclampsia.

CHAPTER 2. LITERATURE REVIEW

Pathophysiology of preeclampsia

The underlying pathophysiology of preeclampsia is the placenta since reversal of the syndrome is only achieved upon its delivery(16)(17). In a normal pregnancy, trophoblastic invasion of all the spiral arteries (terminal branches of the uterine arteries which provide uteroplacental blood) in the placental bed occurs, thereby transforming these vessels from initially small calibre arteries into dilated flaccid vessels. This transformation results in a reduction in the pressure of uteroplacental blood flow and a modest increase in the spiral artery blood flow. This remodelling decreases maternal blood vessel resistance, thereby increasing uteroplacental perfusion(18).

In PE, incomplete transformation of the spiral arteries results in tortuous, thick-walled and narrow arteries with resultant high resistance across the placental bed alongside intermittent uteroplacental hypoperfusion and hypoxia. These processes lead to increased oxidative stress within the placenta, which in turn causes a release of placental derived factors with an imbalance between proangiogenic (sFLT1, VEGF &SENG) and antiangiogenic (PIGF &PGF) factors in favour of antiangiogenic factors. Finally, the maternal systemic inflammatory response is exaggerated with associated endothelial dysfunction and decreased uteroplacental and fetoplacental blood flow(4,8,17).

PE is also associated with higher platelet activation and aggregation response, elevated thrombopoietin levels, elevated thromboxane levels and reduced prostacyclin levels with a shift of prostacyclin thromboxane ratio towards vasoconstriction(16).

Risk factors of preeclampsia

Several maternal risk factors that are associated with preeclampsia have been identified and are divided into significant and moderate risk factors. Significant risk factors include a previous pregnancy complicated by preeclampsia, chronic kidney disease, connective tissue diseases such as Antiphospholipid syndrome (APL) and Systemic lupus erythematosus (SLE), type 1 or type 2 diabetes and chronic hypertension. The moderate risk factors that have been identified are nulliparity, maternal age of 40years

and above, pregnancy interval of greater than 10 years, obesity and body mass index (BMI) of 35kg/m^2 or above, family history of preeclampsia and multifetal gestation(2,(20) . The cut off for an elevated risk of pre-eclampsia is "1 significant risk factor or more than 1 moderate risk factor"(20).
Additional risk factors associated with the development of preeclampsia are assisted reproductive technology, obstructive sleep apnoea and "deficiencies of calcium, zinc, vitamins C and E, and essential fatty acids"(21).

Classification of preeclampsia

Preeclampsia is classified as either mild or severe. Mild PE is preeclampsia without severe features. In contrast, severe PE is characterized by diagnostic elevations in either/or systolic and diastolic BP with or without the presence of new-onset thrombocytopenia, impaired liver and renal function, HELLP syndrome, pulmonary oedema, or visual disturbance(2). Preeclampsia complicated by foetal growth restriction (FGR) is also classified as severe preeclampsia(19). Severe preeclampsia is associated with higher maternal morbidity and mortality than mild preeclampsia(22).
PE is also sub-classified based on the time of diagnosis of the disease or time of delivery, into early onset PE and late onset PE with late onset PE accounting for more than 80% of patients(23). The clinical signs of early onset PE begin prior to 34 completed weeks of gestation, while those of the late onset type occur at or after 34 weeks (19).
Early onset (placental) PE and late onset (maternal) PE are thought to have different pathophysiological features(4). In early onset PE, there is reduced or incomplete vascular "transformation of the spiral arteries"(4). This causes increased resistance in the placental vessels, placental hypoperfusion and therefore placental insufficiency with reduced nutrient supply to the growing foetus. A smaller placental volume is seen in early onset PE. The result is thus FGR. In contrast, late onset PE is linked to little, if any incomplete "transformation of the spiral arteries" (4) and, subsequently placental perfusion is maintained and at times even increased. Histologically, placentas are morphologically comparable to those of healthy pregnancies. FGR is thus not seen in late onset PE which generally presents with milder clinical conditions(21,22).
Early and late onset PE are both associated with maternal and perinatal morbidity and mortality. However, early onset PE confers a significantly higher risk of both maternal cardiovascular (CVS), respiratory, renal, hepatic and central nervous system (CNS) complications and mortality(24).

Complications of Preeclampsia

Maternal, foetal and neonatal morbidity and mortality occur in significantly higher proportions in early onset PE, severe preeclampsia and eclampsia(25).

Maternal complications of PE include eclampsia, placental abruption, disseminated intravascular coagulopathy (DIC), acute respiratory distress syndrome (ARDS), peripartum cardiomyopathy, myocardial infarction, encephalopathy and intracranial haemorrhage(24). Sudden loss of vision due to involvement of the occipital cortex or the retina, although rare, may also occur (26).

The rates of maternal complications vary with the study population, laboratory values used to determine the diagnosis, preceding medical illnesses such as chronic hypertension and SLE, and pre-existing obstetric complications such as placental abruption, intrauterine foetal demise, and eclampsia(11).

Maternal mortality occurring as a result of severe PE is primarily attributable to intracerebral haemorrhage and ARDS(11). Higher mortality is seen in developing countries and this is alluded to poor access to prenatal and proper hospital care, lack of properly trained hospital personnel and resources such as medication, laboratory equipment, and intensive care facilities (27). In KNH, severe and eclampsia are one of the top 3 causes of maternal deaths, accounting for up to 13.9% of maternal mortality and 29.8% of the direct causes of maternal death(28).

Prior history of PE increases a woman's future risk of long term complications of vascular disease, more specifically “hypertension, ischemic heart disease, myocardial infarction, cerebrovascular accidents”(29), in addition to chronic renal failure, and venous thromboembolism. These complications occur more frequently in women with early onset preeclampsia. Patients with a history of PE also suffer an increased risk of death from these complications when compared to non-PE patients (12, 27).

Gestational age and the severity of PE are directly linked to subsequent neonatal and foetal complications. Prenatal complications include intrauterine growth restriction (IUGR), oligohydramnios, and increased rates of preterm delivery. Neonatal complications such as low birth weight, admission to neonatal intensive care unit (NICU), necrotizing enterocolitis (NEC), neonatal sepsis and respiratory distress syndrome (RDS) also occur. Additional complications include neutropenia, periventricular leukomalacia, intraventricular haemorrhage and perinatal death due to preterm delivery (28, 29).

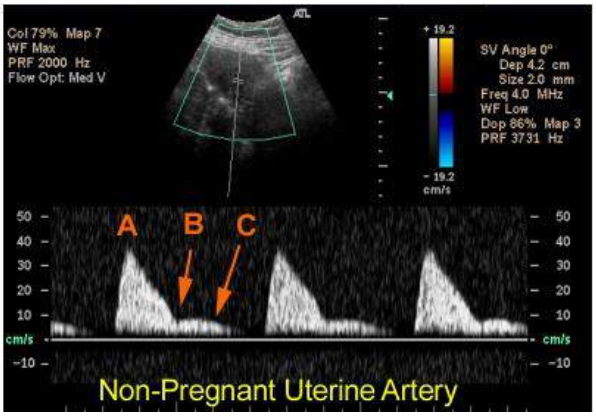
Perinatal mortality rates from severe PE and eclampsia range from 1 in 4 to 1 in 10 (12). These rates correlate with gestation at term with very high rates of up to 800 in 1000 seen with severe early onset PE (27) .

Uterine artery Doppler velocimetry

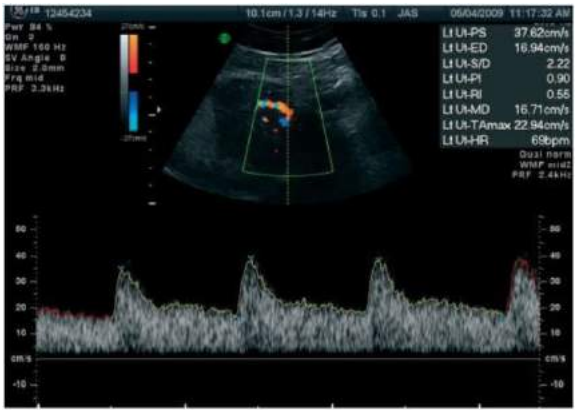
Blood supply to the uterus is through the uterine arteries. In the first trimester and early second trimester of pregnancy, uterine vessels are tortuous with intense spiralling. However, with the advancement of pregnancy, the vessels increase in diameter with a reduction in the degree of tortuosity. Uterine artery Doppler studies can thus be used to provide information on the status of uteroplacental blood flow as aberrations in the uterine vascular waveforms are seen in and are thought to be involved in the pathogenesis of pregnancy disorders such as preeclampsia, FGR and preterm labor (32).

In the non-gravid state the uterine arteries are high resistance low flow vessels and demonstrate a brisk rise and drop during systole, a notch in early diastole and low flow in late diastole as demonstrated in figure A. Throughout pregnancy, uterine blood flow rises to 12 fold due to vascular transformation of the spiral arteries and increased maternal blood flow. This causes an increase in placental perfusion and the UtA waveform then demonstrates low- resistance diastolic flow with the peak end diastolic flow increasing as gestational age increases with the diastolic notch disappearing completely by 26 weeks gestation (33). As a result of these events, the uterine artery Doppler waveform changes with advancing gestation (figures B-D).

A. Non- pregnant patient.



B. First trimester



C. Late Second trimester **D. Third trimester**

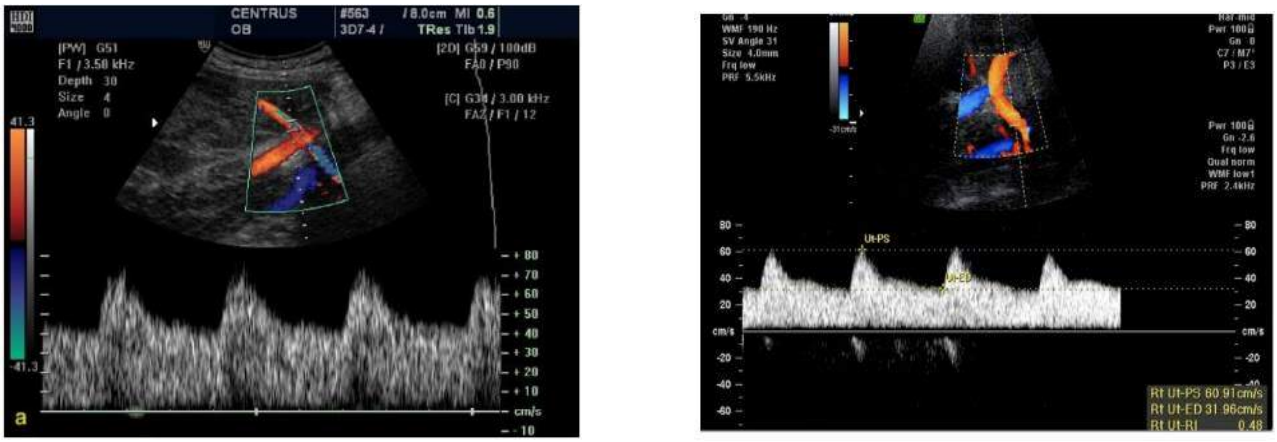
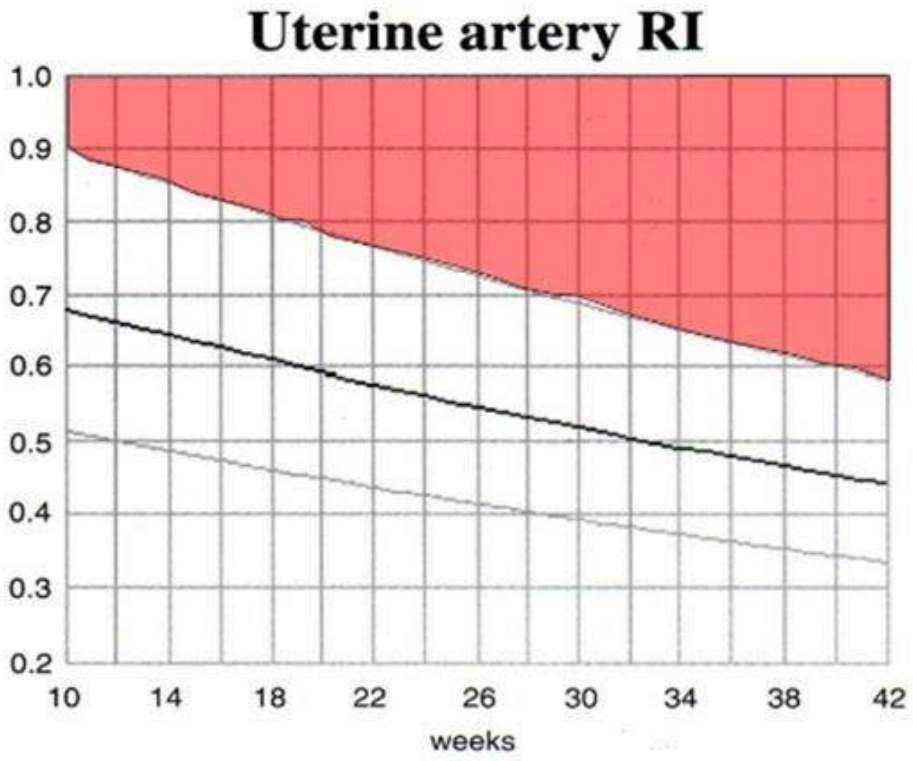


Figure 1: Changes in uterine artery Doppler waveforms in the non-pregnant and pregnant sate

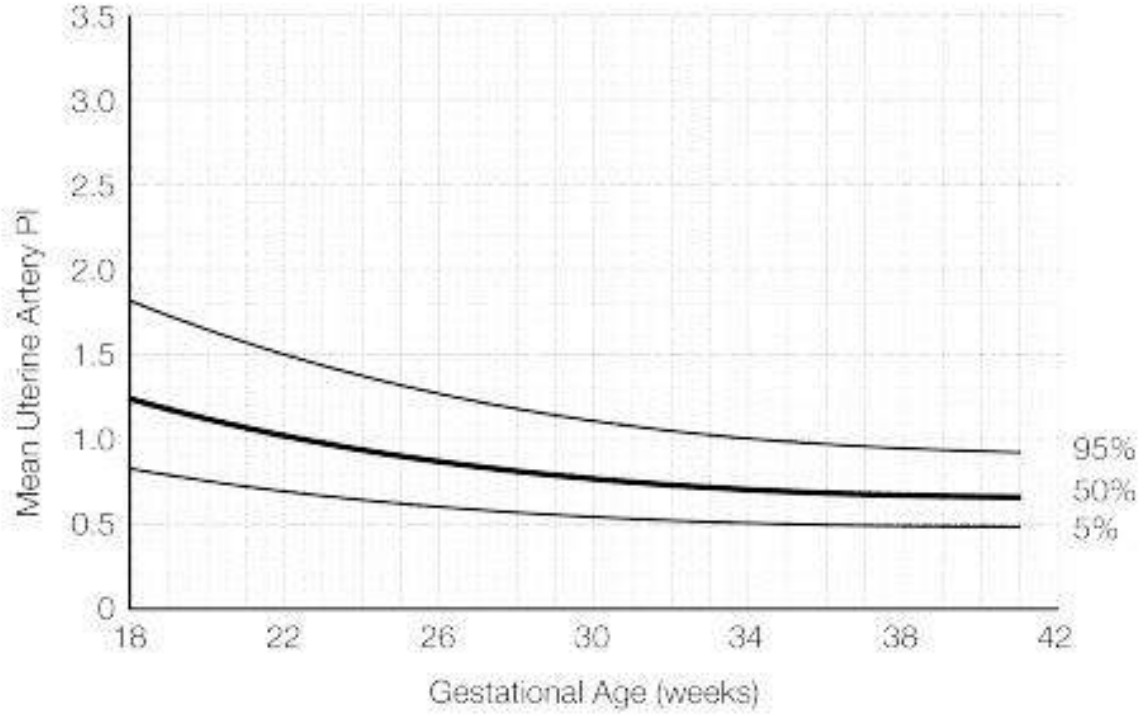
Changes in UtA Doppler indices are also seen throughout pregnancy with a decline in resistive indices (RI) during the first 20 weeks of pregnancy. A UtA RI nomogram is shown below(34).

Significant progressive reduction in the mean UtA Pulsatility index (PI) is seen which continues throughout pregnancy until 34 weeks of gestation(35).



(Ertan AK, Taniverdi HA. Doppler Sonography in Obstetrics. Donald Sch J Ultrasound Obs Gynecol. 2013;7(2):128–48).

Figure 2: Uterine artery Resistive Index nomogram



(Gómez O, Figueras F, Fernández S, Bennasar M, Martínez JM, Puerto B, et al. Reference ranges for uterine artery mean pulsatility index at 11-41 weeks of gestation. Ultrasound Obstet Gynecol. 2008 Aug;32(2):128–32).

Figure 3: Uterine artery Pulsatility Index nomogram (mean 95th and 5th centiles)

Abnormal uterine artery parameters

Abnormal artery waveform and resistive indices are indicators of high resistance flow within the uterine arteries and they can be used to give ancillary evidence of abnormal placentation(36). Abnormal uterine artery waveforms are classified into three: Type I waveform is a resistive index that is above the upper limit of normal. Early diastolic notching is classified as a type II waveform. Type III waveform is associated with the greatest risk for adverse outcomes and is characterized by the presence of a RI above the upper normal limit and the presence of an "early diastolic notch"(36).

A uterine artery score system which factors in UtA PI and the presence of notching is also used to categorize uterine artery waveforms as normal (UAS 0) or abnormal (UAS 1-4) (37).

UAS score/class	Definition
0	Normal blood flow velocity waveforms in both uterine arteries
1	One abnormal parameter (high PI (>1.2) or a diastolic notch) present

2	Presence of two abnormal parameters
3	Presence of three abnormal parameters
4	Four abnormal parameters present (bilateral notch and high PI)

The role of uterine artery Doppler in IUGR

It is hypothesized that the complications that occur in preeclampsia are secondary to hypoperfusion in multiple organs, and, therefore, it follows that high UtA resistance results in a more extensive vasospastic process with more consequences(38).

The role of UtA Doppler in the prediction of foetal and perinatal complications has been extensively investigated with positive results. Research conducted on intrauterine growth restriction (IUGR) foetuses on brain perfusion revealed that brain hypoxia exists long before notable changes in middle cerebral artery (MCA) Doppler are observed and it was, therefore, concluded that UtA Doppler ranks higher than either umbilical artery (UA) or MCA studies in predicting IUGR(14).

Uterine Artery Doppler and severe preeclampsia

In a study conducted by Maged et al on 100 women in Cairo, Egypt, who presented with preeclampsia in the third trimester, 76% of them had features of severe preeclampsia. UtA Doppler studies showed that high UtA RI (0.81-083) was directly associated with HELLP syndrome and acute pulmonary oedema. Patients who developed acute pulmonary oedema had the highest UtA resistive indices at admission (38). It was therefore concluded that specific signs of severe preeclampsia such as HELLP syndrome, and acute pulmonary oedema can be predicted through increased UtA RI in the third trimester in women with preeclampsia.

A similar study conducted on 120 women in Barcelon, Spain, who specifically presented with severe early onset preeclampsia showed that 53% of the patients had abnormal uterine artery Doppler values at inclusion. Maternal features of severe preeclampsia (HELLP, neurologic manifestations, ARF, pulmonary oedema) were more common in those with abnormal uterine Doppler studies compared to those with normal studies (28.1% and 5.1% respectively) (39).

In a study conducted in Italy by Orabona et al on 168 patients in whom no distinction was made between mild preeclampsia and severe preeclampsia, 47% of them developed eclampsia, HELLP, and abruptio placenta. Higher rates of maternal complications were seen in those patients who had high UtA PI and a

MCA (middle cerebral artery) PI to UtA PI ratio. The study concluded that MCA PI/UtA PI ratio is the most accurate predictor of maternal outcomes(40).

Conflicting results were, however, yielded in a study that was conducted on 154 patients with severe preeclampsia in Brazil. 59% of the patients in the study had high uterine artery resistance, evidenced by elevated UtA RI and PI values and uterine artery notching. However, there was no statistical significant association between patients who had normal uterine artery flow and those with increased uterine artery resistance in terms of adverse maternal outcomes(41).

Uterine Artery Doppler in multifetal pregnancy

Uterine artery Doppler RI and PI at all gestational ages are significantly lower in twin pregnancies compared to singleton pregnancies(33). This is attributed, in part, to the larger placenta implantation area which results in contrasting physiological effects of multifetal pregnancy on the uteroplacental circulation. The sensitivities of UtA RI and PI for the detection of PET in twin pregnancies are also significantly lower than in singleton pregnancies(42) and it is for this reason that the role of UtA Doppler in multiple gestations is unclear.

The Effect of Anti-hypertensives on uterine artery Doppler waveforms

Hydralazine, labetalol, methyldopa and calcium channel blockers such as nifedipine, are the principal anti-hypertensives used in the treatment and management of preeclampsia. The effect of these anti-hypertensives on uterine artery resistance, has been studied extensively and it has been established that UtA doppler velocity waveforms remain unchanged with the use of these drugs(8, 41, 42).

STUDY JUSTIFICATION

Preeclampsia is a significant cause of maternal, foetal and neonatal mortality and morbidity in Kenya, and it is the third leading cause of maternal mortality. Obstetric ultrasonography is a safe, widely available, affordable and reliable tool that is used to assess both maternal and foetal well-being. Uterine artery Doppler studies are performed during an obstetric ultrasound and are currently recommended for screening pregnant patients at high risk for developing preeclampsia. A strong correlation between abnormal uterine artery Doppler studies and laboratory findings in severe preeclampsia will guide prompt and timely referral of at-risk patients to the appropriate health care facilities, leading to efficient and lifesaving patient management. Ultimately, this will help to reduce maternal morbidity and mortality.

To the best of my knowledge and literature search, no similar study has been carried out locally. This study will, therefore, form a baseline for further studies and will contribute to the body of scientific knowledge.

STUDY QUESTION

What are the uterine artery Doppler waveforms and indices in patients presenting to Kenyatta National Hospital with severe preeclampsia, and how do they correlate with laboratory findings according to the American College of Obstetrics and Gynaecology criteria?

BROAD OBJECTIVE

To correlate the uterine artery Doppler waveforms and indices with laboratory findings in pregnant patients presenting at KNH with severe preeclampsia.

SPECIFIC OBJECTIVES

In pregnant patients presenting to KNH with severe preeclampsia:

1. To establish the relationship between abnormal uterine artery Doppler findings and elevated serum creatinine.
2. To determine the relationship between abnormal uterine artery Doppler findings and elevated liver transaminases.
3. To establish an association between abnormal uterine artery Doppler findings and thrombocytopenia.
4. To compare uterine artery Doppler and laboratory findings in patients with early onset and late onset severe preeclampsia.

CHAPTER 3. RESEARCH METHODOLOGY

Study Setting:

The study was carried out in Kenyatta National Hospital labour ward. KNH is a level VI referral hospital located in Nairobi. It serves as one of the referral hospitals in Kenya, alongside Moi University Hospital and Kenyatta University Teaching and Referral hospital**.** The KNH labour ward receives approximately 14,400 patients per annum, as at December 2019.

Study Design:

This was a prospective cross sectional study conducted over a period of 5 months from December 2020 to April 2021 on patients with severe preeclampsia admitted in KNH.

Study population:

Consenting women aged 18 years and above with severe preeclampsia were recruited into the study.

Inclusion criteria:

These were patients ≥ 18 years of age with singleton pregnancies presenting with severe preeclampsia.

Exclusion criteria:

The following patient groups were excluded from this study:

1. Patients with chronic renal disease, pre-existing hypertension, gestational diabetes, diabetes mellitus and autoimmune diseases.
2. Multifetal gestation.
3. Patients who declined to give consent.

Sample Size Determination

The following sample size formula was used to determine the sample size:

$$n = \frac{Z^2\,\hat{\mathrm{P}}(1-\hat{\mathrm{P}})}{e^2 + \frac{Z^2\,\hat{\mathrm{P}}(1-\hat{\mathrm{P}})}{N}}$$

n = sample size

z = significance level set at 1.96 corresponding to 95% confidence interval

$\hat{P}$ = percentage of the population with the known characteristic

e = margin of error set at 5%

N= population size which is the average number of patients admitted with preeclampsia which approximates 4800 patients annually. Given that the prevalence of preeclampsia at KNH is 3.6%, the sample size calculated from the equation above came to 53. After adjusting for a 20% attrition, the sample size came to 64.

Sampling Technique:

Purposive consecutive sampling of patients was used to select patients eligible for the study.

Study Procedure

Patients were recruited by the principal investigator from the KNH labour ward soon after admission. A checklist was used to ensure patient eligibility before being entered into the study. Patients' age, sex and clinical information was reviewed to confirm whether or not they met the inclusion criteria. Patients who met the inclusion criteria and who consented to participate in the study were recruited.

The diagnostic criteria that was used for severe PE was systolic BP: ≥160mmHg or diastolic BP ≥110mmHg on 2 or more determinations and urinary proteinuria of 2+ on dipstick analysis in a previously normotensive patient. In the absence of proteinuria, a diagnosis of severe PE was made based on an elevated blood pressure in the presence of deranged liver function tests, renal function tests, thrombocytopenia, pulmonary oedema or new onset visual or cerebral disturbances. The criteria for early onset PE was patients diagnosed with preeclampsia at 34 weeks of gestation or less, while that for late onset PE was gestation above 34 weeks.

All transabdominal obstetric ultrasound examinations were performed by the primary investigator using the Philips HD5 Release 2.1 ultrasound imaging machine available at KNH labor ward that is equipped with a low frequency 3.5–5 MHz transabdominal probe. Foetal number, viability, presentation, the position of the placenta, volume of liquor, estimated foetal weight and biophysical profile was established. The gestational age was also determined using biparietal diameter, head circumference, abdominal circumference, and femur length.

Uterine artery Doppler velocimetry using pulsed wave and color Doppler imaging was performed at the crossover of the uterine and external iliac arteries using an insonation angle of less than 30°, a velocity of more than 60 cm/s, and a sample volume of 2.0 mm. Both arteries were measured three times and the mean results were recorded once 3 similar consecutive waveforms were obtained. The pulsatility index (PI) was calculated electronically using the equation PI = (peak systolic velocity–end diastolic velocity)/time averaged velocity. The resistance index (RI) was also calculated electronically using the equation RI = (peak systolic velocity–end diastolic velocity)/peak systolic velocity. The presence or absence of a notch on both uterine artery waveforms was noted. Ultrasound findings were reviewed with a consultant radiologist to avoid errors.

Data on patients' laboratory findings was obtained from individual patient files and labour ward records and were all coded as either normal or abnormal. The definition for abnormal laboratory results was considered based on the ACOG criteria of severe preeclampsia. Abnormal liver function tests (AST & ALT) were defined as being raised to twice the upper limit of the normal concentration (40 IU/L and 35 IU/L respectively) or higher. Liver transaminases above the upper limit of normal but not meeting the criteria for severe preeclampsia were defined as being elevated. Thrombocytopenia was considered when the platelet count was less than 100 cells /microliter. Abnormal creatinine values were defined as levels above 110 mmol/L.

DATA MANAGEMENT

Each patient was assigned a unique serial identification number. The patient's demographic data, relevant clinical characteristics and uterine Doppler analysis results were captured and recorded on a pretested data abstraction form. The uterine artery Doppler waveforms were reviewed with a consultant radiologist.

The data was subsequently checked for completeness and cleaned prior to entry into REDCap, a non-propriety electronic tool (43), after which it was stored in a password protected laptop.

DATA ANALYSIS

The data that was captured was entered into and analysed on R Studio software using R version 4.0.2 (44), based on validation rules and metadata pulled from REDCap's application programming interface. All data were tested to confirm a normal distribution by using a Kolmogorov–Smirnov test

Continuous variables were described as means with one standard deviation (1 SD) while categorical variables were expressed as frequencies (n) and percentages of the sample. Difference between means for continuous variables were analysed using the Student t-test. Uterine Doppler indices were transformed into Z values to standardize for gestational age.

Univariate analysis was performed in order to reveal the characteristics of the population studied. The chosen parameters were maternal age, gestational age, parity, early onset preeclampsia and late onset preeclampsia. (include)

Bivariate analysis was used to check for any association between abnormal liver transaminases, serum creatinine and platelet count with UtA velocimetry. For continuous data, comparison was made using the Student t-test while analysis for categorical data used Fishers exact test, which is well suited for analysing sample sizes < 100 observations (45) and therefore more appropriate for this study. All tests with a p value of <0.05 were considered significant.

The association between abnormal uterine Doppler results and abnormal laboratory findings that was found to be significant on bivariate analysis was further subjected to multivariate analysis after adjustment for risk factors including maternal age, parity and previous history of preeclampsia by logistic regression, following which odds ratios (OR) and 95% confidence intervals (95% CI) were obtained.

CHAPTER 4: RESULTS

Overall, 80 patients with severe preeclampsia fulfilled the inclusion criteria. 2 patients were later excluded upon being diagnosed with concurrent gestational diabetes mellitus. The third patient who succumbed soon after admission was excluded due to incomplete laboratory results. This left a study population of 77 participants.

Demographic and clinical characteristics of pregnant women with severe preeclampsia at KNH

Table 1 describes the demographic and clinical characteristics of the study population. The patients were aged between 18-42 years with a mean age of 30.4 years. Majority of the patients were multiparous (74.0%) compared to those who were nulliparous (26%). The mean parity was 1.5 (SD=1.2). 51 patients (66.2%) had early onset preeclampsia compared to 26 (33.8%) who had late onset preeclampsia.

Table 1: Demographic and clinical characteristics of pregnant women with severe preeclampsia at KNH

Variable	**Summary Statistic (N=77)**
Mother's age (years) [a]	30.4 (±6.1)
Parity [a]	1.5 (±1.2)
Parity Nullipara Multipara	 20(26.0%) 57 (74.0%)
Systolic BP at admission [a]	179.2 (±21.5)
Diastolic BP at admission [a]	117.2 (±13.2)
Previous history of Preeclampsia [b]	21 (±27.2%)
Timing of preeclampsia Early onset preeclampsia [b] Late onset preeclampsia [b]	 51 (66.2%) 26 (33.8%)
Notes: [a] Statistic provided as mean (1SD) [b] Statistic provided as count (percentage)	

Uterine artery Doppler findings of pregnant women with severe preeclampsia at KNH

Table 2 shows the distribution of normal and abnormal UtA Doppler waveforms and indices in the study population. The most frequent abnormal index was the pulsality index (84.4%). A notch in either uterine artery was seen in 34 (44.2%) of patients.

Table 2: Distribution of uterine artery Doppler indices of pregnant women with severe preeclampsia at KNH

Doppler Indices Results (N=77)		
Finding	**Normal n(%)**	**Abnormal n(%)**
Pulsatility Index	12 (15.6)	65 (84.4)
Resistive Index	31 (40.3)	46 (59.7)
Notching	43 (55.8)	34 (44.2)

An abnormal uterine artery score was defined as a score ranging from 1-4, which was based on right and left uterine artery pulsatility indices and the presence or absence of a notch in either uterine artery. A normal score was seen in 13 (16% of patients) while 64 (83.1%) of patients had an abnormal UtA score. The most frequent abnormal score was 2 (26%). The distribution of uterine artery scores in the study population is demonstrated in figure 4.

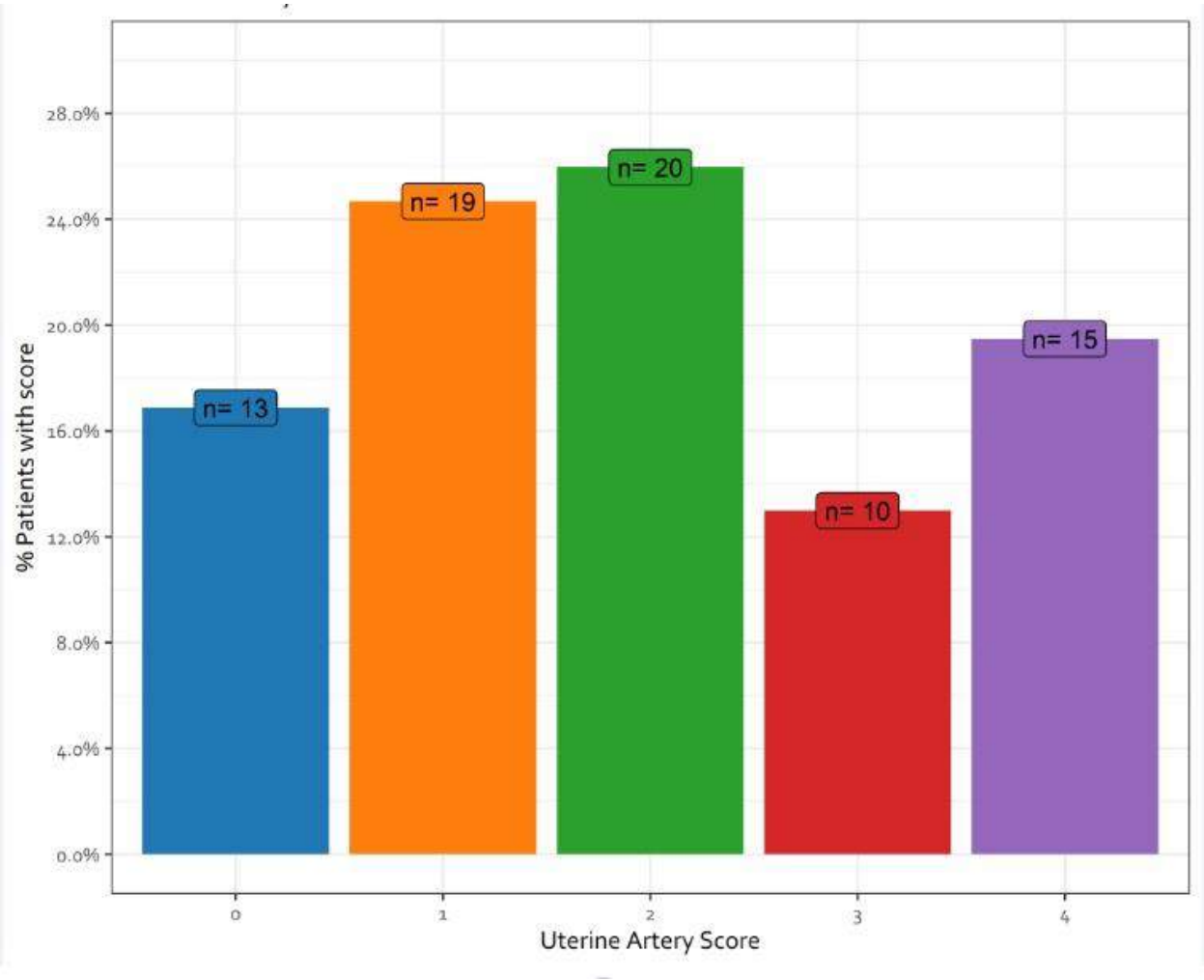
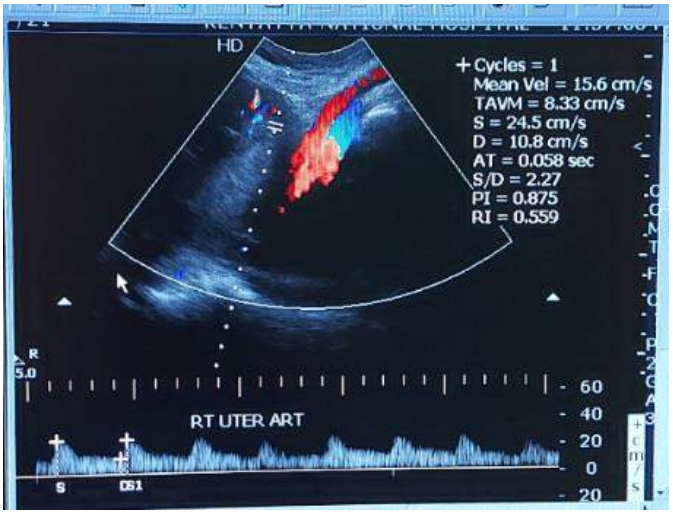
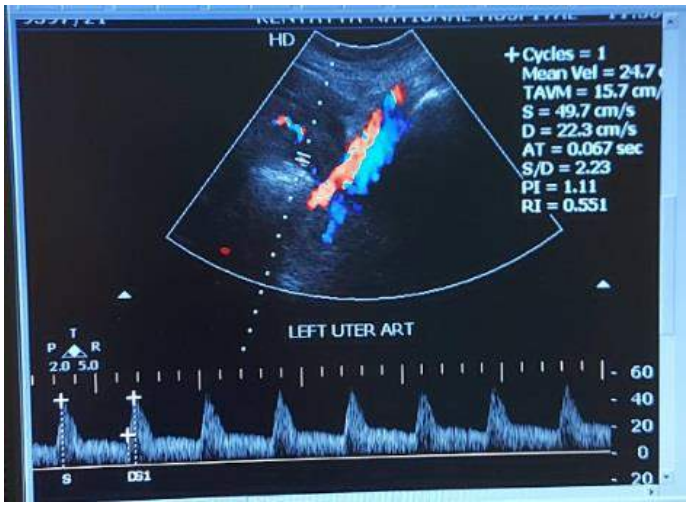


Figure 4: Uterine artery score distribution of pregnant women with severe preeclampsia at KNH

Figure 5a and 5b shows normal uterine artery Doppler findings in a patient who had normal bilateral UtA Doppler waveforms and indices and a uterine artery score of 0.



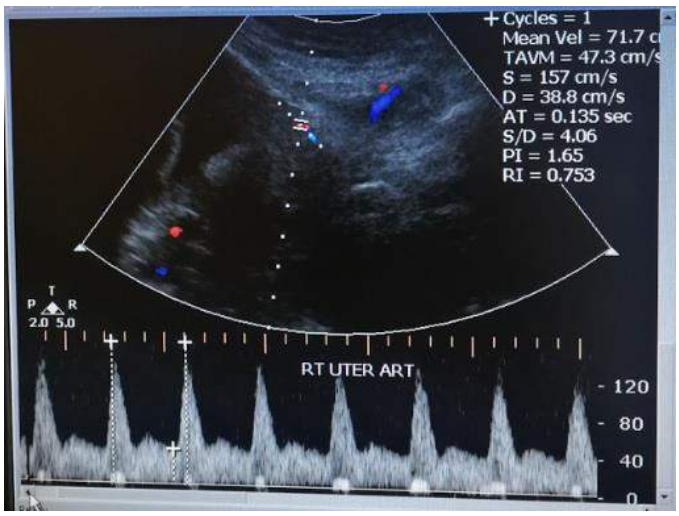
5a



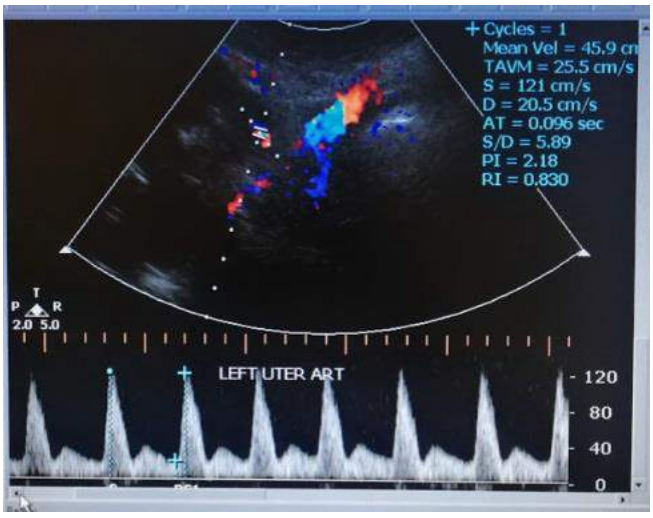
5b

Figure 5a and 5b showing normal right and left uterine artery Doppler waveforms and indices in a patient who had severe preeclampsia.

Figure 6a and 6b shows uterine artery Doppler findings in a patient with bilateral abnormal uterine artery notching, bilateral uterine RI above the 95th percentile, bilateral uterine artery PI above the 95th percentile and a cumulative UtA score of 4.



6a



6b

Figure 6a and 6b showing abnormal right and left uterine artery Doppler waveforms and indices in a patient who had severe preeclampsia.

Laboratory findings of pregnant women with severe preeclampsia at KNH

26 (33.8%) patients demonstrated either liver dysfunction, renal insufficiency or thrombocytopenia, while 51 (66.2%) had normal findings. 8 (10.4%) patients had elevated AST levels that met the criteria for liver dysfunction, while 13 (16.9%) were found to have elevated ALT levels that met the criteria for hepatic dysfunction. Overall, the mean liver transaminases were elevated with a mean AST of 64.2 (SD±123.1) and a mean ALT of 57.2 (SD±94.1). 14 (18.2%) patients in the study had elevated creatinine levels. The mean creatinine was normal at 95.2 (SD±55.5). Only 7 (9.1%) patients had thrombocytopenia and the mean platelet count was normal at 218.7 (SD±84). Only one patient (1.3%) in the study population had abnormal liver transaminases, abnormal creatinine and thrombocytopenia. The frequency of patients with abnormal individual laboratory values is provided in table 3.

Table 3: Distribution of laboratory values in pregnant women with severe preeclampsia at KNH

Laboratory parameter	**Normal n (%)**	**Abnormal n (%)**
AST	69 (89.6)	8 (10.4)
ALT	64 (83.1)	13 (16.9)
Creatinine	63 (81.8)	14 (18.2)
Platelet Count	70 (90.9)	7 (9.1)

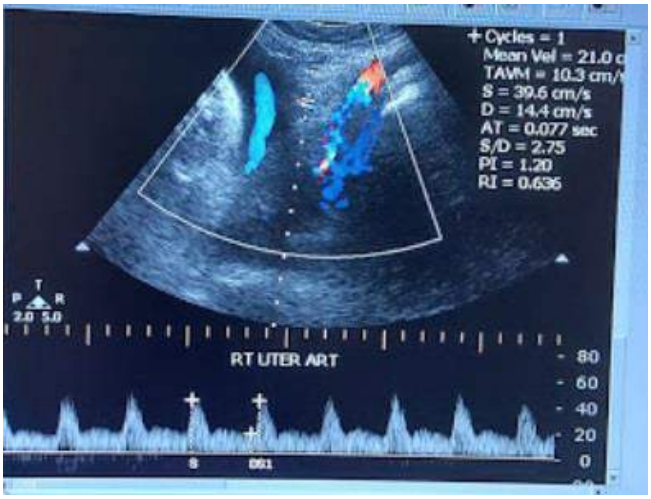
Bivariate analysis of the association between abnormal uterine artery Doppler findings and elevated liver transaminases

In bivariate analysis, a statistically significant correlation was found between the presence of a persistent uterine artery notch and abnormally elevated ALT levels (p value < 0.05). The association between elevated UtA RI above the 95th percentile and abnormally elevated ALT levels was also found to be significant (p value <0.05). No significant association was found between elevated ALT and elevated UtA PI, elevated UtA RI or abnormal UtA scores. No significant association was found between elevated AST levels and either elevated UtA PI, elevated UtA RI, abnormal UtA notching or abnormal UtA scores. Table 4 summarizes these findings.

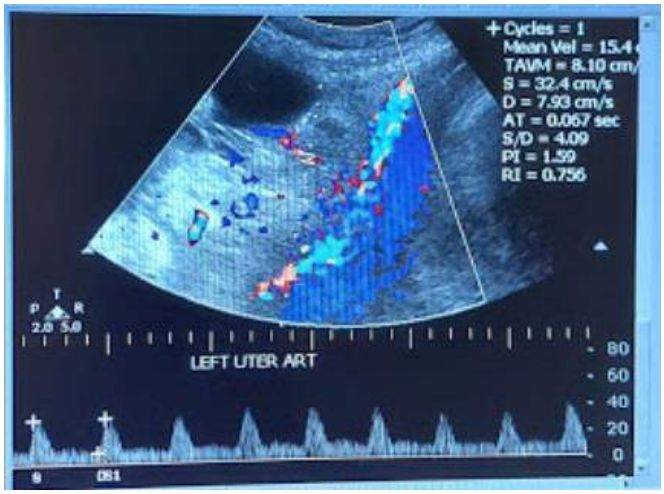
Table 4: Bivariate analysis of uterine artery Doppler indices and elevated liver transaminases

Laboratory parameter	Uterine artery Doppler parameter	Odds Ratios (95% CI)	P value
Abnormally elevated ALT	Abnormal Pulsatility Index	2.47 (0.3 - 115.95)	0.67
	Abnormal Resistive Index	10.35 (1.38 - 466.33)	**0.0113**
	Notching	9.52 (1.85 - 95.76)	**0.0017**
	Abnormal Uterine Score	2.74 (0.34 - 128.03)	0.45
Abnormally elevated AST	Abnormal Pulsatility Index	1.32 (0.14 - 65.18)	1
	Abnormal Resistive Index	2.15 (0.35 - 23.32)	0.46
	Notching	2.27 (0.41 - 15.82)	0.45
	Abnormal Uterine Score	1.47 (0.16 - 71.86)	1

Figure 7a and 7b shows uterine artery Doppler findings in a patient with severe preeclampsia who had an elevated ALT levels of 279 IU/L and elevated AST level of 346 IU/L indicative of hepatic dysfunction. The patient had an early right uterine notch. A notch was, however absent in the left uterine artery.



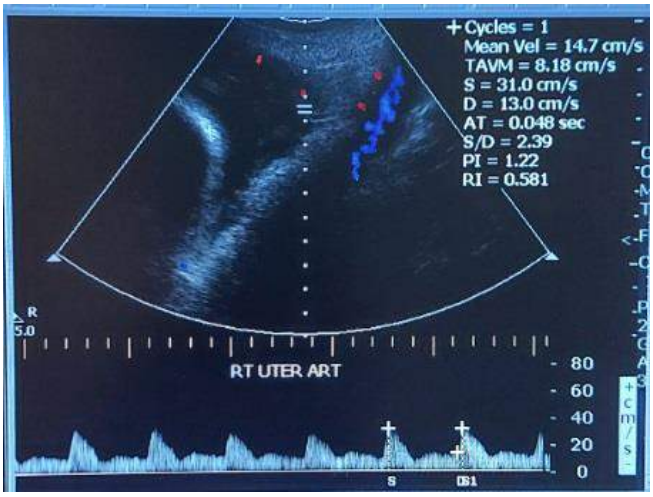
7a



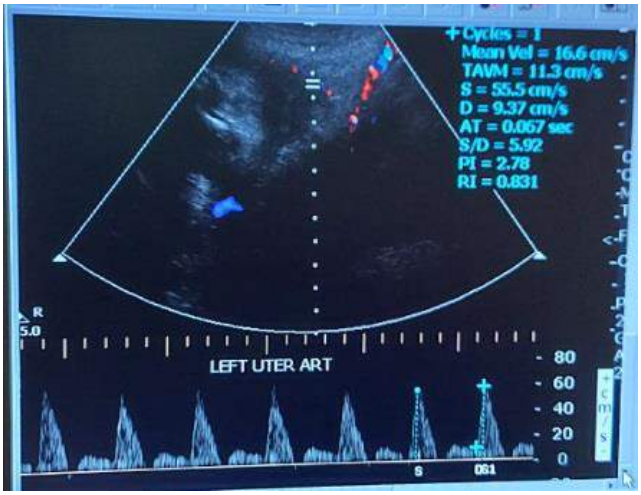
7b

Figure 7a and 7b showing right uterine artery notching and normal left uterine artery waveform in a patient with severe preeclampsia who had elevated AST and ALT levels.

Figure 8 demonstrates uterine artery Doppler findings in a patient with severe preeclampsia who had elevated left UtA RI above the 95th percentile and bilateral notching with markedly elevated AST and ALT levels (938IU/L and 687 IU/L respectively).



8a



8b

Figure 8a and 8b showing bilateral uterine artery notching in a patient with severe preeclampsia who had elevated AST and ALT levels.

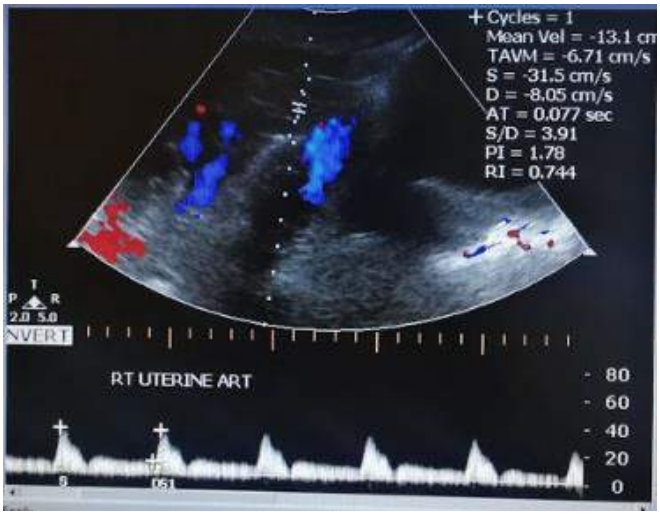
Bivariate analysis of the association between abnormal uterine artery Doppler findings and elevated serum creatinine

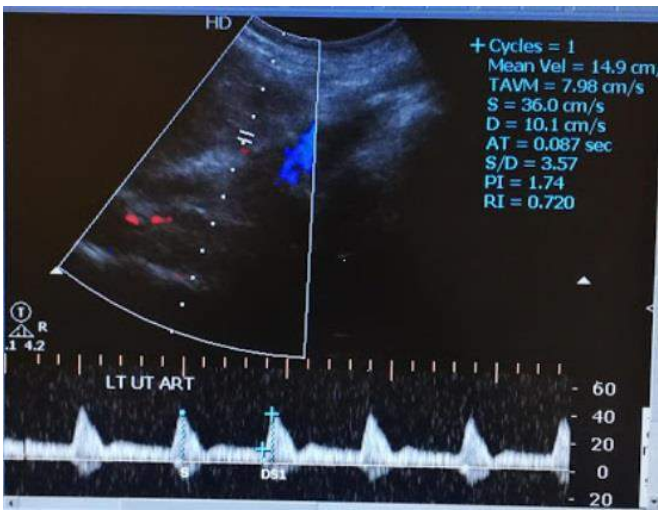
The presence of an abnormal notch in either uterine artery was significantly associated with abnormal creatinine levels (p value <0.05). however, no statistically significant relationship was found between elevated UtA PI, elevated UtA RI or an abnormal UtA score and elevated serum creatinine levels. These findings are summarized in table 5.

Table 5: Bivariate analysis of uterine artery Doppler indices and elevated serum creatinine

Laboratory parameter	Uterine artery Doppler parameter	Odds Ratios (95% CI)	P value
Elevated creatinine	Abnormal Pulsatility Index	1.13 (0.2 - 11.93)	1
	Abnormal Resistive Index	0.88 (0.23 - 3.47)	1
	Notching	6.22 (1.44 - 38.26)	**<0.05**
	Abnormal Uterine Score	1.27 (0.23 - 13.24)	1

Figure 9 shows uterine artery Doppler waveforms and indices in patient with bilateral uterine artery notching and elevated creatinine level of 151mmol/L.





9a 9b

Figure 9a and 9b showing bilateral uterine artery notching in a patient with severe preeclampsia who had elevated creatinine levels

Bivariate analysis of the association between abnormal uterine artery Doppler findings and thrombocytopenia.

In bivariate analysis, no significant association was established between abnormal uterine artery Doppler findings and thrombocytopenia. This is outlined in table 6.

Table 6: Bivariate analysis of uterine artery Doppler indices and thrombocytopenia

Laboratory parameter	Uterine artery Doppler parameter	Odds Ratios (95% CI)	P value
Thrombocytopenia	Abnormal Pulsatility Index	Inf (0.26 – Inf)	0.5878
	Abnormal Resistive Index	4.43 (0.5 - 213.54)	0.2313
	Notching	3.48 (0.52 - 38.95)	0.2304
	Abnormal Uterine Score	Inf (0.29 – Inf)	0.5947
Note: *An odds ratio of infinity means that the lists are highly dependent (not independent), as one is contained in other and therefore not suitable for fisher's exact test of independence .			

Multivariate analysis of the association of uterine artery Doppler findings and elevated liver transaminases

In multivariate analysis the findings were further analysed while adjusting for the mother's age, parity and previous history of preeclampsia.

After adjusting for these patient characteristics, the association between UtA notching, abnormal UtA RI and abnormally elevated ALT remained significant (OR 74.85, 95% CI 8.07 – 2035.35) and (OR 16.24, 95% CI 2.52 – 335.80) respectively. It was also established that multiparity was associated with a greater likelihood of abnormally elevated ALT and AST levels in patients with severe preeclampsia compared to nulliparity (p value= 0.004 and 0.005 respectively).

Table 7: multivariate analysis of uterine artery notching and abnormally elevated ALT

	Outcome = Abnormal ALT (n=13)	
	Odds Ratios (95% CI)	**p-value**
Uterine artery Notching	74.85 (8.07 – 2035.35)	**0.002**
Abnormal Resistive Index	16.24 (2.52 – 335.80)	**0.015**

Multivariate analysis of the association of uterine artery Doppler findings and elevated creatinine

After adjusting for maternal age, parity, previous history of preeclampsia, the association between uterine artery notching and creatinine remained significant (OR 6.15, 95% CI 1.56 – 32.44). The presence of a notch, whether single or double, was significant in predicting elevated creatinine levels. Prediction values for a single notch were (OR 8.89, 95% CI 1.97 – 49.00) while that for a double notch was (OR 4.76, 95% CI 1.04 – 25.76). No significant association was found between abnormal UtA PI, RI or scores and abnormal creatinine.

Table 8: multivariate analysis of uterine artery notching and elevated creatinine

	Outcome = elevated creatinine (n=14)	
	Odds Ratios (95% CI)	**p-value**
Uterine artery Notching	6.15 (1.56 – 32.44)	**0.016**

Comparison of uterine artery Doppler findings in early and late onset preeclampsia in pregnant women seen at Kenyatta National Hospital

When classified into early and late onset preeclampsia, higher percentages of abnormal uterine artery pulsatility indices, abnormal uterine artery resistive indices and abnormal uterine artery scores were seen in those with late onset preeclampsia. However, 24 (47.1%) patients with early onset preeclampsia had abnormal uterine artery notching compared to 10 (38.5%) who had late onset preeclampsia. Table 9 compares the frequencies and percentages of uterine artery parameters between patients with early onset and late onset preeclampsia.

Table 9: Differences in uterine artery Doppler parameters between early and late onset preeclampsia in women with severe preeclampsia at KNH

Variable	**Early onset (n=51)**		**Late onset (n=26)**	
	Normal	**Abnormal**	**Normal**	**abnormal**
Pulsatility index	10 (19.6%	41 (80.4%)	2 (7.7%)	24 (92.3%)
Resistive index	22 (43.1%)	29 (56.9%)	9 (34.6%)	17 (65.4%)
Notching[a]	27 (52.9%)	24 (47.1%)	16 (61.5%)	10 (38.5%)
Uterine artery score[b]	10 (19.6%)	41 (80.4%)	3 (11.5%)	23 (88.5%)

a- normal = no notch

b- abnormal uterine artery scores = score 1-4

Comparison of laboratory findings in early onset and late onset preeclampsia

The prevalence of abnormal laboratory parameters was higher in the group with early onset preeclampsia compared to those with late onset preeclampsia. All cases of thrombocytopenia were seen in patients with early onset preeclampsia. Table 10 summarises the frequencies of abnormal laboratory parameters seen in early and late onset preeclampsia.

Table 10: Frequency of abnormal laboratory values in patients with early onset and late onset preeclampsia in women with severe preeclampsia at KNH

	Elevated AST (n=8)	Elevated ALT (n=13)	Elevated Creatinine (n=14)	Thrombocytopenia (n=7)
Early onset preeclampsia	7 (13.7%)	11 (21.6%)	10 (19.6%)	7 (13.7%)
Late onset preeclampsia	1 (3.8%)	2 (7.7%)	4 (15.4%)	0 (0%)

The mean liver transaminases in the patients with early onset preeclampsia were higher than the upper limit of normal. The mean AST in this group was 79 (SD±150) while the mean AST in patients with late onset preeclampsia was normal at 35.2 (SD±20). The mean ALT in patients with early onset preeclampsia was 69.3 (SD±113.4) while that in patient with late onset preeclampsia was 33.4 (SD±17.9). This difference in means was found to be statistically significant (p value <0.001). Both groups had normal mean creatinine values with a mean of 96.8 (SD±61.1) in the early onset group and 92 (SD±43.23) in the group with late onset preeclampsia. Normal mean platelet values were also demonstrated in both groups with a mean of 211.4 (SD± 95.5) in early onset preeclampsia and 233 (SD± 53.7) in late onset preeclampsia.

DISCUSSION

Our study is among the first studies done in Africa to outline the use of uterine artery Doppler analysis in the assessment of, or prediction of liver dysfunction, renal dysfunction and thrombocytopenia in patients with severe preeclampsia. It sought to establish a relationship between uterine artery Doppler waveforms and indices, and abnormal laboratory in patients with severe preeclampsia. It also compared uterine artery Doppler and laboratory findings in patients with early onset preeclampsia and those with late onset preeclampsia.

The study demonstrates a significant correlation between elevated UtA resistive indices above the 95th percentile, the presence of a notch, and liver dysfunction. These findings support the hypothesis that inadequate transformation of spiral arteries that is seen in preeclampsia is associated with increased uterine artery resistance and the systemic vasospastic process contributes to liver injury by causing necrosis of hepatocytes(48,49). Our study showed that of the liver transaminases, the association between abnormal ALT levels and abnormal uterine artery Doppler findings was significant, while that of abnormal AST level was not significant. This could be explained by literature that reports that ALT is a more specific marker of hepatocyte injury compared to AST (48) since AST is found in other organs such as the heart and the kidney besides the liver(49).

An association between uterine artery notching and elevated creatinine levels was also seen. The presence of a notch reflects abnormal maternal vascular tone and raised uterine artery impedance (50) which is linked to elevated renal vascular resistance that is consistently seen in patients with preeclampsia(51). These results are comparable to studies that have shown that high uterine artery resistance is associated with an extensive systemic vasospastic process (36,54) and that persistence of uterine artery notching is associated with high vascular resistance, systemic endothelial damage, and ultimately renal dysfunction (53). We postulate that the glomerular capillary occlusion that occurs in severe preeclampsia (54) may also be associated with increased uterine artery impedance and notching.

The study showed that most of the patients presenting to Kenyatta National Hospital with severe preeclampsia have early onset preeclampsia. This finding is similar to another study conducted in KNH by Ndwiga et al (55) and an analysis carried out by Robillard et all that showed significantly high numbers of severe early onset preeclampsia in low income countries compared to high income countries (56). Our study also demonstrated that patients with early onset preeclampsia are more likely to have abnormal uterine artery findings, and they are also more likely to have higher liver transaminases and creatinine levels, and thus liver and renal dysfunction. Our data also suggests that thrombocytopenia is only seen in

patients with severe early onset preeclampsia. These findings support other studies that show that early and late onset preeclampsia are associated with different biochemical markers, clinical presentation and hemodynamic states (4) and high maternal morbidity rates (23). The findings are compatible with studies done by Meler (2010) and Gong (2012) which demonstrated that early onset preeclampsia is associated with a higher risk of maternal complications if abnormal uterine artery flow was present (39) and that hepatic dysfunction, renal dysfunction and thrombocytopenia are more likely to occur in patients with early onset severe preeclampsia (57). They also conform with the assertion that uterine artery Doppler studies principally identify the severe, early onset complications of defective placentation(58). Our findings were, however, in contrast to the findings by Weitzner et al which demonstrated that creatinine levels were not significantly different between patients with early and late onset preeclampsia(59).

Ancillary findings of the study were that majority of the patients presenting to KNH with severe preeclampsia were multiparous and not nulliparous women. Multiparous women also had a greater likelihood of having abnormal liver transaminases, abnormal platelet values and abnormal creatinine levels. This is in contradistinction to studies that have shown that nulliparity, and not multiparity, is a risk factor for preeclampsia (60,61) .

While previous studies have demonstrated a relationship between abnormal uterine artery Doppler findings and maternal and fetal outcome, this study goes a step further to demonstrate a relationship between abnormal Doppler notching and abnormally elevated liver transaminases and creatinine. This is, therefore, a significant addition and contribution to literature available on the use of uterine artery Doppler in patients with severe preeclampsia.

Our study, however has a few limitations. The presence of uterine artery notching is subjective and no uniform definition of the presence of a notch is available and this can lead to reader bias. This was, however, mitigated by reviewing the uterine artery Doppler tracing with a consultant radiologist experienced in obstetric sonography. The association between thrombocytopenia and elevated uterine artery pulsatility and resistive indices could also not be studied due to the small number of patients in the study who presented with thrombocytopenia. Our analysis also looked at the association between normal and abnormal (>95th percentile) uterine artery pulsatility indices but did not analyse the association between specific numerical values for the pulsality indices and abnormal laboratory parameters. This may be explored in further studies as uterine artery PI values are more objective than notching.

.

CONCLUSION

Based on the findings of this study, we concluded that the presence of a persistent uterine artery notch is associated with liver and renal dysfunction in patients with severe preeclampsia. Elevated uterine artery resistive indices are also associated with liver dysfunction. The presence of abnormal notching is also seen in more cases of early onset preeclampsia compared to late onset preeclampsia.

The findings of our study also suggest that multiparity is associated with an increased risk of elevated liver transaminases and thrombocytopenia in patients with severe preeclampsia.

While previous studies have demonstrated a relationship between abnormal uterine artery Doppler findings and maternal and fetal outcome, this study goes a step further to demonstrate a relationship between persistent uterine artery Doppler notching, abnormally elevated uterine artery resistive indices and abnormally elevated liver transaminases, and creatinine

This study done at Kenyatta National hospital builds on the existing evidence that uterine artery Doppler studies are a valuable resource in the assessment of complications in pregnant patients with severe preeclampsia.

RECOMMENDATIONS

Studies focussing on uterine artery Doppler correlation with abnormal laboratory parameters in patients with severe preeclampsia with a larger sample size are warranted in order to build up on the available data.

As demonstrated in this study, the presence of a persistent uterine artery notch in patients with severe preeclampsia is associated with an increased risk of liver and renal insufficiency. This is seen with greater frequency in those with early onset preeclampsia compared to those with late onset preeclampsia. We, therefore recommend that all patients on management for severe preeclampsia should have routine uterine artery Doppler evaluation included in their routine obstetric ultrasound scan.

We also recommend that multiparous patients with a diagnosis of severe preeclampsia and the presence of persistent uterine artery notching should be monitored closely with laboratory assessments for hepatic dysfunction and thrombocytopenia, as they are more likely to present with high liver transaminases and low platelet counts.

REFERENCES

1. Duley L. The Global Impact of Pre-eclampsia and Eclampsia. Vol. 33, Seminars in Perinatology. 2009. p. 130–7.

2. ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol. 2019 Jan 1;133(1):e1–25.

3. Pregnancy-Induced (ACOG) Hypertension in. Hype Rte N Sion. Hypertension in Pregnancy. 2013. 1-100. p.

4. Raymond D, Peterson E. A critical review of early-onset and late-onset preeclampsia. Vol. 66, Obstetrical and Gynecological Survey. 2011. p. 497–506.

5. Dolea C, Abouzahr C. Global burden of hypertensive disorders of pregnancy in the year 2000. Global Burden of Disease. 2000.

6. Osungbade KO, Ige OK. Public health perspectives of preeclampsia in developing countries: implication for health system strengthening. [Internet]. Vol. 2011, Journal of pregnancy. Hindawi Limited; 2011 [cited 2021 May 20]. p. 481095. Available from: /pmc/articles/PMC3087154/

7. Authors, Ayumba A, Ogutu O, Osoti A, Nyamai L, Ab; K, et al. HIGH PREVALENCE AND SEVERITY OF POSTPARTUM RETINOVASCULAR CHANGES FOLLOWING PRE-ECLAMPSIA WITH SEVERE FEATURES COMPARED TO NORMAL PREGNANCY.

8. Ndwiga C, Odwe G, Pooja S, Ogutu O, Osoti A, Warren CE. Clinical presentation and outcomes of preeclampsia and eclampsia at a national hospital, Kenya: A retrospective cohort study. PLoS One [Internet]. 2020 Jun 1 [cited 2021 May 20];15(6 June). Available from: /pmc/articles/PMC7274433/

9. Nankali A, Malek-Khosravi S, Zangeneh M, Rezaei M, Hemati Z, Kohzadi M. Maternal complications associated with severe preeclampsia. J Obstet Gynecol India. 2013 Apr;63(2):112–5.

10. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: A WHO systematic analysis. Lancet Glob Heal. 2014;2(6).

11. Ghulmiyyah L, Sibai B. Maternal Mortality From Preeclampsia/Eclampsia. Vol. 36, Seminars in Perinatology. 2012. p. 56–9.

12. Hodgins S. Pre-eclampsia as underlying cause for perinatal deaths: Time for action. Vol. 3, Global Health Science and Practice. Johns Hopkins University Press; 2015. p. 525–7.

13. Sotiriadis A, Hernandez-Andrade E, da Silva Costa F, Ghi T, Glanc P, Khalil A, et al. ISUOG Practice Guidelines: role of ultrasound in screening for and follow-up of pre-eclampsia. Ultrasound Obstet Gynecol. 2019 Jan 1;53(1):7–22.

14. Meler E, Figueras F, Mula R, Crispi F, Benassar M, Gómez O, et al. Prognostic role of uterine artery doppler in patients with preeclampsia. Fetal Diagn Ther [Internet]. 2010 Jan [cited 2019 Oct 3];27(1):8–13. Available from: https://www.karger.com/Article/FullText/258048

15. Owolabi O, Riley T, Juma K, Mutua M, Pleasure ZH, Amo-Adjei J, et al. Incidence of maternal near-miss in Kenya in 2018: findings from a nationally representative cross-sectional study in 54 referral hospitals. Sci Rep [Internet]. 2020;10(1):1–10. Available from: https://doi.org/10.1038/s41598-020-72144-x

16. Granger JP, Alexander BT, Llinas MT, Bennett WA, Khalil RA. Pathophysiology of preeclampsia: Linking placental ischemia/hypoxia with microvascular dysfunction. Vol. 9, Microcirculation. 2002. p. 147–60.

17. George EM, Granger JP. Recent insights into the pathophysiology of preeclampsia. Vol. 5, Expert Review of Obstetrics and Gynecology. 2010. p. 557–66.

18. Lyall F. The human placental bed revisited. Placenta. 2002;23(8–9):555–62.

19. Staff AC, Benton SJ, Von Dadelszen P, Roberts JM, Taylor RN, Powers RW, et al. Redefining preeclampsia using placenta-derived biomarkers. Vol. 61, Hypertension. 2013. p. 932–42.

20. Hypertension in pregnancy Quality standard [Internet]. 2013. Available from: www.nice.org.uk/guidance/qs35

21. Editorials R ISK F ACTORS FOR P REECLAMPSIA [Internet]. 2001 [cited 2019 Oct 24]. Available from: www.nejm.org

22. Hitti J, Sienas L, Walker S, Benedetti TJ, Easterling T. Contribution of hypertension to severe maternal morbidity. Am J Obstet Gynecol. 2018 Oct 1;219(4):405.e1-405.e7.

23. Gathiram P, Moodley J. pre-eclampsia: its pathogenesis and pathophysiolgy. Cardiovasc J AFRICA • [Internet]. [cited 2019 Oct 7];27(2):71–8. Available from: www.cvja.co.za

24. Lisonkova S, Sabr Y, Mayer C, Young C, Skoll A, Joseph KS. Maternal morbidity associated with early-onset and late-onset Preeclampsia. Obstet Gynecol. 2014 Oct 10;124(4):771–81.

25. Kongwattanakul K, Saksiriwuttho P, Chaiyarach S, Thepsuthammarat K. Incidence, characteristics, maternal complications, and perinatal outcomes associated with preeclampsia with severe features and hellp syndrome. Int J Womens Health. 2018;10:371–7.

26. Swende TZ, Abwa T. Reversible blindness in fulminating preeclampsia. Ann Afr Med. 2009 Sep 1;8(3):189–91.

27. Danso KA, Opare-Addo HS. Challenges associated with hypertensive disease during pregnancy in low-income countries. Int J Gynaecol Obstet [Internet]. 2010 Jul [cited 2019 Oct 26];110(1):78–81. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20362990

28. Edward Oburu N, Of Nairobi U. MATERNAL MORTALITY AT KENYATTA NATIONAL HOSPITAL (NAIROBI, KENYA) 2000-2008 A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT FOR THE DEGREE OF MASTER OF MEDICINE IN OBSTETRICS/GYNAECOLOGY OF THE UNIVERSITY OF NAIROBI BY. 2009.

29. Leslie MS, Briggs LA. Preeclampsia and the Risk of Future Vascular Disease and Mortality: A Review. J Midwifery Womens Health [Internet]. 2016 May 1 [cited 2020 May 13];61(3):315–24. Available from: http://doi.wiley.com/10.1111/jmwh.12469

30. Yildirim G, Güngördük K, Aslan H, Gül A, Bayraktar M, Ceylan Y. Preeklampsi, eklampsi ve HELLP sendromu olgularinda perinatal ve maternal sonuçlari{dotless}n karşi{dotless}laşti{dotless}ri{dotless}lmasi{dotless}. J Turkish Ger Gynecol Assoc. 2011;12(2):90–6.

31. Maria Suppo de Souza Rugolo L, Regina Bentlin M, Enoir Petean Trindade C, de Souza Rugolo S. Preeclampsia: Effect on the Fetus and Newborn [Internet]. Available from: http://neoreviews.aappublications.org/

32. Degner K, Magness RR, Shah DM. Establishment of the Human Uteroplacental Circulation: A Historical Perspective. Vol. 24, Reproductive Sciences. SAGE Publications Inc.; 2017. p. 753–61.

33. Sciscione AC, Hayes EJ. Uterine artery Doppler flow studies in obstetric practice. Am J Obstet Gynecol [Internet]. 2009 [cited 2019 Oct 27];201(2):121–6. Available from: http://dx.doi.org/10.1016/j.ajog.2009.03.027

34. Ertan AK, Taniverdi HA. Doppler Sonography in Obstetrics. Donald Sch J Ultrasound Obs Gynecol. 2013;7(2):128–48.

35. Gómez O, Figueras F, Fernández S, Bennasar M, Martínez JM, Puerto B, et al. Reference ranges for uterine artery mean pulsatility index at 11-41 weeks of gestation. Ultrasound Obstet Gynecol. 2008 Aug;32(2):128–32.

36. Digiacinto D, Graves M. Uterine Artery Doppler and Its Value in Predicting Preeclampsia.

37. Li H, Gudnason H, Olofsson P, Dubiel M, Gudmundsson S. Increased uterine artery vascular impedance is related to adverse outcome of pregnancy but is present in only one-third of late third-trimester pre-eclamptic women. Ultrasound Obstet Gynecol. 2005 May;25(5):459–63.

38. Maged AM, Elnassery N, Fouad M, Abdelhafiz A, Al Mostafa W. Third-trimester uterine artery Doppler measurement and maternal postpartum outcome among patients with severe pre-eclampsia. Int J Gynecol Obstet. 2015 Oct 1;131(1):49–53.

39. Meler E, Figueras F, Bennasar M, Gomez O, Crispi F, Gratacos E. The prognostic role of uterine artery Doppler investigation in patients with severe early-onset preeclampsia. Am J Obstet Gynecol. 2010;202(6):559.e1-559.e4.

40. Orabona R, Gerosa V, Gregorini ME, Pagani G, Prefumo F, Valcamonico A, et al. The prognostic role of various indices and ratios of Doppler velocimetry in patients with pre-eclampsia. Clin Exp Hypertens. 2015 Feb 1;37(1):57–62.

41. Pinto De Melo BC, De Amorim MMR, Katz L, Coutinho I, Verssimo G. Uterine artery doppler in the third trimester of pregnancy and postnatal outcome of patients with severe preeclampsia. Hypertens Pregnancy. 2010 May;29(2):135–47.

42. Sebire NJ. Routine uterine artery Doppler screening in twin pregnancies? Ultrasound Obstet Gynecol [Internet]. 2002 Dec 1 [cited 2020 May 4];20(6):532–4. Available from: http://doi.wiley.com/10.1046/j.1469-0705.2002.00856.x

43. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)-A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform [Internet]. 2009 Apr [cited 2021 Jun 4];42(2):377–81. Available from: /pmc/articles/PMC2700030/

44. R Core Team (2020). — European Environment Agency [Internet]. [cited 2021 Jun 4]. Available from: https://www.eea.europa.eu/data-and-maps/indicators/oxygen-consuming-substances-in-rivers/r-development-core-team-2006

45. Winters R, Winters A, Amedee RG. Statistics: A brief overview. Ochsner J [Internet]. 2010 [cited 2021 Jun 4];10(3):213–6. Available from: /pmc/articles/PMC3096219/

46. Hammoud GM, Ibdah JA. Preeclampsia-induced Liver Dysfunction, HELLP syndrome, and acute fatty liver of pregnancy [Internet]. Vol. 4, Clinical Liver Disease. John Wiley and Sons Inc.; 2014 [cited 2021 May 11]. p. 69–73. Available from: https://aasldpubs.onlinelibrary.wiley.com/doi/full/10.1002/cld.409

47. Brady CW. Liver Disease in Pregnancy: What's New. Hepatol Commun [Internet]. 2020 Feb 1 [cited 2021 May 11];4(2):145–56. Available from: https://aasldpubs.onlinelibrary.wiley.com/doi/full/10.1002/hep4.1470

48. Liver Enzyme - an overview | ScienceDirect Topics [Internet]. [cited 2021 May 11]. Available from: https://www.sciencedirect.com/topics/medicine-and-dentistry/liver-enzyme

49. Giannini EG, Testa R, Savarino V. Liver enzyme alteration: A guide for clinicians [Internet]. Vol. 172, CMAJ. Canadian Medical Association; 2005 [cited 2021 May 11]. p. 367–79. Available from: /pmc/articles/PMC545762/

50. Khong SL, Kane SC, Brennecke SP, Da Silva Costa F. First-trimester uterine artery doppler analysis in the prediction of later pregnancy complications. Dis Markers. 2015;2015.

51. Chesley's Hypertensive Disorders in Pregnancy - 4th Edition [Internet]. [cited 2021 May 16]. Available from: https://www.elsevier.com/books/chesleys-hypertensive-disorders-in-pregnancy/taylor/978-0-12-407866-6

52. Pachamuthu1 U, Dhanapal2 M, Subramanian3 V. Hypertensive Disorders of Disorders of Pregnancy, Foetal Growth Restriction, Uterine Artery Diastolic Notch. STUDY PERSISTENT UTERINE ARTERY DIASTOLIC NOTCH A Predict Hypertens Disord PREGNANCY FOETAL GROWTH Restrict. 2016;(11409).

53. Choi EK, Choi HM, Lee YH, Yoo YK, Cho JS, Park YW, et al. The Relationship of Early Diastolic Notch in Uterine Artery Doppler Velocimetry and the Renal Function of Patients with Pregnancy Induced Hypertension. Korean J Obstet Gynecol. 2001 Jan 1;41(1):191–9.

54. Moghaddas Sani H, Zununi Vahed S, Ardalan M. Preeclampsia: A close look at renal dysfunction. Vol. 109, Biomedicine and Pharmacotherapy. Elsevier Masson SAS; 2019. p. 408–16.

55. Ndwiga N, Ndwiga C, Alfred Osoti A dr., Sripad Pooja P dr., George Odwe G dr., Warren C dr. 104. The profile of early versus late onset preeclampsia-eclampsia at Kenyatta National Hospital: A retrospective cohort study. Pregnancy Hypertens. 2018

Oct;13:S75.

56. Robillard PY, Dekker G, Chaouat G, Elliot MG, Scioscia M. High incidence of early onset preeclampsia is probably the rule and not the exception worldwide. 20th anniversary of the reunion workshop. A summary. Vol. 133, Journal of Reproductive Immunology. Elsevier Ireland Ltd; 2019. p. 30–6.

57. Gong YH, Jia J, Lü DH, Dai L, Bai Y, Zhou R. Outcome and risk factors of early onset severe preeclampsia. Chin Med J (Engl). 2012;125(14):2623–7.

58. Lees C. Uterine artery Doppler: Time to establish the ground rules [Internet]. Vol. 16, Ultrasound in Obstetrics and Gynecology. John Wiley & Sons, Ltd; 2000 [cited 2021 May 16]. p. 607–9. Available from: https://obgyn.onlinelibrary.wiley.com/doi/full/10.1046/j.1469-0705.2000.00328.x

59. Wójtowicz A, Zembala-Szczerba M, Babczyk D, Kołodziejczyk-Pietruszka M, Lewaczyńska O, Huras H. Early-and Late-Onset Preeclampsia: A Comprehensive Cohort Study of Laboratory and Clinical Findings according to the New ISHHP Criteria. Int J Hypertens. 2019;2019.

60. Fox R, Kitt J, Leeson P, Aye CYL, Lewandowski AJ. Preeclampsia: Risk Factors, Diagnosis, Management, and the Cardiovascular Impact on the Offspring. J Clin Med [Internet]. 2019 Oct 4 [cited 2021 Jun 5];8(10):1625. Available from: /pmc/articles/PMC6832549/

61. Luo ZC, An N, Xu HR, Larante A, Audibert F, Fraser WD. The effects and mechanisms of primiparity on the risk of pre-eclampsia: A systematic review. In: Paediatric and Perinatal Epidemiology [Internet]. John Wiley & Sons, Ltd; 2007 [cited 2021 Jun 5]. p. 36–45. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-3016.2007.00836.x

APPENDICES

A. ELIGIBILITY CHECKLIST

THE ROLE OF UTERINE ARTERY DOPPLER AS AN ADJUNCT TO ABNORMAL LABORATORY PARAMETERS IN PATIENTS WITH SEVERE PREECLAMPSIA AT KNH

STUDY CHECKLIST

STUDY INFORMATION:

Research Committee protocol No. _____

Investigator: Dr. Martha Kitili_____

Study site: KNH_____

SUBJECT INFORMATION:

Age		
Pre-existing hypertension	**Absent ( )**	**Present ( )**
Pre-existing chronic renal disease	**Absent ( )**	**Present ( )**
Pre-existing diabetes mellitus	**Absent ( )**	**Present ( )**
Autoimmune disease	**Absent ( )**	**Present ( )**
	If present, which one _____	
No. of foetuses	**Singleton ( )**	**Multifetal ( )**
	No. of fetuses if >1:_____	

B. QUESTIONNAIRE

PATIENT CHARACTERISTICS	
Patient identifier (Serial number)	
Age	
Gestational age	
Parity	
Blood pressure at admission (mm/Hg)	
Proteinuria level:	
Right uterine artery Doppler parameters	RI- PI- Notch- absent ( ) or present ( )
Left uterine artery Doppler parameters	RI- PI- Notch- absent ( ) or present ( )
Uterine artery score	0 ( ) 3 ( ) 1 ( ) 4 ( ) 2 ( )
Laboratory Findings	Serum AST Level: _____ Serum ALT level: _____ Serum Creatinine level: _____ Platelet count: _____

C. PATIENT CONSENT FORM

PARTICIPANT INFORMED CONSENT FORM

FOR ENROLLMENT IN THE STUDY

Title of Study: THE ROLE OF UTERINE ARTERY DOPPLER VELOCIMETRY AS A PROGNOSTIC TOOL IN IN PATIENTS WITH SEVERE PREECLAMPSIA AT KENYATTA NATIONAL HOSPITAL

Principal Investigator\and institutional affiliation: DR. MARTHA KITILI (MMED, UON)

Co-Investigators and institutional affiliation: N/A

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in a medical research: i) Your decision to participate is entirely voluntary ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal
iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol No. _____

WHAT IS THIS STUDY ABOUT?

The researcher listed above is interviewing individuals who have been diagnosed with high blood pressure occurring in pregancy. The purpose of the interview is to find out whether there is a relationship between abnormal uterine artery Doppler findings and laboratory findings such as abnormal liver function, kidney function and platelet count. Participants in this research study will be asked questions about their age, their parity, last normal menstrual period, and preexisting medical condition (Diabetes mellitus, renal disease and antiphospholipid syndrome). Participants will also have the choice to undergo the uterine artery Doppler analysis.

There will be approximately 95participants in this study randomly chosen. We are asking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen: You will be interviewed by a trained interviewer in a private area where you feel comfortable
answering questions. The interview will last approximately 3 minutes, after which an
obstetric ultrasound and uterine artery Doppler analysis will be performed.
The ultrasound is expected to last 20-35 minutes.

After the interview and ultrasound is complete, we will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others. The reasons why we may need to contact you include: to follow up on any complications you may or may not develop.

ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

We will do everything we can to ensure that the ultrasound is done in private. Furthermore, all study staff and interviewers are professionals with special training in these examinations/interviews.

In case of an injury, illness or complications related to this study, contact the study staff right away at the number provided at the end of this document. The study staff will treat you for minor conditions or refer you when necessary.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

We will refer you to a hospital for care and support where necessary. Also, the information you provide will help us better understand whether there is a direct association of abnormal uterine artery findings and signs of severe preeclampsia. This information is a contribution to science and may assist in developing antenatal care protocols in at risk patients.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

No. The test will be conducted as part of a routine obstetric ultrasound will be charged at the standard KNH rates. There are no additional costs

WILL YOU GET REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?

There will be no refunds

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study:	**Yes**	**No**
I agree to have my uterine artery Doppler characteristics preserved for later study:	Yes	No
I agree to provide contact information for follow-up:	Yes	No

Participant printed name: _____

Participant signature / Thumb stamp _____ Date_____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name____Dr. Martha Ndanu Kitili_____ **Date**: _____

Signature _____

Role in the study:____Principle investigator____

Researcher's contacts:

Mobile number: 0725568527

Email address: marthandanu@gmail.com

Supervisor's Name:_____Dr. A. Aywak_____

Role in the study: LEAD SUPERVISOR

Supervisor's contacts:

Mobile number:

Email address:

Witness Printed Details

Name_____ **Signature /Thumb stamp: _____**

Contact information_____ **Date**: _____

D. KIBALI CHA MGONJWA

MAELEZO KUHUSU UTAFITI/WARAKA WA IDHINI

Kichwa cha Utafiti: THE ROLE OF UTERINE ARTERY DOPPLER VELOCIMETRY A PROGNOSTIC TOOL IN PATIENTS WITH SEVERE PREECLAMPSIA AT KENYATTA NATIONAL HOSPITAL

Mpelelezi mkuu \ na ushirika wa kitaasisi: DR. MARTHA KITILI (MMED, UON)

Wachunguzi wa ushirikiano na ushirika wa kitaasisi: N/A

Utangulizi:

Napenda kukuambia juu ya utafiti unaofanywa na watafiti waliotajwa hapo juu. Madhumuni ya fomu hii ya idhini ni kukupa habari utahitaji kukusaidia kuamua ikiwa sio mshiriki katika utafiti**..** Jisikie huru kuuliza maswali yoyote juu ya madhumuni ya utafiti, nini kinatokea ikiwa unashiriki katika utafiti, hatari na faida zinazowezekana, haki yako kama kujitolea, na kitu kingine chochote kuhusu utafiti au fomu hii ambayo haiko wazi**.** Wakati tumejibu maswali yako yote kwa kuridhika kwako, unaweza kuamua kuwa kwenye masomo au la. Utaratibu huu unaitwa 'ridhaa iliyo na habari'. Mara tu utakapoelewa na kukubali kuwa katika masomo, nitakuomba utie saini jina lako kwenye fomu hii. Unapaswa kuelewa kanuni za jumla zinazotumika kwa washiriki wote katika utafiti wa matibabu **:** i) Uamuzi wako wa kushiriki ni wa hiari kabisa

ii) Unaweza kujiondoa kutoka kwa masomo wakati wowote bila kutoa sababu ya kujiondoa kwako

iii) Kukataa kushiriki katika utafiti hakuathiri huduma unayostahiki katika kituo hiki cha afya au vifaa vingine. Tutakupa nakala ya fomu hii kwa rekodi zako.

Naweza kuendelea? NDIO/ LA

Utafiti huu umedhibitishwa na Itifaki ya Kamati ya Maadili ya Kitaifa ya Kenya ya Chuo Kikuu cha Maadili na Utafiti cha No. ___

UTAFITI HUU NI JUU YA NINI?

Mtafiti aliyeorodheshwa hapo juu anahoji watu ambao wamegunduliwa na preeclampsia kali. Madhumuni ya mahojiano ni kujua ikiwa kuna uhusiano kati ya matokeo ya usiokuwa ya kawaida ya artery Doppler na matokeo ya maabara kama vile kazi ya ini isiyo ya kawaida, utendaji wa figo na hesabu ya chembe.

Washiriki wa utafiti huu wataulizwa maswali juu ya umri wao, usawa wao, kipindi cha kawaida cha hedhi, na hali ya matibabu inayoenea (ugonjwa was sukari, ugonjwa wa figo, na antiphospholipid syndrome). Washiriki pia watakuwa na chaguo la kufanyiwa utafiti wa uterine artery Doppler.

Kutakuwa na washiriki takriban 95part katika utafiti huu waliochaguliwa kwa nasibu. Tunaomba idhini yako kufikiria kushiriki katika utafiti huu.

NINI ITAFANYIKA KAMA UTAKUBALI KUWA KATIKA FUNDO HILI LA UTAFITI?

Ikiwa unakubali kushiriki katika utafiti huu, mambo yafuatayo yatatokea:

Utahojiwa na mhojiwa aliyefunzwa katika eneo la kibinafsi ambapo unahisi raha kujibu maswali.

Mahojiano haya yatadumu takriban dakika 3, baada ya hapo uchambuzi wa kizuizi cha mkojo na njia ya kutuliza ya uterine itafanywa. Ultrasound inatarajiwa kudumu dakika 20-35.

Baada ya mahojiano na ultrasound imekamilika, tutauliza nambari ya simu ambapo tunaweza kuwasiliana nawe ikiwa ni lazima. Ikiwa unakubali kutoa habari yako ya mawasiliano, itatumiwa tu na watu wanaofanya kazi kwa utafiti huu na hautabadilishwa na wengine. Sababu ambazo tunaweza kuhitaji kuwasiliana nawe ni pamoja na: kufuata shida zozote ambazo unaweza au ambazo huwezi kuzipata.

JE KUNA ATHARI ZAIDI ZA UTAFITI HUU?

Utafiti wa matibabu una uwezo wa kuanzisha hatari za kisaikolojia, kijamii, kihemko na za mwili. Jaribio linapaswa kuwekwa kila wakati ili kupunguza hatari. Hatari moja ya kuwa katika masomo ni upotezaji wa faragha. Tutaweka kila kitu unachotwambia kama siri iwezekanavyo. Tutatumia nambari ya kukutambulisha katika hifadhi ya data ya kompyuta iliyolindwa na nywila na tutaweka rekodi zetu zote za karatasi katika baraza la mawaziri lililofungwa faili. Walakini, hakuna mfumo wa kulinda usiri wako unaweza kuwa salama kabisa, kwa hivyo bado inawezekana kwamba mtu angegundua kuwa ulikuwa kwenye utafiti huu na anaweza kupata habari juu yako.

Pia, kujibu maswali katika mahojiano inaweza kuwa mbaya kwako. Ikiwa kuna maswali ambayo hutaki kujibu, unaweza kuyaruka. Una haki ya kukataa mahojiano au maswali yoyote yaliyoulizwa wakati wa mahojiano.

Tutafanya kila tuwezalo kuhakikisha kuwa ultrasound inafanywa kwa faragha. Kwa kuongezea, wafanyikazi wote wa masomo na mahojiano ni wataalamu walio na mafunzo maalum katika mitihani / mahojiano haya.

Katika kesi ya jeraha, ugonjwa au shida zinazohusiana na utafiti huu, wasiliana na wafanyikazi wa utafiti mara moja kwa nambari iliyotolewa mwishoni mwa waraka huu. Wafanyikazi wa masomo watakutendea kwa hali ndogo au kukuelekeza wakati inahitajika.

JE! KUNA FAIDA ZOZOTE ZA KUPATA NDANI YA MASOMO HAYA?

Tutakuelekeza hospitalini kwa utunzaji na usaidizi inapohitajika. Pia, habari unayotoa itatusaidia kuelewa vizuri ikiwa tunaweza kutabiri shida zinazowezekana kwa wagonjwa walio na preeclampsia. Habari hii ni mchango kwa sayansi na inaweza kusaidia kukuza itifaki za utunzaji wa ujauzito kwa wagonjwa walio katika hatari.

JE! KUJISAJILI KATIKA UTAFITI HUU UTAKUGHARIMU PESA NGAPI?

Utafiti huu hautakugharimu pesa zaidi kuliko utakazolipa kufanya ultrasound ambayo daktari atakuwa amekuagizia. Gharam ya ultrasound ni ile ambayo KNH inalipisha.

JE! UTAREGESHEWA PESA AMBAZO UTAKUWA UMELIPIA ULTRASOUND UTAKAYO AGIZIWA NA DAKTARI?

Hakutakuwa na fidia

KAMA UNA MASWALI KATIKA SIKU ZA USONI?

Ikiwa una maswali zaidi au wasiwasi juu ya kushiriki katika utafiti huu, tafadhali piga simu au tuma ujumbe wa maandishi kwa wafanyikazi wa utafiti kwa nambari iliyotolewa chini ya ukurasa huu.

Kwa habari zaidi juu ya haki zako kama mshiriki wa utafiti unaweza kuwasiliana na Katibu / Mwenyekiti, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 barua pepe uonknh_erc@uonbi.ac.ke.

Wafanyikazi wa masomo watakulipa kwa malipo yako kwa nambari hizi ikiwa simu ni ya mawasiliano yanayohusiana na masomo.

UNA CHAGUZI ZINGINE ZIPI?

Uamuzi wako wa kushiriki katika utafiti ni wa hiari. Uko huru kukataa kushiriki katika masomo na unaweza kujiondoa kwenye masomo wakati wowote bila ukosefu wa haki au upotezaji wa faida yoyote.

TAARIFA YA IDHINI

Taarifa ya Mshiriki

Nimesoma fomu hii ya idhini au nimesomewa. Nimepata nafasi ya kujadili utafiti huu na mshauri wa masomo. Nimepata maswali yangu kujibiwa kwa lugha ambayo naelewa. Pia nimeelezewa hatari na faida za utafiti huu. Ninaelewa kuwa ushiriki wangu katika utafiti huu ni wa hiari na kwamba naweza kuchagua kujiondoa wakati wowote. Nakubali kwa bure kushiriki katika utafiti huu.

Ninaelewa kuwa juhudi zote zitafanywa kuweka habari kuhusu utambulisho wangu siri.

Kwa kusaini fomu hii ya idhini, sijapeana haki yoyote ya kisheria ambayo mimi kama mshiriki wa utafiti wa utafiti.

Ninakubali kushiriki katika utafiti huu: Ndio La

Ninakubali kuhifadhiwa sifa zangu za uterine

artery Doppler kwa masomo ya baadaye: Ndio La

Ninakubali kutoa habari ya mawasiliano kwa kufuata Ndio La

Jina la Mshiriki lililochapishwa _____

Saini ya mshiriki/ kuchapa kwa kidole _____ Tarehe_____

Taarifa ya mtafiti

Mimi, aliyetengwa, nimeelezea kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki aliyetajwa hapo juu na ninaamini kwamba mshiriki ameelewa na ametoa ridhaa yake kwa hiari na kwa hiari yake.

Jina la mtafiti____DR. MARTHA NDANU KITILI **Tarehe_____**

Saini _____

Jukumu katika masomo: _MTAFITI MKUU

Anwani za mtafiti:

Namba ya simu ya mkononi: 0725568527 Barua pepe: marthandanu@gmail.com

Jina la Msimamizi: DR. ANGELINE AYWAK

Jukumu katika masomo: MSIMAMIZI MKUU

Anwani za mtafiti:

Namba ya simu ya mkononi: 0722200803 **Barua pepe: angeline.aywak@uonbi.ac.ke**

Maelezeo ya shahidi

Jina_____ Habari ya mawasiliano_____

Saini ya mshiriki/ kuchapa kwa kidole _____ Tarehe_____