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DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

POSTPARTUM RETINOVASCULAR FINDINGS AMONG WOMEN HAVING PRE ECLAMPSIA WITH SEVERE FEATURES COMPARED TO NORMAL PREGNANCY AT KENYATTA NATIONAL HOSPITAL

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2018

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DEDICATION

This work is dedicated to Mrs. Viewlance Machocho Mwachanya and Ms. Amara Machocho.

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Abstract

Background

Hypertensive disorders in pregnancy (HDP) complicate approximately 10 % of pregnancies and 2-8% of this is attributable to pre-eclampsia-eclampsia. The global burden of HDP remains high, it is estimated to contribute to 14% of direct obstetric causes of maternal deaths comparable to 16% in sub-Saharan Africa. Hypertensive retinopathy complicates about 40-100% of pregnancies with hypertensive disorders and its severity worsens with progression of hypertension.

Reactive retinal vessel changes mirror cardiovascular changes in the course of normal pregnancy. Retinal vessel changes are thought to compare with placental vasculature changes and where severe changes are noted, it may indicate placental insufficiency. There are limited studies on the utility of fundoscopy in assessing target organ damage and prognosis in pre-eclampsia in low resource settings. Explorative data on the association between retinovascular changes and umbilical artery Doppler studies can be useful in predicting clinically relevant placental site changes and fetal outcomes.

Objectives

To compare postpartum maternal retinovascular (RV) findings between pregnancies complicated with preeclampsia with severe features (PES) and normal pregnancies at Kenyatta National Hospital (KNH).

Methods

A comparative cross sectional study was conducted between May 2017 and March 2018.The study was conducted in KNH, a regional Teaching and Referral hospital. Sixty five women within 72 hours postpartum following pregnancies complicated with PES (n=30) or normal pregnancy (n=35) and without preexisting ocular or medical cormobidities were interviewed on sociodemographic and reproductive health characteristics and clinical parameters obtained from medical records. Visual acuity assessment was done using a portable LogMAR chart and non mydriatic fundus photography used for retinovascular evaluation. RV changes were graded using Keith Wagner grading.

Postpartum retinovascular findings and severity grades were analyzed and presented as percentages and compared between the two groups using Chi square or Fisher's exact test. Odds ratios (OR) of retinovascular changes following pre-eclampsia compared to normal pregnancy was estimated. A p value of <0.05 and 95% confidence interval (CI) that doesn't include the null value were considered significant.

Results

Overall prevalence of hypertensive retinovascular change was 90.8 %(83.3% in PES versus 97.1% in normal pregnancies.). We found statistically significantly greater odds, OR 5.05 CI (0.93, 27.6) of severe retinovascular changes after pregnancies complicated with PES (p=0.045).

Conclusion

There prevalence of maternal retinovascular changes within 72 hours postpartum was high after both pregnancies complicated with PES and normal pregnancy, but not statistically significant difference noted. PES was associated with greater odds of severe postpartum retinovascular changes compared to normal pregnancy.

Recommendation

The high prevalence of RV changes depicts the need for larger prospective studies to assess disease progression and long term effects. Sensitize caregivers on eye disease in HDP.

Abbreviations

ACOG	American College of Obstetricians and Gynecologists
DIC	Disseminated Intravascular Coagulation.
HELLP	Hemolysis Elevated liver enzymes Low platelets.
HIF	Hypoxia Inducible Factor
ISSHP	International Society for the Study of Hypertension
KNH	Kenyatta National Hospital
KOGS	Kenya Obstetrical and Gynecological Society
NICU	Neonatal Intensive Care Unit
NK	Natural Killer
PIGF	Platelet Growth Factor
RAAS	Renin Angiotensin Aldosterone System
RI	Resistive Index
RV	Retinovascular
Sflt	Soluble fms-like tyrosine kinase
SPET	Severe Preeclampsia
TGF-B	Transforming Growth Factor Beta
TNF-α	Tumor Necrosis Factor Alpha

VEGF Vascular Endothelial Growth Factor

VEGFR-1 Vascular Endothelial Growth Factor Receptor 1

WHO World Health organization

PES Pre eclampsia with severe features

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CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

1.1: Introduction

Overall, HDP occurs in about 10% of all pregnancies and of this; 2-8% is due to pre-eclampsia and eclampsia(1). A World Health Organization (WHO) multicountry survey reports a country (Kenya) incidence of pre-eclampsia of 1.97% while a retrospective review at Kenyatta National Hospital in 2004 reported the incidence of hypertensive disorders in pregnancy at 6.5%,55% of which was pre-eclampsia and 37% was eclampsia (2,3).

Preeclampsia and eclampsia are still major causes of maternal and perinatal morbidity and mortality. Globally, it is estimated that 14% of direct obstetric causes of maternal deaths is due to hypertensive diseases of pregnancy (4) (5), which also compares to the sub Saharan region estimate of 16%.In 2015, 666 cases of pre eclampsia were admitted at Kenyatta National Hospital with a case fatality rate of 2.3%.

In the setting of hypertension, 40-100% of women in pregnancy develop hypertensive retinopathy and its severity directly correlates with severe forms of hypertensive disease in pregnancy. Eclampsia is especially associated with greater severity which can lead to cortical blindness with anterior optic neuropathy being rare. This is despite of only 25- 50 % being symptomatic i.e. having blurred vision and visual field defects. Although the retinal vessels are most commonly affected, other structures that may be affected include; the choroid, optic nerve, visual cortex and conjunctiva. The most common retinal vessel change is terminal arteriolar vasospasm and is with occurrence of systemic hypertension (6).

The fundus provides a good site for visualization of vessels i.e. retinal vessels. Changes in the retinal arterioles may indirectly reflect the state in the placental vasculature and fetal status (7). Retinal vascular changes once noted require further diagnostic and therapeutic measures. Notably, there are no fundoscopically visible changes reported with the retinal vessels in the course of normal pregnancy (6).However Samantha et al demonstrated arteriolar and venular caliber changes in tandem with blood pressure changes during the course of normal healthy pregnancy. Retinal vascular dilatation supports the hypothesized concept that peripheral vasodilatation tempers the increased cardiac output and circulatory volume. This was thought to be due to the increase in vasodilatory molecules e.g. nitric oxide, prostacyclin and prostaglandins in healthy pregnancy and also increased resistance to vasopressors e.g. Angiotensin 2 (8).

The fundus provides a unique site to study micro vascular changes making fundoscopic examination useful in assessing disease progression. The most common finding is arteriolar attenuation but serious ocular lesions can also occur including central retinal vein occlusion, acute ischemic optic neuropathy (AION), retinal detachment, retinal arteriole occlusion, macula tear, choroidal ischemia and central serous retinopathy (9).

The evaluation and management should be undertaken by an all-inclusive team in order to decrease maternal-fetal risks and improve on disease prognosis.

In order to characterize the clearly visible retinal changes in postpartum women having PES (pre eclampsia with severe features) compared to physiological findings in normotensive women, we conducted an analytical cross sectional study at Kenyatta National Hospital, Nairobi Kenya.

1.2: Literature review

1.2.1: Definition

The World Health Organization (WHO) observes that there are controversies and uncertainties in screening, diagnosis, management and severity classification of severe preeclampsia. General consensus however is that new onset hypertension in pregnancy (with persistent diastolic blood pressure >90 mm Hg) with existing substantial proteinuria (>0.3 g/24 h) can be used as criteria for identifying pre-eclampsia. Preeclampsia is mostly graded as mild or severe (10). Severe grading is when any of the following is present: severe range hypertension (> 160/110mmhg), heavy proteinuria (>1g/liter) or substantial maternal end organ dysfunction e.g. renal or liver insufficiency (11).

The International Society for the Study of Hypertension (ISSHP) 2014 defines pre-eclampsia as new episode of hypertension, blood pressure greater than or equal to, 140mmhg/90mmhg with one or more of: Proteinuria (24hour urine protein > 300mg/ day, protein/creatinine ratio 0.3, dipstick proteinuria especially with values greater than 1 g/dl (2+), renal insufficiency (creatinine >90 umol/L), liver impairment (elevated transaminases and/or severe right upper quadrant or epigastric pain), neurological dysfunction (e.g. eclampsia, altered mental status, blindness, stroke, or more commonly hyperreflexia, severe headaches, persistent visual scotomata), uteroplacental dysfunction (fetal growth restriction), hematological complications (thrombocytopenia, DIC, hemolysis) (12). The ISSHP guide does not clinically distinguish between early onset and late onset pre-eclampsia, mild and severe pre-eclampsia. Instead the condition should be regarded as that which can evolve to a life threatening one at any time to both the mother and the baby.

The American College of Obstetricians and Gynecologists (ACOG) classifies pre-eclampsia into pre-eclampsia without severe features and pre-eclampsia with severe features (PES). Severe features of pre-eclampsia include: Blood pressure equal to or greater than 160/110mmhg, thrombocytopenia, platelet count <100000 / ul, progressive renal insufficiency, pulmonary edema, impaired liver, cerebral and visual functions. Eclampsia is defined as new onset grand mal seizures in a woman with pre-eclampsia.

Even though visual symptomatology is a recognized feature of severity in pre-eclampsia, no precise recommendation is provided for diagnosis and follows up of these patients.

1.2.2: Aetiology and pathogenesis

The pathophysiologic mechanism of pre-eclampsia remains largely speculative. It is hypothesized that a defective placentation due to inadequate trophoblastic invasion leads to release of factors that cause widespread micro vascular endothelial dysfunction, proteinuria and hypertension.

The placental derived factors implicated include; tumor necrosis factor alpha (TNF-α), homocysteine, soluble Fas ligand, oxidized lipid products, anti-phospholipid antibodies, neurokinin B, soluble endoglin and soluble fms-like tyrosine kinase (Sflt). Neither the primary trigger nor the molecular mechanism of abnormal placental development is known. Placental hypoxia is thought to be an early event and an important regulator in this process (13) (14).

Recent advances have been made in trying to fully understand the role of the anti-angiogenic factors in placental development and trophoblastic invasion. Excessive oxidative stress, inflammation, immune maladaptation, alteration of renin angiotensin-aldosterone system

(RAAS) and genetic susceptibility are additional factors that contribute to pathogenesis of pre-eclampsia (15).

Placental development and angiogenic imbalance

During placental development, cytotrophoblasts invade maternal spiral arteries in the decidua and myometrium thus transforming them to low resistance, high caliber capacitance vessels thus enabling adequate perfusion. In pre-eclampsia, the cytotrophoblastic invasion is only up to the decidua-myometrial junction. Altered signaling and regulation during the angiogenic process may lead to incomplete cytotrophoblastic invasion.

Invasive cytotrophoblasts express vascular endothelial growth factor (VEGF), platelet growth factor (PIGF), vascular endothelial growth factor receptor 1 (VEGFR-1or Sflt) Their expression is altered in pre-eclampsia as depicted in immunohistochemistry studies.VEGF is essential in angiogenesis and vasodilatation. Soluble fms tyrosine like kinase 1 (SFlt1) antagonizes the actions of VGEF and PGIF and has been shown in vitro to decrease placental invasiveness. Soluble transforming growth factor beta (TGF-B) co receptor (soluble endoglin) inhibits angiogenesis and causes increased capillary permeability and hypertension (13–15).Several investigators have shown that there is increased level of Sflt in women with pre-eclampsia (16,17).

Placental hypoxia and ischemia

While partial remodeling of uterine spiral arteries due to incomplete cytotrophoblastic invasion is a known causal mechanism of pre-eclampsia, it is unknown whether placental hypoxia and ischemia results from or causes pre- eclampsia. In pre-eclampsia, hypoxia inducible factor (HIF)

alters the expression of angiogenic factors.VEGFR-2, sFLt-1, Tie-1, Tie-2 and TGF B3 are targets of HIF-1 regulation (18).

Primarily, trophoblast invasion is key to successful placental development and progression of pregnancy. Placenta hypoxia and ischemia resultant from inadequate placentation is perhaps an important sequelae.

Renin-angiotensin-aldosterone system (RAAS)

In normal pregnancy, plasma levels of angiotensin and aldosterone are increased. In preeclampsia the RAAS is suppressed with an increased sensitivity to the vasoactive peptide angiotensin 2 and other vasoconstrictors compared to normal pregnancies (19). Angiotensin 2 hypersensitivity may be due to formation of angiotensin auto antibodies that activate angiotensin receptors.

Immunologic/ Inflammatory alterations

The gravid uterus is immunologically privileged and allows development of the fetal-placental unit. Maladaptation of the immune system is an important contributing factor to inadequate invasion by the cytotrophoblasts. Women who are immune suppressed from untreated immunodeficiency virus have a lower incidence of preeclampsia compared to the general population (20).

A significant level of chemokines, macrophages, and dendritic cells at placentas with preeclampsia is consistent with the theory of inflammation causing immune maladaptation thus impaired trophoblast invasion. Natural Killer (NK) cells present at the maternal-fetal interface

are thought to contribute to the pathogenesis of preeclampsia possibly due to the role in vascular remodeling..

Oxidative stress

One of the mechanisms for impaired placentation may be oxidative stress in the placenta. The production of free radicals contributes to vascular conditions such as atherosclerosis and is therefore thought to contribute to placental atherosis. Markers of high oxidative stress in preeclampsia include high levels of lipid peroxidation, increased superoxide and isoprostane generation (21).

Genetics

A strong paternal component is suggested in studies. Fathers to a pre-eclamptic pregnancy had an increased risk of fathering a similar pregnancy despite change of partner (15). After controlling for body mass index, age and smoking status, women's risk of severe preeclampsia increased two- to four times with the presence of pre-eclampsia in a first-degree relative (22).

Maternal endothelial dysfunction

Vasopressive substances released from the diseased placenta probably causes widespread endothelial damage. In pre-eclamptic women, the following serum markers of endothelial activation and dysfunction are deranged: Von Willebrand antigen, soluble E-selectin, platelet derived growth factor, endothelin and cellular fibronectin. Systemic vasoconstriction that ensues and exaggerated sensitivity to vasopressors like angiotensin 2 and norepinephrine contribute to the increase in blood pressure (15).

1.2.3: Retinal vessel changes

The etiopathologic process of micro vascular changes is that of vascular endothelial dysfunction i.e. vasospasm and capillary leakage. Retinal, choroidal and optic nerve head vasculature are affected (23). It is estimated that 40 to 100% of pregnancies complicated with hypertensive disease have retinal changes which correlate with the severity of hypertension (6).

Tadin et al found 45% of pre-eclamptic patients had opthamoscopically verified hypertensive retinopathy according to the Keith–Wagner classification (KW) (24). Forty women were analyzed retrospectively: ten had grade I, six had grade II and two had grade III. The four grades as per the KW classification include:

Box 1. Keith Wagner Grading

Grade 1:- Mild generalized arterial attenuation, especially of terminal branches
Grade 2:- More severe Grade 1 + focal arteriolar attenuation
Grade 3:- Grade 2 + hemorrhage, cotton wool spots, hard exudate, macula & retinal edema.
Grade 4:- Grade 3+ optic disc swelling (papilloedema)

Bhandari et al reported ocular fundus changes in 44% of patients with pregnancy induced hypertension (25), no residual changes were observed up to a week post delivery. In the hospital based prospective observational study, more changes were seen in eclampsia (61%) than severe pre-eclampsia (50%) and mild pre-eclampsia (25%). 32% had Grade I retinal vascular changes. 8% had Grade II and 4% had III retinal vascular changes. Macular edema was seen in 4% of cases. A prospective cross-sectional study at a tertiary University hospital (Burkina Faso) found that hypertensive retinal changes were present in 26% of those who suffered from eclampsia / pre-eclampsia (26). In 1991 a descriptive study at KNH reported 60% occurrence of ocular

fundus changes in the left eye and 58% in the right eye in pre-eclampsia, eclampsia patients (27).The study recommended photo-documentation of fundus findings for all patients studied to ensure standardization of findings.

EVALUATION OF RETINOVASCULAR CHANGES

Fundoscopy helps not only to make a diagnosis but also assess severity, progression and response to treatment especially with repeated examinations. Non mydriatic digital fundus imaging is both a sensitive and specific screening and diagnostic tool for diabetic retinopathy (28) (29). Ahmed et al (29), in determining the sensitivity and specificity of digital imaging for diabetic retinopathy screening, found an agreement of 86% in retinopathy grading between non mydriatic digital imaging and dilated fundus examination. In a comparative study of fundal photography modalities, the non mydriatic modality was more sensitive to smart phone photography in detecting diabetic retinopathy (30).

Ocular fundus imaging can easily characterize fundus changes particularly with the retinal vessels that depict hypertensive effects on systemic vascular system. The clinical course of fundal changes can be divided into three stages:

Spasm of retinal arterioles

Constriction of the arteriolar lumen is the earliest change seen on normal arterioles. It can be focal, multifocal or it can be generalized. Addition of varying degrees of localized constrictions in patients with generalized constrictions suggests an active disease process. Spastic arteriolar constrictions are proved when there is variation in location and degree with subsequent examinations. Prompt diagnosis and management of angiospastic changes may prevent development of retinopathy and generalized progression of the illness. The most common retinovascular change is arteriolar spasm occurring in about 70% of pre eclampsia cases (23)

Arteriolar spasm superimposed on arteriolar sclerosis

The main signs of retinal vasculosclerosis are arterio-venous nicking, focal narrowing of retinal vessels and generalized arteriolar attenuation which may be associated with straightening of the arterioles. Decreased translucency of vessel walls, vascular sheathing and reflex changes are less significant clinical signs when occurring without the main signs.

Stage of retinopathy

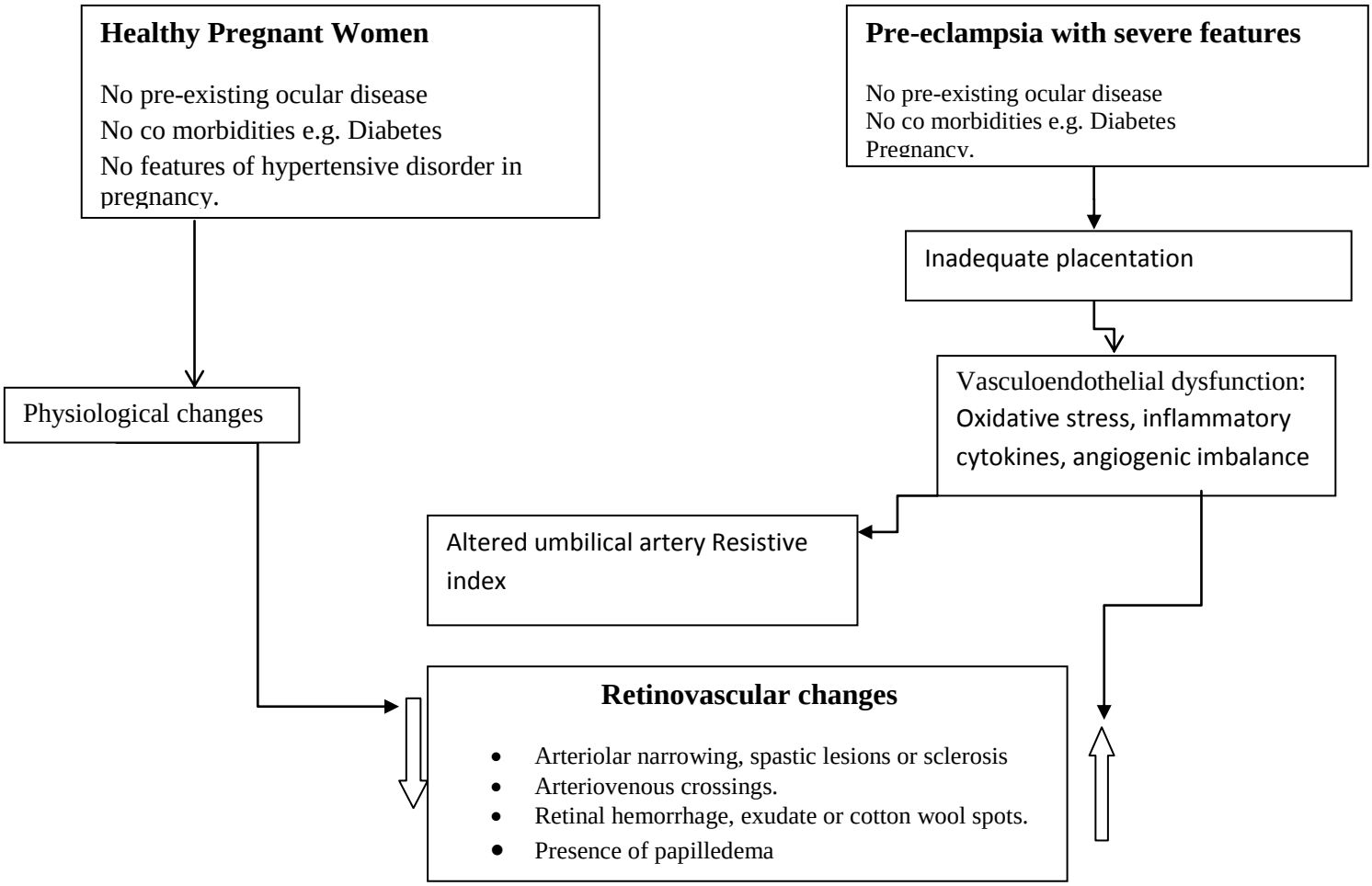
This is seen in case of continued constriction of retinal arterioles and manifests with retinal edema, retinal hemorrhages and exudates. With increasing severity of hypertension and vasospasm, papilloedema develops. Other complications that can manifest include optic atrophy/neuritis, transient cortical blindness, central retinal artery thrombosis, , proliferative retinopathy, choroidal infarcts, purtscher like retinopathy, occlusion of the retinal artery and vein, ischemic optic neuropathy and paralysis of extra ocular muscles.

Significant correlation has been demonstrated between severity of hypertension and hypertensive retinopathy (7) (24). Therefore hypertensive retinopathy directly correlates with severity of hypertension making fundoscopic examination a valuable tool in diagnosis. Progressive worsening of retinovascular changes is considered in many studies as a sign of increasing severity of hypertensive disorders in pregnancy and adverse fetal outcomes (6,9,24,25). Severe retinovascular changes necessitates timely delivery to balance optimum maternal visual function vis a vis chance of survival for the newborn (6). Placental status i.e. placental insufficiency and low birth weight could indirectly be indicated by retinal changes in preeclampsia (31). A case reported of PES before 20 weeks of gestation described papilloedema on fundoscopic exam and a concurrent Doppler study showed umbilical resistive index reading of 0.84.Her condition deteriorated further and there was absence of end diastolic flow on repeat Doppler necessitating

termination of the pregnancy (32). Doppler studies of the umbilical artery provide useful information on status of placental vascular impedance. It has also been shown to be an early and more sensitive marker of intrauterine fetal compromise than biophysical profile scoring (33,34).

1.2.4: Conceptual framework.

Pre-eclampsia with severe features has been associated with retinal vascular changes due to systemic maternal vascular endothelial dysfunction (vasospasm and capillary leak). The changes are progressive from retinal arteriolar constriction, vasculosclerosis to retinopathy that manifests as retinal edema, hemorrhages and exudates which can also result in papilledema. Healthy pregnant women could have physiologic retinovascular changes but is reported not to be prominent as in cases of pre-eclampsia with severe features. An evaluation of key predictable variables based on fundoscopic examination in pre-eclamptic patients with severe features and healthy pregnant women will help in describing the pathophysiologic relationship between pre-eclampsia with severe disease and the fundoscopic features. This model assumes that the presence and severity of pre- eclampsia has a modulatory role in retinovascular changes as observed in ocular disease in pre-eclampsia. Gallani et al, applied such a model to demonstrate how modifiable factors such as exercise, nutrition, medication therapy adherence have a causal relationship with cardiovascular risk factors and ultimately with severe hypertensive features (blood pressure levels, target organ damage) (35).


Healthy Pregnant Women
No pre-existing ocular disease
No co morbidities e.g. Diabetes
No features of hypertensive disorder in pregnancy.
Pre-eclampsia with severe features
No pre-existing ocular disease
No co morbidities e.g. Diabetes
Pregnancy.
Inadequate placentation
Vasculoendothelial dysfunction: Oxidative stress, inflammatory cytokines, angiogenic imbalance
Physiological changes
Altered umbilical artery Resistive index
Retinovascular changes
Arteriolar narrowing, spastic lesions or sclerosis
Arteriovenous crossings.
Retinal hemorrhage, exudate or cotton wool spots.
Presence of papilledema

1.3: Justification.

Pre-eclampsia/eclampsia is a multisystemic disease with end organ complications. It may result in sudden onset and chronic maternal and fetal complications including retinal injury. New onset cerebral and visual disturbances is among the criterion for diagnosis of pre-eclampsia with severe features (36). Review articles estimate that 25% of pre-eclampsia patients and 50% of eclampsia patients report visual symptoms (6) (23).

A correlation between the severity of hypertension and ocular vascular changes has been found and is applied as a predictive indicator for adverse fetal and maternal outcomes and termination of pregnancy (6,24). Bhandari et al in an observational study reported higher grades of retinal changes in patients having preeclampsia with severe features and thus recommended ocular examinations in each and every patient with preeclampsia and eclampsia (25).The vascular changes can persist up to 6 weeks post-delivery and arteriolar vasoconstriction may remain as a permanent feature of preeclampsia (37).

This study intends to compare physiological ocular fundus changes with pathological findings in patients with preeclampsia with severe features. Findings will provide baseline information on the prevalence of these changes in the local setting. Explorative data on the association between retinovascular changes and umbilical artery Doppler studies can be useful in predicting clinically relevant placental site changes and fetal outcomes.

1.4: Research question

Is there a difference in postpartum maternal retinovascular findings between pregnancies complicated with preeclampsia with severe features and normal pregnancies at Kenyatta National Hospital in the year 2016/2017?

1.5: Objectives.

1.5.1: Broad objective

To compare postpartum maternal retinovascular findings in women having preeclampsia with severe features with that of normal pregnant women at Kenyatta National Hospital.

1.5.2: Specific objectives

a) To compare the prevalence of abnormal postpartum maternal retinovascular findings between pregnancies complicated with pre eclampsia with severe features versus normal pregnancies at Kenyatta National Hospital.

b) To compare the severity of postpartum maternal retinovascular findings between those having pre-eclampsia with severe features and normal pregnant women at Kenyatta National Hospital.

c) To determine the association between maternal retinovascular findings with antenatal umbilical Doppler studies in the subset of women having pre eclampsia with severe features.

CHAPTER 2: METHODOLOGY

2.1: Study design.

We conducted an analytical cross sectional study. Variables measured included independent (pre-eclampsia/eclampsia versus none) and dependent variables (retinovascular changes versus none) in the immediate postpartum period at one time point (within 72 hours post delivery). This comparison allowed for evaluation of whether the exposure to preeclampsia with severe features

had any statistically significant association with retinovascular changes. This design provided invaluable explorative data and was less costly.

2.2: Study Site and setting.

The study was conducted at Kenyatta National Hospital postnatal wards**.** KNH is the largest national teaching and referral hospital in Kenya. It provides both low-risk and high-risk antenatal and postnatal care services. It receives patients with severe forms of disease. Each month there are about 1700 deliveries at KNH. The post delivery setting provided a suitable environment for recruitment and evaluation of study participants. The institutional prevalence of pre eclampsia is at 5%.There is also a multidisciplinary team approach for high risk patients including ophthalmologists and obstetricians. However the performance of fundoscopy for patient with hypertensive disease in pregnancy at the local setting is not routine but available if indicated. The medical outpatient clinic provided a digital non mydriatic camera for fundoscopic examination.

2.3: Study Population.

The study population comprised women who were within 72 hours postpartum and were admitted at Kenyatta National Hospital (KNH) following pre-eclampsia with severe features or normal healthy pregnancies. Severe features of pre-eclampsia include: Blood pressure equal to or greater than 160/110mmhg, thrombocytopenia (platelet count <100000 / ul), deranged liver function, renal function derangement, impaired cerebral and visual functions and pulmonary edema. Normal pregnancies were those not complicated with either diabetes, hypertensive disorders of pregnancy, chronic renal disease, cardiac disease, systemic vascular diseases.

2.3.1: Inclusion Criteria.

Participants in the study were both healthy women and pre-eclamptic women with any one of the severe features in the post partum period admitted and delivered in KNH and who consented for evaluation. They were aged 14 years and above. Only those with clear ocular media permitting examination of the posterior segment of the eye got recruited into the study. They were then evaluated within 24 hours following a vaginal delivery and within 72 hours following a caesarean section. This was in line with the time to discharge period in the institution. Only postpartum women who were stable enough to undergo examination were enrolled in the study.

2.3.2: Exclusion Criteria.

We excluded participants with preexisting medical conditions with potential eye systemic effects e.g. diabetes mellitus, hypertensive disease, chronic renal disease, cardiac disease and systemic vascular disease. Those with underlying ocular co-morbidity (cataract, corneal opacities, glaucoma, history of ocular trauma or surgery, laser surgery included) or known to have pre-eclampsia superimposed on chronic hypertension were also excluded from the study.

2.4: Sample size and sampling Procedure.

Study participants were recruited, interviewed and evaluated from immediate post delivery time to within 24 hours if vaginal delivered 72 hours if surgical delivery. In prior studies, the prevalence of retinal vessel changes varied between 40 -100% among women with hypertensive disease in pregnancy (6) (37).

This was a comparative study comparing prevalence of retinovascular changes between preeclamptic patients and the normal population hence the formula for comparing proportions was used to calculate sample size as follows:

$$n = \frac{2(Z_{1-\alpha/2}+Z_{1-\beta})^2 P_{av}(1-P_{av})}{(P_0-P_1)^2}$$

n is the sample size required in each group

$Z_{1-\alpha/2}$ refers to the level of significance or confidence interval – 1.96 for 95% CI

$Z_{1-\beta}$ refers to the power of obtaining difference between the two groups – 0.84 for 80% power

P_0 – Proportion of patients with retinopathy among patients without pre-eclampsia – 35%

P_1 –Proportion of patients with retinopathy among patients with pre-eclampsia – 70%

P_{av} – Average outcome in the two groups – 52.5%

Substituting into the formula:

n = **32** patients per group will be studied to detect a minimum effect size of 35% between the two groups of patients.

2.5: Research procedure.

Study participants were recruited in the post natal wards. A pilot study was done on three postpartum women following normal pregnancy and three postpartum women following pre-eclampsia with severe features at post-natal wards in KNH using structured questionnaires before the study to test for its reliability and validity. Two research assistants were also trained on study procedure and recruitment of study participants.

Systematic random sampling was used where the k^{th} patient (k=2, i.e. patient 2, 4, 6….) admitted everyday in the postnatal register was selected for the study. With an estimated daily admission of 4 patients, 2 patients were selected daily during the study period until the required sample size (n=64) was met. Post partum women following normal pregnancies and following pre eclampsia with severe features (PES) who met the eligibility criteria were approached, consented. Study participants were interviewed on socio- demographic, focused past medical and ocular history. Selected clinical and laboratory findings were obtained from clinical records as per the questionnaire. The participants were then directed and guided to the medical outpatient clinic where visual acuity assessment was done using a portable logMAR chart after which digital fundus photos were taken using the non mydriatic fundus camera. The visual acuity testing was done while the participant was standing three meters away from the chart and the fundus photography was done while the patient was seated on a chair taking at most a total of ten minutes. This evaluation was done by an optical technician at the medical outpatient clinic assisted by the principal researcher and findings recorded in a predetermined questionnaire. Fundoscopic changes seen on either right or left eye was recorded as positive findings and graded using the Keith Wagner classification. This grading was done by an ophthalmologist together with the principal investigator. Patients with positive ocular findings or evidence of disease were referred for ophthalmological care and follow up.

2.6: Data Variables.

For objectives 1 and 2, the exposure variable was normal pregnancy versus pregnancy complicated with pre eclampsia with severe features versus. Independent variables and potential confounders included; age, parity, blood pressure, gestational age at delivery, duration from diagnosis to evaluation, visual acuity, creatinine levels, liver enzymes, platelet count, (Hemolysis

Elevated liver enzymes Low platelets) HELLP syndrome. Dependent variables included; retinovascular changes as found in fundus photos i.e. generalized arteriolar or focal arteriolar narrowing, retinal hemorrhages, retinal detachment, exudates and presence of papilledema.

For aim 3 the exposure variable was type and severity of retinovascular findings while the outcome variable was antenatal umbilical RI. Other variables included birth weight, neonatal mortality, APGAR score and NICU admission.

2.7: Data Collection.

A pretested interviewer administered structured questionnaire was administered to obtain ocular and medical history. Visual and fundal examination findings were also recorded in the questionnaire. Data collected on medical history was corroborated with available patient records in the post-natal ward for accuracy. The questionnaires were translated from English to Kiswahili, then local and then back-translated into English to ensure accuracy. A proposed standardized operating procedure for umbilical artery resistive index measurement was put up at ultrasonography rooms in KNH and the radiology department, University of Nairobi. The SOP proposed was in line with prior studies and recommendations (34,39–43). This was in collaboration with the unit heads a month prior to data collection commencement.

2.8: Data analysis methods.

Data was cleaned to get rid of inconsistencies (missing values, duplicates and values that were out of range) then entered into and analyzed using statistical program for social scientists (SPSS^{R}) version 22 software package. The study population was described using socio-demographic and clinical variables. The descriptive variables included demographic data, visual acuity, retinovascular findings and umbilical Doppler readings which were summarized and

presented in terms of proportions (categorical data). Normal pregnancy and pre-eclampsia with severe disease groups were compared in relation to their descriptive variables using Chi square test (or Fishers exact tests for small cells) for proportions as measured from categorical variables. Retinovascular findings and severity grades were analyzed and are presented as percentages and compared between the two groups using Chi square or Fisher's exact test. Odds ratios (OR) is calculated and presented as an estimate of relative risk (RR) of retinopathy associated with pre-eclampsia. Statistical significance is interpreted at a P value less than 0.05 or confidence interval that doesn't include the null value.

2.9: Data Confidentiality and Storage.

Unique identity numbers was used for each participant for anonymity. Filled questionnaires were kept under lock and key after the study. The data was also stored and backed up in electronic computer devices with only access to the researcher by use of password.

2.10: Research ethics.

2.10.1: Informed Consent

Informed consent was sought from participants in a language they best comprehended.

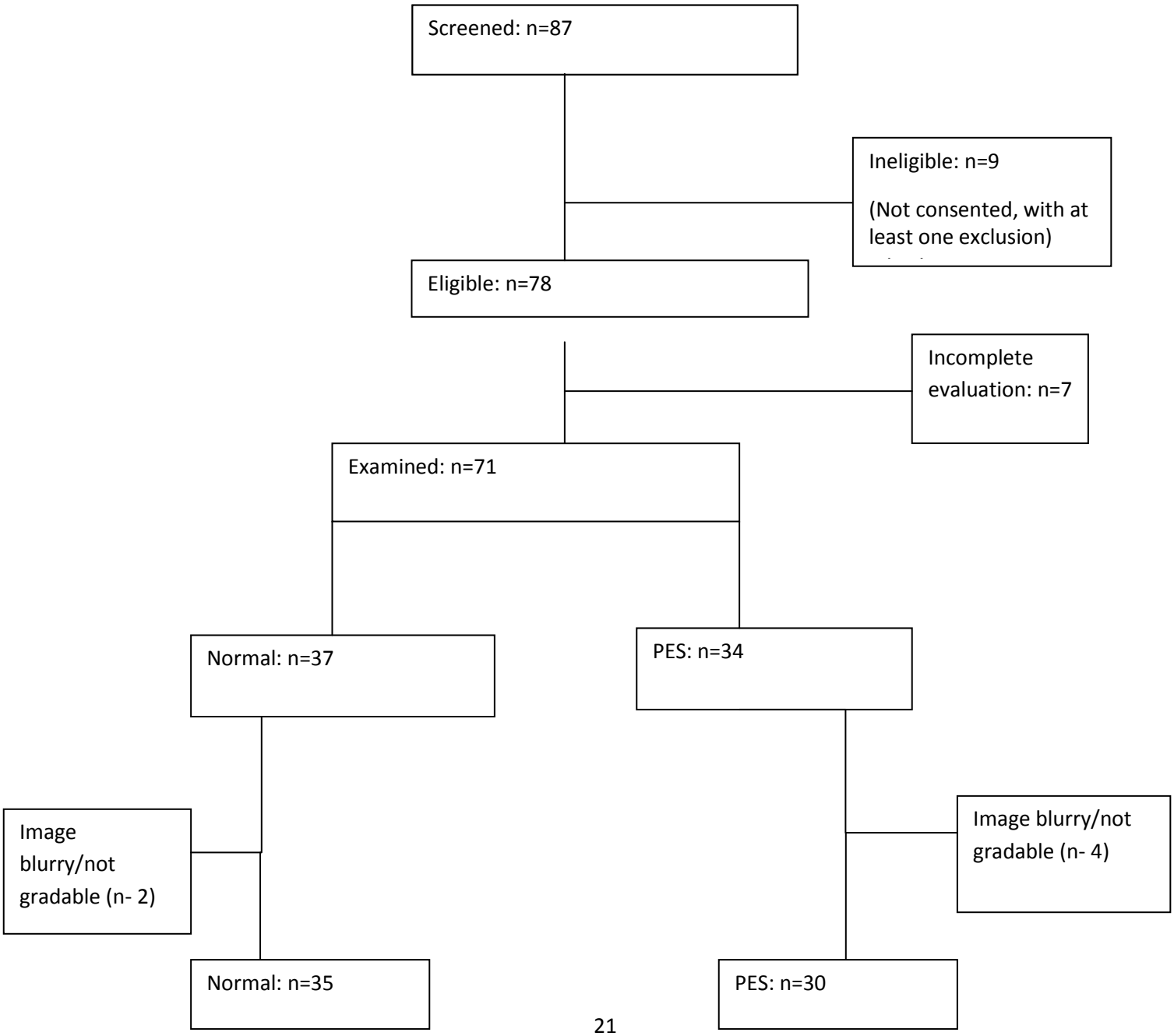
2.10.2: Ethics Approval

Ethical approval was obtained from Kenyatta National Hospital University of Nairobi Ethics Review Committee (P663/09/2016). A feedback report including recommendations was provided and disseminated through the Department of Obstetrics and Gynecology, KHN symposia and the Annual KOGS conference.

Participants took part in the study voluntarily and could withdraw at any point without receiving substandard care. Confidentiality of all participants' records was ensured and ocular examinations were performed at no cost to the participants.

RESULTS

Figure 1: Flow chart



Of the 87 women approached, 78(74%) consented and 71(91%) underwent complete evaluation (Figure1.) A total of 65(92%) women were included in the final analysis, 30(46%) in the PES group and 35(54%) in the normal pregnancy group.

TABLE1: BASELINE SOCIO-DEMOGRAPHIC AND OBSTETRIC CHARACTERISTICS OF THE STUDY PARTICIPANTS

		PES or Normal		
		PES n (%)	Normal n (%)	p-value
Age group	16-25years	7 (23.3)	14 (40.0)	0.352
	26-35years	17 (56.7)	15 (42.9)	
	36-45years	6 (20.0)	6 (17.1)	
Level of Education	Primary	8 (26.7)	11 (32.4)	0.514
	Secondary	12 (40.0)	16 (47.1)	
	Post-Secondary	10 (33.3)	7 (20.6)	
Parity	One	12 (40.0)	12 (35.3)	0.698
	>one	18 (60.0)	22 (64.7)	
Gestation age at delivery weeks	</=34	12 (40.0)	3 (8.6)	**0.002**
	35-37	7 (23.3)	5 (14.3)	
	>37	11 (36.7)	27 (77.1)	

		PES n (%)	Normal n (%)	p-value
Visual acuity Left	Normal	21 (70.0)	28 (80.0)	0.351
	Not normal(>0.2)	9 (30.0)	7 (20.0)	
Visual acuity Right	Normal	25 (83.3)	27 (77.1)	0.534
	Not normal(>0.2)	5 (16.7)	8 (22.9)	

PES- pre eclampsia with severe features

Normal- normal pregnancy

Between March 2017 and May 2018 seventy eight women within the postpartum period were enrolled. Seventy one then completed examination out of which thirty five (normal) and thirty (PES) had gradable images. The baseline socio-demographic and obstetric characteristics of the study participants are summarized in table 1.The characteristics of study participants were comparable between the two exposure groups except for gestational age at delivery. The mean age was 29 years. Almost 75% had secondary or higher level of education and up to two thirds of the participants were multiparous. Compared to normal pregnancy, women with PES (pre eclampsia with severe features) were more likely to deliver at or less than 34 weeks gestation (40% versus 8.6%).Women with PES compared to normal pregnancies were more likely to deliver at or more than 37 weeks (77% versus 36.7%).Visual acuity of more than 0.2 on the LogMAR chart was considered not normal, occurred in less than 30% for either eye and was similar between the two groups. There was significant association between gestational age at

delivery and severe pre- eclampsia (p= 0.002) with those with PES likely to deliver at less than 34 weeks compared to those with uncomplicated pregnancy.

TABLE 2: OCULAR AND NON OCULAR COMPLAINTS REPORTED BY STUDY PARTICIPANTS

	PES or Normal		
	PES	Normal	
Complaints	n (%)	n (%)	p-value
Blurred vision	10(33)	1(2.9)	**0.01**
Lid swelling	2 (6.7)	0(0)	0.209
Ocular pain	8(27.6)	1(2.9)	**0.005**
Lacrimation	1(3.3)	0(0)	0.476
Chest pain	1(3.3)	0(0)	0.462
Headache	8(26.7)	2(5.7)	**0.02**
Epigastric pain	7(23.3)	0(0)	**0.002**
Cough	1(3.3)	0(0)	0.462

PES- pre eclampsia with severe features

Normal- normal pregnancy

The most frequently reported ocular symptom was blurriness of vision but still in only 17% of respondents. Ocular pain was the second at 14%, up to one quarter in those with PES and only 3% among the normal. However, the most recorded non ocular complaint was headache in 15% of respondents followed by epigastric pain in10% of participants all of which were in the PES group.

TABLE 3: Prevalence of retinovascular changes in PES and Normal pregnancy groups

	KW Grade			
PES or Normal	Grade 0 n (%)	Grade 1-4 n (%)	Odds ratio (95% confidence)	P value
Normal	1 (2.9)	34 (97.1)	0.15 (0.02, 1.34)	0.055
PES	5 (16.7)	25 (83.3)		

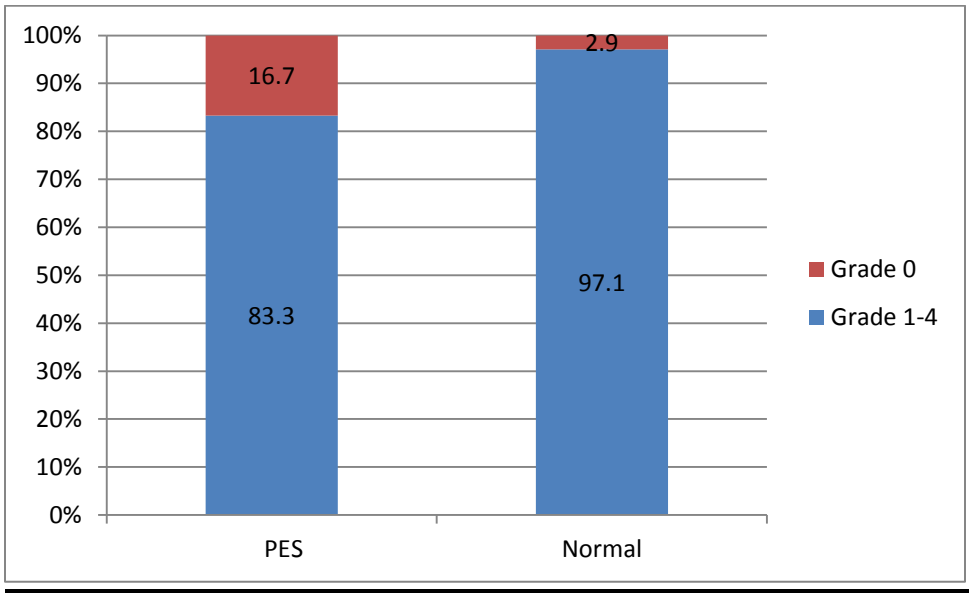
PES- pre eclampsia with severe features group

KW- Keith Wagner

Normal- normal pregnancy group

The overall prevalence of retinovascular changes within 72 hours postpartum was 90.8% and was comparable between the normal pregnancies (97.1%) and pregnancies complicated with PES (83.3%) (Figure 2). The odds ratio (OR) of retinovascular changes was lower but statistically insignificant in the PES group (OR 0.15, 95% Confidence Interval (CI) [0.02-1.34]) (Table 3)

Figure 2: Prevalence of abnormal postpartum maternal retinal findings



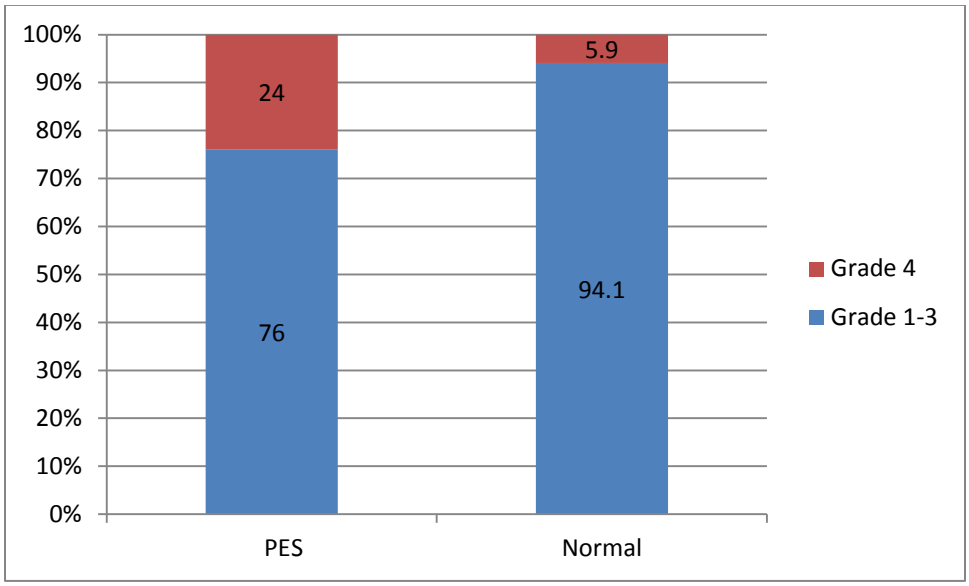
PES- pre eclampsia with severe features group

Normal- normal pregnancy group

TABLE 4: Severity of Keith Wagner grade in PES compared to normal pregnancy

	KW grade			
PES or Normal	Grade 1-3 n (%)	Grade4 n (%)	Odds ratio (95% confidence)	P value
Normal	32 (94.1)	2 (5.9)	5.05 (0.93, 27.6)	**0.045**
PES	19 (76)	6 (24)		

Figure 3: Severity of Keith Wagner grades in PES compared to normal pregnancy group.



PES- pre eclampsia with severe features group

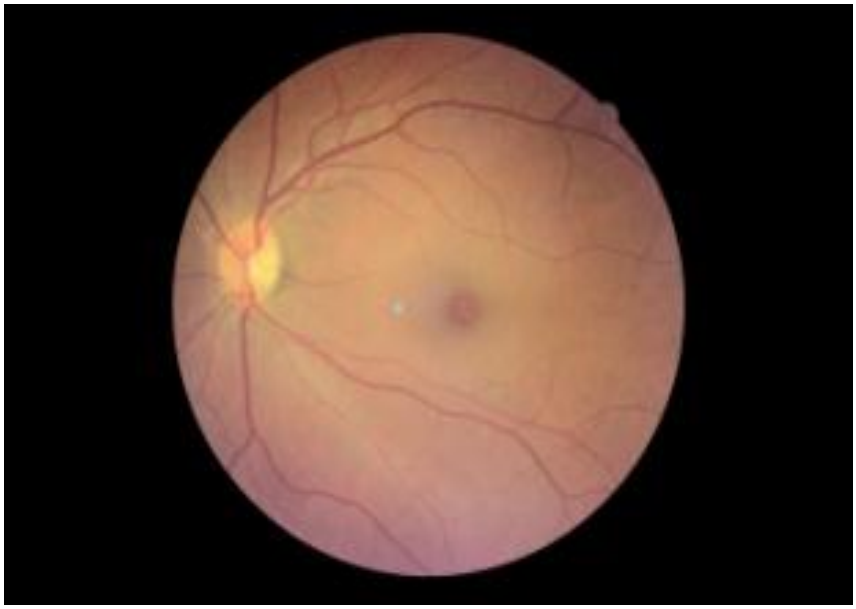
Normal- normal pregnancy group

The prevalence of severe retinovascular changes (KW 4) was higher in the PES n=6(24%) compared to normal pregnancy group n=2(5.9%) (Figure 3)

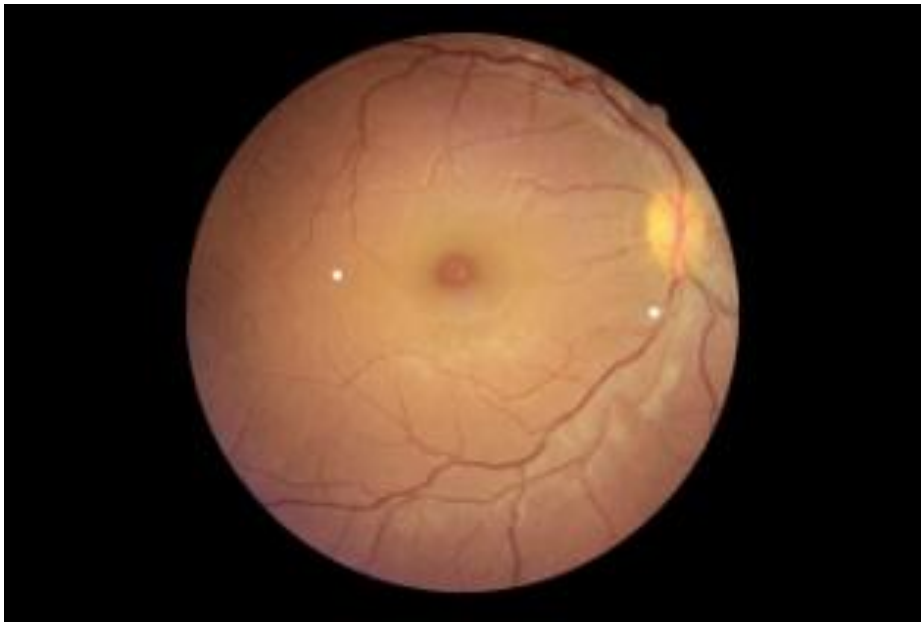
The odds ratio of having severe retinovascular change was 5 fold greater among the PES group compared to the normal pregnancy group. However this increase was not statistically significant. (OR 5.05, 95% C.I [0.93-27.6], P=0.05) (Table 4).

Selected images of fundoscopic findings among postpartum women showing normal and RV changes

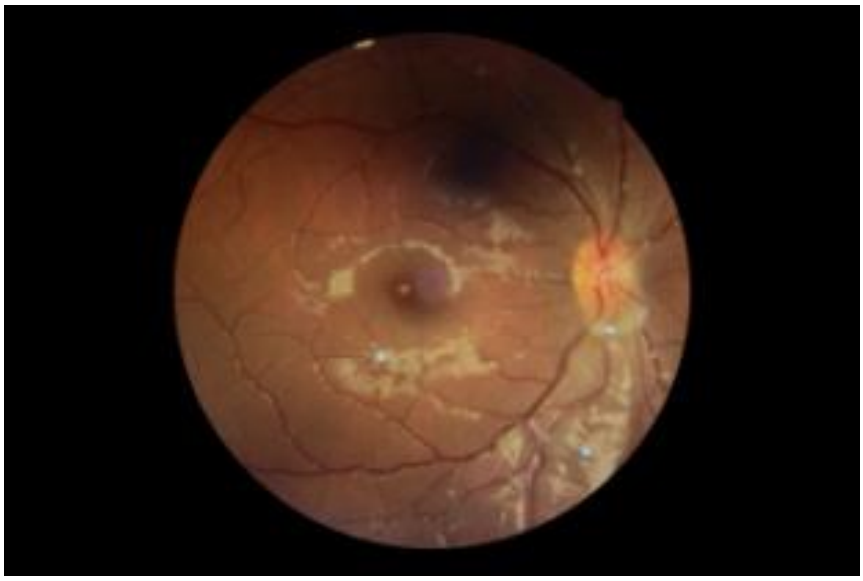
Picture 1: Normal fundus photo



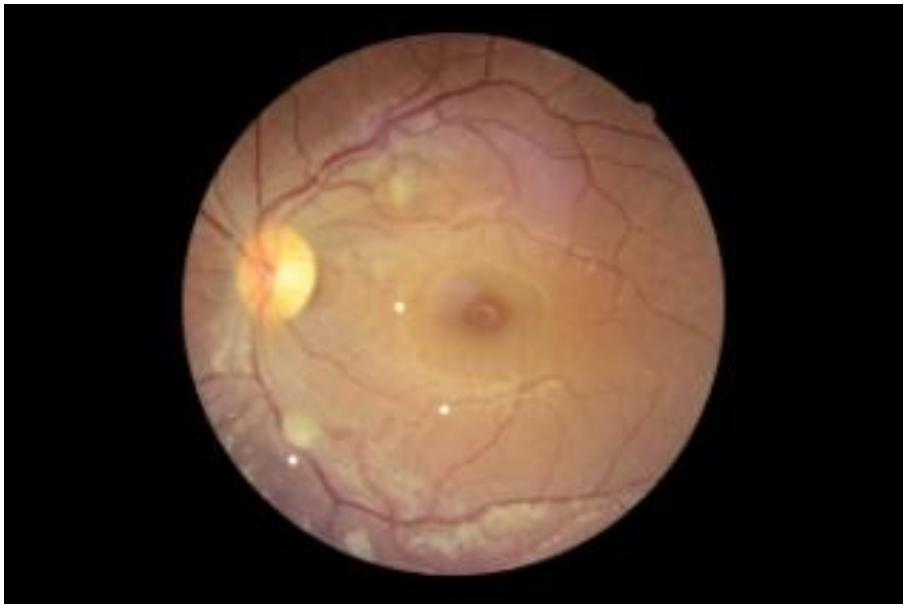
Picture 2: Increased retinal vessel tortuosity



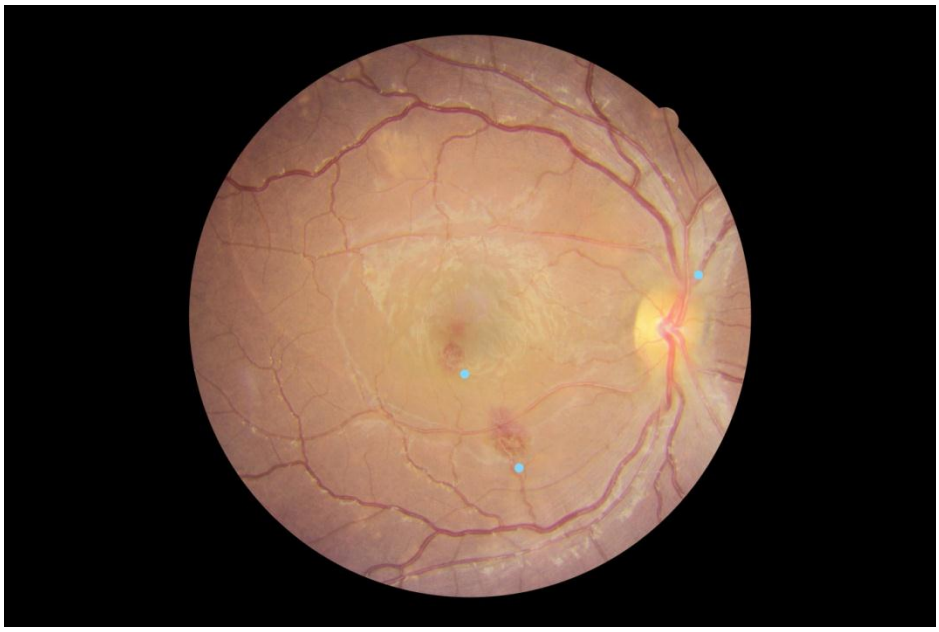
Picture 3: Macula and retinal edema



Picture 4: Cotton wool spots



Picture 5: Flame shaped haemorrhage



DISCUSSION

In this study that compared pregnancy complicated with PES versus normal, we found a comparably high prevalence of retinovascular changes in the early postpartum period in both the normal (97%) and PES (83%) groups. Although RV changes were more common in the normal group compared to the PES group, it was not statistically significant and could have been explained by the time from delivery to exam which was within 72 hours. Furthermore, changes in retinal microvasculature caliber mirroring the physiological rise and fall of mean arterial pressure in the course of normal pregnancy has been described (8,44) returning to baseline at 6 months postpartum (8). Vasodilators (nitric oxide, prostacyclin, prostaglandins) and vasoconstrictors (Angiotensin II) have been postulated to play a role in these temporal changes.

A higher prevalence of RV changes has been reported previously. Reddy et al, 1983 found 90% of severe pre-eclampsia cases with retinal vascular changes while Naval et al, 1965 reported 78.6% (25). A local study in this similar setting, done 25 years ago reported 60% occurrence of ocular fundus changes in the left eye and 58% in the right eye in pre-eclampsia, eclampsia patients (27). However, these studies were limited to pregnancy complicated with hypertension and did not have a comparative group of normal pregnancy.

We found that KW grade 3 retinovascular change was the most prevalent in both normal (88.6%) and PES (60.0%) patients in the current study. This is explained by the majority of patients having retinal edema on fundus exam; 83% left eye (LE), 77% right eye (RE) in the normal pregnancy group and 57% LE, 63% RE in PES group. Grade 2 overall was 2% and grade 4 overall was 12%, no grade 1 retinal vessel change was recorded. Previous studies found a predominance of grade 1 retinopathy of between 8-52.6% (25) (7) (24).

A significant association between retinovascular changes and pregnancy complicated with PES was reported in this setting. KW Grade 4 retinopathy was significantly higher in the PES group than in the normal pregnancy group. This is consistent with other studies on hypertensive retinopathy in pregnancy induced hypertension that reported positive association between severity of retinopathy and hypertension (7) (9) (25) (45) (24). Although Rasdi et al, 2011 in a prospective observational study and Gupta et al, 2008 in a retrospective study found no positive association; they notably measured for association based on only blood pressure criteria classification of severity of hypertensive disease (31) (46).

In this study, there was no significant association between grade of severity of retinovascular changes and abnormal umbilical artery resistive index. This was however an exploratory

objective for the purpose of this study. Changes in the retinal arterioles may indirectly reflect the state in the placental vasculature and fetal status and progression of hypertension and worsening of severity of retinopathy can be a predictive indicator of adverse fetal outcomes (7) (31) (47).

Our study strengths includes being the first study in this setting to use a high definition fundus camera which also has the advantage of eliminating time constraints compared to performing a clinical fundoscopic exam. Digital fundus photography also ensured standardization of findings. In addition, as opposed to other studies that only assessed pregnancy complicated with PES, our study had a normotensive group for comparison. The inclusion of the normal pregnancy group also provides invaluable baseline data for larger prospective studies.

The limitations of this study are largely due its cross-sectional nature. We limited our study to the first 72 hours postpartum and had no retinal vessel evaluation from antepartum to postpartum period which could describe any progressive changes in RV findings. Having limited our study to immediate postpartum, when pregnancy and labour related changes have not resolved, we could have found higher prevalence of retinovascular changes in both groups. This high prevalence could have lowered the power to detect group differences. Mothers who were clinically unstable were excluded from the study thus not represented in the sample. Examination of the PES mothers post delivery however was an optimum time suggesting a point where disease progress necessitated intervention. The disease process is progressive thus maximal changes can be captured at or around delivery. Furthermore, this study provides baseline data that can inform future longitudinal studies.

CONCLUSION

In the immediate postpartum period, the prevalence of retinovascular changes was high in both groups (pregnancies complicated with pre eclampsia with severe features (PES) and among normal pregnancies) but no statistically significant difference was noted. The odds of severe retinovascular changes were greater for pregnancies complicated with PES as compared to normal pregnancies. In exploratory analysis, there was no significant association between severity of grade of retinovascular changes and abnormal umbilical artery resistive index.

RECOMMENDATIONS

The high prevalence of RV changes requires more studies to assess progression resolution and long term effect. Population based studies with if possible a pre pregnancy fundal photograph and follow up beyond 6 weeks postpartum would be critical. Involve ophthalmologists for definitive tests (Optical Coherence Tomography (OCT) for suspected serious retinal conditions. Also to sensitize caregivers to understand various ocular conditions associated with hypertension in pregnancy and to handle them in a multidisciplinary manner.

TIMELINES

Activity	Feb-June 2016	July 2016	Aug 2016	Sept 2016	Oct 2017	Nov 2017	Dec 2017	Jan 2018	Feb 2018	March 2018	April 2018	May 2018	June 2018
Proposal development													
Proposal presentation													
Ethical review													
Data collection													
Data analysis													
Thesis development													
Thesis presentation													

BUDGET

	PARTICULARS	**TOTAL(Ksh)**
1	Proposal writing, review and internet.	**6,000**
2	Fundus camera charges @ 1000	**60,000**
3	Photocopying services and binding services	**8,000.**
4	Stationery	**4,000**
5	Data entry and analysis	**40,000**
6	Contingencies @ 10 % of total cost	**12,000**
	Grand Total.	**130,000**

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APPENDICES

APPENDIX 1: SAMPLE QUESTIONNAIRE

A.DEMOGRAPHIC DATA

1. Date __ __ / __ __ / __ __ __ __
2. Name (initials) _____ Participant ID _____
3. Religion Christian ☐ Muslim ☐ Hindu ☐
4. County _____
5. Level of Education: Primary ☐ Secondary ☐ Post-secondary ☐
6. Age (years) _____
7. Parity _____

B. Medical history

Have you ever been diagnosed or treated for any of the following?

1. Diabetes or any Diabetes related complications Yes ☐ No ☐
2. Hypertensive disease Yes ☐ No ☐
3. Renal disease Yes ☐ No ☐
4. Cardiac disease Yes ☐ No ☐
5. Systemic vascular disease Yes ☐ No ☐

C. Ocular history

Complaints:

6. Blurred vision Yes ☐ No ☐
7. Lid swelling Yes ☐ No ☐
8. Pain Yes ☐ No ☐
9. Lacrimation Yes ☐ No ☐
10. None ☐
11. Other _____

Ocular diseases or conditions

12. Glaucoma Yes ☐ No ☐
13. Cataract Yes ☐ No ☐
14. Corneal opacities Yes ☐ No ☐
15. Ocular trauma Yes ☐ No ☐
16. Previous ocular/ laser surgery Yes ☐ No ☐

D. Clinical records and examination.

17. Blood pressure: Systolic _____ Diastolic _____

18. Platelet count _____

19. Renal function: Creatinine (umol/l)_____

20. Proteinuria _____

21. Liver function: AST _____ (iu/l) ALT _____(iu/l)

22. Pulmonary edema: Present ☐ Absent ☐

23. Cerebral and visual symptoms: Present ☐ Absent ☐

24. Gestational age at delivery _____

25. Duration of delivery to study (Hrs)_____

26. Umbilical artery RI: Abnormal for GA ☐ Normal for GA ☐

27. Visual Acuity: Lt _____ Rt _____

28. Neonatal birth weight(Kgs)

29. APGARS score at 5 minutes. 0-3 ☐ 4-6 ☐ 7-10 ☐

30. NICU admission: Yes ☐ No ☐

E. Fundoscopic photo findings

31. Focal arteriolar narrowing: Present ☐ Absent ☐

32. Generalized arteriolar narrowing: Present ☐ Absent ☐

33. Dot and blot hemorrhages: Present ☐ Absent ☐

34. Cotton wool spots: Present ☐ Absent ☐

35. Hard exudates: Present ☐ Absent ☐

36. Papilloedema: Present ☐ Absent ☐

37. Macular edema: Present ☐ Absent ☐

38. Retinal edema: Present ☐ Absent ☐

39. Retinal detachment: Present ☐ Absent ☐

40. Hypertensive choroidopathy: Present ☐ Absent ☐

41. Others. _____

42. Grade:_____

APPENDIX 2: KEITH WAGNER GRADING OF HYPERTENSIVE RETONIPATHY

Grade 1:- Mild generalized arterial attenuation, particularly of small branches.

Grade 2:- More severe Grade 1 + focal arteriolar attenuation.

Grade 3:- Grade 2 + hemorrhages, hard exudates, cotton wool spots.

Grade 4:- Grade 3+ optic disc swelling (papilledema)

APPENDIX 3: CONSENT FORM

TITLE: POSTPARTUM RETINAL FINDINGS IN MOTHERS WITH PRE ECLAMPSIA WITH SEVERE FEATURES COMPARED TO NORMAL PREGNANCY AT KENYATTA NATIONAL HOSPITAL.

INTRODUCTION

Pregnancy can be complicated by high blood pressure and very high blood pressure can affect the major body organs including the kidney, brain, lungs, placenta and the eye. Evaluation of changes in blood vessels at the back of the eye will aid in identifying very high blood pressure disease .Doctors are therefore able to take good care of patients.

OBJECTIVES

The study will compare these eye changes between post delivery mothers with very high blood pressure and those without. Specifically we will aim to establish the magnitude of occurrence of eye changes in mothers with high blood pressure and how severe those changes are. Also in those mothers with severe hypertension, we will want to find out if blood flow to the placenta is compromised.

BENEFITS

The study will provide researchers with knowledge on eye changes which can be useful in better management of patients. Mothers with eye changes will be referred to the eye clinic for a comprehensive management.

RISKS

There are no immediate of later risk of suffering any complication while taking part in this study.

VOLUNTARISM

This consent is not sought under any coercion and you reserve the right to withdraw from the study at any particular point. This study will use a visual chart to check visual acuity and an eye camera to examine for changes in mothers after delivery.

RESEARCH PROCEDURE

This will involve checking how good your eyesight is and then taking a photo of the back of your eye while you are seated.

FOLLOW UP

If you will be found with eye changes, you will be referred to the eye clinic for specialized care.

CONFIDENTIALITY

Your information will be handled with utmost confidence. All the details will be stored under lock and key.

INFORMATION ON RESEARCHERS

Principal researcher: Dr. Ayumba Albert, phone-0726868932, mail- ayumbaalb@gmail.com.

KNH-UON ETHICS& RESEARCH COMMITTEE

Tel: (254-020) 2726300-9 Ext 44355, mail- uonknh_erc@uonbi.ac.ke, web- www.erc.uonbi.ac.ke.

CONSENT BY PATIENT/ NEXT OF KIN FOR PARTICIPATION IN STUDY.

I…… hereby consent to undergo fundoscopic photography the nature and effect of which has been explained to me by Dr. /Mr…….

I also consent to such further measures as may be found necessary during the course of the examination.

Date……..... Signed……..

I confirm that I have explained to the patient and nature of effect of this procedure.

Date……..Signed……

Witness: Date……..Signed…….

IDHINI YA KUSHIRIKI KATIKA UTAFITI: HOSPITALI KUU YA KENYATTA.

UTANGULIZI

Mimba inaweza kuwa ngumu na shinikizo la damu na shinikizo la damu juu sana inaweza kuathiri kuu viungo vya mwili ikiwa ni pamoja na figo, ubongo, mapafu, placenta na jicho. Tathmini ya mabadiliko katika mishipa ya damu nyuma ya jicho misaada katika kutambua ugonjwa juu sana shinikizo la damu .Doctors hiyo ni uwezo wa kuchukua huduma nzuri ya wagonjwa.

MALENGO

Utafiti huo kulinganisha mabadiliko haya jicho kati ya akina mama baada kujifungua na shinikizo la damu sana na wale bila. Hasa sisi na lengo la kuanzisha ukubwa wa tukio la mabadiliko ya macho akina mama na shinikizo la damu na jinsi kali mabadiliko hayo ni. Pia katika akina mama wale walio na shinikizo la damu kali, sisi wanataka kujua kama damu kati yake na placenta ni kuathirika.

FAIDA YA KUSHIRIKI

utafiti itatoa watafiti na maarifa juu ya mabadiliko jicho ambayo inaweza kuwa na manufaa katika usimamizi bora ya wagonjwa. Akina mama na mabadiliko jicho itakuwa inajulikana kliniki ya jicho kwa usimamizi wa kina

MADHARA

Hakuna haraka ya hatari ya baadaye ya mateso matatizo yoyote wakati kuchukua sehemu katika utafiti huu.

UHURU WA KUSHIRIKI

idhini hii si kutatua chini ya kutumia nguvu yoyote na wewe haki ya kujiondoa kutoka utafiti katika hatua yoyote fulani. Utafiti huu utatumia Visual chati kwa kuangalia kutoona vizuri na kamera jicho kuchunguza kwa mabadiliko katika mama baada ya kujifungua.

UTARATIBU WA UTAFITI

Hii itahusisha kuangalia jinsi nzuri jicho lako ni na kisha kuchukua picha ya nyuma ya jicho lako wakati wewe ni ameketi

FUATILIA

Hii itahusisha kuangalia jinsi nzuri jicho lako ni na kisha kuchukua picha ya nyuma ya jicho lako wakati wewe ni ameketi

USIRI

Maelezo yako itakuwa kubebwa kwa kujiamini mkubwa. maelezo yote itakuwa kuhifadhiwa chini ya kufuli na ufunguo

TAARIFA JUU YA WATAFITI

Mtafiti mkuu: Dr. Ayumba Albert, phone-0726868932, mail- ayumbaalb@gmail.com.

KNH-UON MAADILI & UTAFITI WA KAMATI

Simu: (254-020) 2726300-9 Ext 44355, barua pepe- uonknh_erc@uonbi.ac.ke, mtandao

-www.erc.uonbi.ac.ke.

IDHINI KWA MGONJWA / pili ya jamaa KWA USHIRIKI KATIKA KUJIFUNZA.

Mimi ..... hili ridhaa ya kufanyiwa fundoscopic kupiga picha asili na athari ambayo imekuwa alielezea kwangu na Dk /Mr..... .....

Mimi pia kukubaliana na hatua hizo za zaidi kama inaweza kupatikana muhimu wakati wa kozi ya mitihani.

Tarehe .... Signed ....

Mimi kuthibitisha kwamba nilivyoeleza kwa mgonjwa na asili ya athari za utaratibu huu.

Tarehe ....Signed .....

Shahidi: Tarehe ....Signed .....

APPENDIX 4: STANDARD OPERATING PROCEDURE

UMBILICAL RESISTIVE INDEX MEASUREMENT.

1. Patient in a recumbent position.

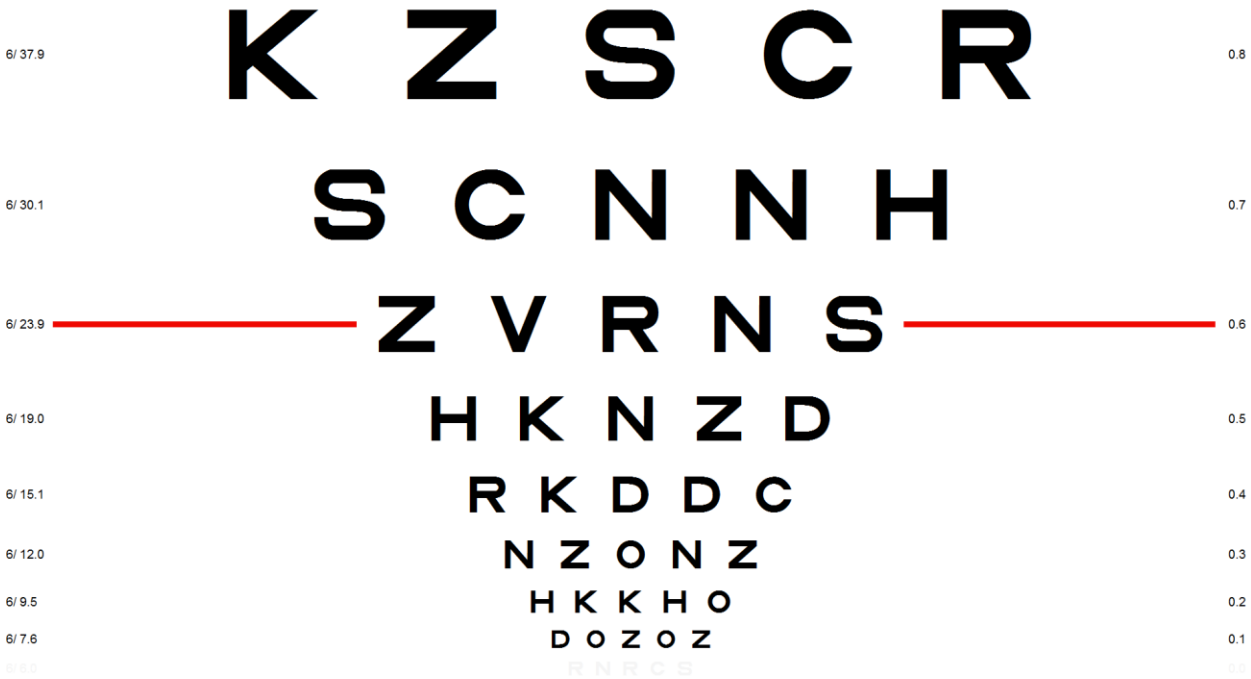
2. Identify a segment of free floating umbilical cord.

3. Select the umbilical artery (UA), zoom in and place the Doppler ultrasound gate in a segment of cord flowing at close to 0 degrees to the transducer.

4. Ensure recording is done with minimal fetal activity and with absence of fetal breathing (fetal apnea).

4. If there is reversed flow, the UA is reexamined close to the placental insertion, because this segment of the UA is the last part to develop reversed flow.

APPENDIX 5: LOG MAR CHART



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Ref: KNH-ERC/A/20

23rd January 2017

Dr. Ayumba Albert
Reg. No.H58/76049/2014
Dept. of Obs/Gynae
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Ayumba

REVISED RESEARCH PROPOSAL: "POSTPARTUM RETINAL FINDINGS IN MOTHERS WITH PRE ECLAMPSIA WITH SEVERE FEATURES COMPARED TO NORMAL PREGNANCY AT KENYATTA NATIONAL HOSPITAL (P663/09/2016)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above revised proposal. The approval period is from 23rd January 2017 – 22nd January 2018.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Kindly arrange to submit a copy of registration by Pharmacy and Poisons Board and approval when ready..

Protect to discover