# PREVALENCE, CLINICAL CHARACTERISTICS, MATERNAL AND PERINATAL OUTCOMES OF PATIENTS WITH RECURRENT PREECLAMPSIA AT KENYATTA NATIONAL HOSPITAL: A CROSS-SECTIONAL STUDY

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A research dissertation submitted in partial fulfilment of the requirements for the award of the degree of Master of Medicine Department of Obstetrics and Gynecology, Faculty of Health Sciences, University of Nairobi.

## **DECLARATION**

I certify that this is my authentic original work and that it has not been submitted forany other university's degree program.

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## LIST OF ABREVIATIONS

ACOG	American College of Obstetricians and Gynecologists		
APLS	Antiphospholipid Antibody syndrome		
BP	Blood Pressure		
CS	Cesarean Section		
DM	Diabetes Mellitus		
HTN	Hypertension		
ICU	Intensive Care Unit		
ISSHP	International society for the study of hypertension in pregnancy		
KNH	Kenyatta National Hospital		
NBU	Newborn Care Unit		
NICU	Neonatal Intensive Care Unit		
PNC	Post Natal Care		
RCT	Randomized Control Trial		
SLE	Systemic Lupus Erythematosus		
SSA	Sub Saharan Africa		
WHO	World Health Organization		

#### **OPERATIONAL DEFINITIONS**

**Preeclampsia** is defined by the International Society for the Study of Hypertension in Pregnancy (ISSPH) as a new onset of hypertension with either proteinuria or end-organ dysfunction that occurs after 20 weeks of gestation.

**Preeclampsia with severe features**: this has been defined, based on ISSPH, as preeclampsia with severe hypertension with any end-organ damage, whereby:

1. Severe hypertension is defined as having a systolic blood pressure of at least 160 mmHg or adiastolic blood pressure of at least110 mmHg on two separate occasions at least four hours apart.

2. The end organ damage include:

a. central nervous system (visual disturbance, headache, or seizures),

b. hepatic injury (elevated ALT and AST, > 2 times the upper limit of the normal, orsevere right upper quadrant pain or epigastric pain),

c. kidney injury (serum creatinine >97.2micromol/L or doubling of serum creatinine concentration in the absence of other renal disease),

- d. lung injury (pulmonary edema),
- e. hematologic (thrombocytopenia <100,000 platelets/microL), and

f. vascular abnormalities (disseminated intravascular coagulopathy)

**Recurrent Preeclampsia:** According to Van Oostward MF et al (AJOG 2015) a woman who had preeclampsia in a previous pregnancy and now develops pre-eclampsia in a subsequent pregnancy is considered as having a recurrent preeclampsia.

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#### ABSTRACT

**Introduction:** Hypertensive disorders in pregnancy are a significant cause of maternal morbidity and mortality globally. The recurrence rate of preeclampsia ranges from 6% to 25%, with the variability depending on patient characteristics and demographic differences and various comorbidities as risk factors. This study sought to determine the prevalence, clinical characteristics, maternal and perinatal outcomes of patients with recurrent pre-eclampsia at Kenyatta National Hospital (KNH).

**Methodology**: This was a descriptive cross-sectional study conducted at the KNH from 3rd October 2021 to 31st March 2021. Postpartum women with recurrent preeclampsia were interviewed and additional data extracted from files. Sociodemographic, clinical characteristics, maternal and perinatal outcomes of patients with recurrent pre-eclampsia was expressed using percentages, mean (standard deviation) median (interquartile ranges) and proportions respectively. Pearson's Chi square was used for categorical variables to assess the clinical characteristics associated with adverse fetal and maternal outcomes P values of 0.05 was considered statistically significant. Logistic regression analysis was used to model for factors associated with morbidity.

#### Results

Out of 553 patients who had preeclampsia, 343 had new onset preeclampsia and were ineligible, 58 had preeclampsia superimposed on chronic hypertension and 152 patients had recurrent preeclampsia. The prevalence rate was 27 (95% CI: 23.8 - 31.2 Thirty-eight percent had early onset preeclampsia, 53 % had preterm deliveries <37 weeks gestation. Ninety nine percent had at least 1 antenatal visit while 77% had at least 4 visits. Thirty percent were given calcium supplements, and 20% got low dose aspirin for prevention of preeclampsia. Only 9 % had pre-existing comorbidities.

There were no adverse maternal outcomes, 32.9% had pregnancy related comorbidities with 15.9% having HELLP syndrome, 3.9% having postpartum haemorrhage and acute kidney injury respectively. Caesarean section rate was 78%. Fifty three percent had pretern births, 42% were admitted in the newborn unit, 17% had foetal growth restriction and 12.5% had Stillbirths. Patients with less than 4 antenatal visits and no prenatal calcium supplement was associated with adverse maternal outcomes. Foetal growth restriction was associated with pretern births.

#### Conclusion

Prevalence of recurrent preeclampsia is high 27.5%. The average age of patients is 32 years with a high ANC attendance. However, there is low use of aspirin and calcium for prevention of preeclampsia. There is a high caesarean section rate but no mortality reported. A high proportion of patients had preterm births resulting in newborn unit admissions. We recommend managing such patients in facilities that can conduct caesarean sections, screening for fetal growth restriction and offer newborn care for preterm neonates.

#### **CHAPTER ONE: INTRODUCTION**

#### **1.1. Background of the study**

According to the International society for the study of hypertension in pregnancy (ISSPH) preeclampsia has been characterized as a new onset of hypertension with either proteinuria or target organ dysfunction commencing at 20 weeks' gestation (1).

Preeclampsia is ardently linked to increased maternal and perinatal morbidity and mortality globally (2– 5) and in Sub-Saharan Africa in particular (6,7).

Every year, between 2% and 10% of pregnancies are negatively impacted by preeclampsia. The preponderance varies from one country to the next (3). The World Health Organization (WHO) reports that pre-eclampsia harms 2.8 percent of live births in developing countries and 0.4 percent of live births in developed countries (3,8,9). Despite numerous studies conducted to learn more about the pathogenesis of preeclampsia, the precise etiology of the condition is yet to be established (10).

The findings of numerous research in various parts of the world on risk factors and predictors of recurrent preeclampsia are inconclusive owing to variation across populations and ethnic and religious communities (11).

The paucity of data shows a need for regional epidemiology data on determinants of recurrent preeclampsia.

Earlier studies by Campbell DM et al in 1985, Sibai BM et al in 1986, and Lie RT et al in 1998 revealed a recurrence rate of preeclampsia ranging from 7 to 10 (12–14). According to research conducted by Mahande et al in Moshi, Tanzania, 24.6 percent of individuals with preeclampsia experienced a recurrence in a future pregnancy (15). Van Rijn et al. found that 25% of individuals with preeclampsia had a recurrence in the subsequent pregnancy in research he conducted in the Netherlands (16).

According to Firoz T et al, the failure to predict recurrent preeclampsia early leads to delays in diagnosis and appropriate treatment, resulting in significant obstetricand neonatal mortality from preeclampsia (17).

Von Dadelszen P et al states that clinical prediction of recurrent pre-eclampsia based on identified risk factors would aid in surveillance and avoidance of complications, resulting in improved childbirth outcomes in preeclamptic patients (18). As per North R et al and Sibai BM et al, research findings on the predictors of recurrent preeclampsia have fixated on nulliparous gravid women and defined risk factors evaluated at 14-16 weeks of gestation, which include maternal age,hypertension, body mass index, familial history of preeclampsia, and medical comorbidities (19,20). However, the majority of these investigations were performed in countries outside of Africa and the generalizability of these findings to women in Kenyan settings may be limited.

#### 1.2. Problem statement

Preeclampsia is among the leading causes of maternal and neonatal morbidity and mortality worldwide, especially in Sub-Saharan Africa.

Despite numerous studies the cause and pathogenesis of preeclampsia is still vague and not clearly delineated. There is paucity of data due to limited studies on the predictors and prevention of recurrent preeclampsia. The inability to have an early prediction of recurrence of preeclampsia, leads to delays in diagnosis and effective treatment, consequently resulting in high maternal and perinatal mortality from pre-eclampsia.

Clinical prediction of recurrent preeclampsia, based on identifiable risk factors, will help in surveillance and prevention of complications: thus, improve obstetric and neonatal outcome of women who are predisposed to preeclampsia. Research on the predictors of recurrent preeclampsia have focused on nulliparous pregnant women and identified risk factors measured at 14-16 weeks' gestation including maternal age, mean arterial blood pressure, body mass index, family historyof preeclampsia, and comorbidities (9,10). However, most of these studies were done in countries outside of Africa and the generalizability of these findings to women in Kenyan settings may be limited.

#### **CHAPTER TWO: LITERATURE REVIEW**

#### 2.1. Introduction

According to Van Oostward MF et al (AJOG 2015) a woman who had preeclampsia in a prior pregnancy and now develops preeclampsia in a subsequent pregnancy is considered to have recurrent preeclampsia (21). Several studies have shown that preeclampsia tends to recur. Previous studies by Campbell DM et al in 1985, Sibai B.Met al in 1986 and Lie RT et al in 1988 have reported the recurrence rate of pre-eclampsia ranging from 7 to 10 times (12–14). Mostello D, et al (2008), in a population-based study in Missouri USA, reported a prevalence of recurrent Preeclampsia to be 14.7% (22). Van Oostward MF et al did a meta-analysis that analyzed studies and reported an overall prevalence rate of recurrent preeclampsia of 20.7%. (21,22). A study done in Moshi, Tanzania by Mahande et al, published in 2013 established a 25% of patients with prior preeclampsia had a recurrence (15). This was in tandem with the findings of a study done by Van Rijn in Netherlands established that 25% of patients with preeclampsia had a recurrence (23).

#### 2.1.1. Clinical characteristics and risk factors associated with recurrent pre-eclampsia.

**Maternal gestational age:** Mostello et al, 2008, in a population-based study in Missouri USA, reported that patients with an earlier onset of preeclampsia had a higher risk of recurrence (22). A study by Poon et al elucidated that the risk for late- onset PE escalates by 4% with per annum after attaining age 32 (24). Nonetheless, maternal age is not linked with a higher chance of getting early-onset PE (24). A recent meta-analysis, by Meazaw et al, of factors associated with preeclampsia and eclampsia in sub-

Saharan Africa, showed that both young maternal age (<35 years) and those with old maternal age ( $\geq$  35 years) have equal predisposition to develop preeclampsia. However, this study did not show whether there is association of maternal age with recurrent preeclampsia (25).

Parity: Meazaw et al. in the 2020 meta-analysis mentioned above established that primiparous women

have 2.5 times higher chances of developing preeclampsia/eclampsia as comparison to multiparous women in sub-Saharan Africa (25).

Antenatal Care (ANC) visits: Meazaw et al in the aforementioned meta-analysis conducted in 2020, established that patients who didn't attend antenatal clinic while gravid had a nearly three times higher risk of having preeclampsia/eclampsia as compares to clients who had ANC visits (25).

**Previous preeclampsia/eclampsia:** In the same Meta-analysis alluded to earlier done by Meazaw to establish the factors associated with preeclampsia in Sub Saharan Africa showed that women who had a history of preeclampsia or eclampsia were nearly six times higher risk of developing pre-eclampsia or eclampsia as compared to women whohad no history of preeclampsia or eclampsia in past pregnancies (25).

A 2016 meta-analysis of cohort studies done by Bartsch et al. demonstrated that women with preeclampsia in an antecedent pregnancy had the highest pooled relative risk of having recurrent preeclampsia (8.4, 7.1 to 9.9) (26). Duckitt et al did a systemic reviewof studies in 2005 that showed that patients with an antecedent history of preeclampsiahad a seven-fold increased risk of having a recurrence (27).

Zhong-Cheng Luo NA et al (2007) did a study on primiparous women that showed patients with preeclampsia in a single pregnancy had a 15% risk of recurrence in the next pregnancy and 32% risk of recurrence if she had pre-eclampsia in 2 pregnancies (28). It has been postulated that the multisystemic nature of the disease influences the likelihood of recurrence. To avoid adverse outcomes patients with a history of pre-eclampsia need close follow up in subsequent pregnancies (29).

Hernandez-Diaz S et al in 2009 did a population-based study that established arecurrence rate of preeclampsia to be 14.7% if she had preeclampsia in one pregnancy and 31.9% for women who had PE in the previous two pregnancies (30).

Previous studies by Odegard RA et al (2000), van Rijn BB et al (2006) and LangenveldJ et al (2010) respectively did studies that elucidated that a prior history of pre-eclampsia predisposes one to having early onset preeclampsia in subsequent pregnancy as opposed tolate-onset preeclampsia (16,29,31).

According to Ronsmans et al (2003), early onset PE (<32 weeks) is linked with poor pregnancy outcomes and a higher maternal and perinatal morbidity and mortality (32).

**Family history of preeclampsia/eclampsia:** Meazaw MW et al in the 2020 aforementioned metaanalysis that analyzed studies that looked at factors associated with preeclampsia and eclampsia in SSA demonstrated that family history of preeclampsia or eclampsia predisposed women to a 1.68 times higher risk of developingpreeclampsia or eclampsia during pregnancy (25).

A study by Boyd et. Al, showed that a familial history of preeclampsia predisposes an individual to a higher risk of developing preeclampsia (33). A higher incidence of preeclampsia leads to an escalated risk of recurrence (33).

**Comorbidities:** Bartsch E et al. in the aforementioned meta-analysis published in 2016 reported that a wide array of commodities such as; renal disease, chronic hypertension, diabetes mellitus, and autoimmune diseases like systemic lupus erythematosus and antiphospholipid syndrome, are linked with an elevated risk of developing PE (26). Meazaw MW et al in the study referred to earlier demonstrated that patients with chronic hypertension increased twice as likely to develop preeclampsia in comparison the general population without chronic hypertension (25). In the same sub-Saharan African study, by Meazaw MW et al, Anaemia in pregnancy predisposed patients to a threefold elevated risk of getting preeclampsia as opposed to those without such a history (25).

**High BMI**: A study by Mostello D, et al (2008), did show that the recurrence rate of preeclampsia increases with maternal BMI (22). Likewise, Meazaw MW et al demonstrated that in Sub-Saharan Africa women with high BMI were 1.4 times more likely to develop hypertensive disorders in pregnancy as compared to women with a lower BMI (25).

#### 2.1.2. Outcomes of recurrent pre-eclampsia

Preeclampsia has been linked with adverse outcomes such as elevated maternal and perinatal morbidity and mortality globally in general (2–5) and Sub-Saharan Africaspecifically (6,7).

Firoz T et al in 2011, observed that the inability to have an early prediction of a possible recurrent preeclampsia, leads to delays in diagnosis and effective treatment, consequently resulting in adverse outcomes associated with pre-eclampsia (17). Moreover, recurrence has also been linked to admission to Intensive care unit and long hospital stay (17).

#### 2.1.3. Prevention interventions of recurrent pre-eclampsia

**Calcium supplements for prevention of pre-eclampsia:** W.H.O and A.C.O.G concur on the benefits of use of calcium supplements in the prevention of preeclampsia (34,35).

A 2018 Cochrane systematic review that analyzed 27 studies where more than half lived in geographic regions where they consumed foods with low calcium found that calcium supplementation of more than 1 gram from 20 weeks' gestation to delivery significantly reduced the risk of preeclampsia (relative risk [RR] 0.45, 95% CI 0.31-0.65, 13 trials) and gestational hypertension (RR 0.65, 95% CI 0.53-0.81) in comparison with those who got placebo or no treatment in the cohort (36).

Antiplatelets for prevention of pre-eclampsia: A Cochrane review of 60 RCTs involving 37 720 women recommended the following:Low-dose acetylsalicylic acid for the prevention of pre-eclampsia in women at high risk of developing the condition (37). The low-dose acetylsalicylic acid / aspirin for the prevention of pre-eclampsia and its related complications should be initiated before 20weeks of pregnancy (37). Low dose refers to a dose of 50 -150 mg of Aspirin. Initially 75 mg of Aspirin was recommended by WHO but a study by Van Doorn et al recommends using a dose of Aspirin; 150 mg per day (38).

The WHO recommends use of antiplatelets for patients with at least one of the following risk factors: history of preeclampsia; chronic hypertension, renal disease, systemic lupus erythematosus diabetes

mellitus, and multiple gestation. The recommendations can be adjusted or adapted based on local data on the epidemiology of pre-eclampsia. W.H.O recommends use of antiplatelet agents prior to12 weeks', if possible, if there is a delay latest by 20 weeks' gestation (34).

#### **2.2. Theoretical Framework**

This study has adopted the 2-stage theory as postulated by Chris Redman et al in 1999 (39). The theory proposes that a poorly perfused placenta (Stage 1) produces factors that lead to clinical manifestation of preeclampsia (Stage 2). This theory explains the etiology, pathogenesis of preeclampsia and thus informs the laid down strategies which prevent and manage this disease.

The first stage involves placental under perfusion and second stage the maternal syndrome that leads to multisystemic manifestation of the disease. The placenta is central to the pathogenesis of preeclampsia (40). It is composed of decidua basalis frommaternal part and four fifths is from fetal tissues. Human placenta has two independent placenta is each other the fetoplacental and maternal placental circulation. The spiral arterioles are specifically linked in the pathogenesis of preeclampsia. Endovascular trophoblasts invade up to decidual segments of the spiral arterioles by week 12 and by 18<sup>th</sup> week another wave of trophoblasts invades up to the myometrial segments. This process replaces the endothelial lining and the muscular arterial wall by fibrinoid formation. The spiral arterioles thereby become distended, tortuous, and funnel-shaped thus the spiral arterioles turn into a low resistance, low

pressure, high flow system (39).

In Pre-eclampsia there is failure of the second wave of endovascular trophoblast migration and there is reduction of blood supply to the fetoplacental unit. The diminished placental blood flow leads to hypoxia and ischemia. This leads to release of inflammatory mediators such as cytokines, interleukin 6. It culminates in endothelialdysfunction is due to oxidative stress and the inflammatory mediators. There are geneticfactors, immunologic factors that influence the manifestation of the disease.

Vasospasm results from the imbalance of vasodilators decrease in Prostaglandin, nitricoxide and increase in vasoconstrictors Angiotensin-II, Thromboxane A2, Endothelin. Thus, manifesting as an increase in blood pressure. The damaged endothelium leads toloss of proteins via the urine causing proteinuria. The leaking of proteins and decrease on oncotic pressure causes edema (41). The placental insufficiency causes growth restriction. The leaky capillaries and elevated blood pressure in the brain causes cerebral edema, blurred vision and convulsions.

The fact that some underlying diseases, maternal and genetic factors will remain the same then it creates a high likelihood of recurrence. The following observations and medical phenomena give credibility to this theory. Diseases associated with vascular insufficiency such as hypertension, diabetes, systemic lupus erythematosus, renal disease, acquired and inherited thrombophilia's increase the risk of abnormal placentation and preeclampsia.

Obstetric conditions that increase placental mass like hydatidiform mole, hydrops fetalis, diabetes mellitus and multiple gestation result in relative ischemia and are associated with preeclampsia. Preeclampsia is more common in women who live at high altitudes above 3100 meters above sea level because of the low oxygen concentration (40). The aim of this study is therefore to quantify the magnitude of recurrent preeclampsia in our study population. Then assess the risk factors that will influence the recurrence of the disease. These include the maternal constitutional factors that influence the manifestation of the disease such as age, diabetes, systemic lupus erythematosus, chronic hypertension, high body mass index, the onset of preeclampsia in the previous pregnancy. There are strategies that have been proven tobe effective in reducing incidence and recurrence of preeclampsia such as use of low dose aspirin, Calcium supplementation and attendance of antenatal clinic. The study will assess if the patients adhered to these mitigation strategies or missed out. Finally assessing the fetal and maternal outcomes of the women who had recurrent preeclampsia (39). Being a cross sectional study, it will focus on quantifying the prevalence, risk factors and outcomes but will not assess the temporal association of the risk factors and the outcome.

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The two-stage theory of Preeclampsia by Chris Redman Et Al (1999)



#### 2.2.1. Conceptual Framework



Source: (Zephania Ashira, 2021).

Figure 1:Conceptual framework.

Women who have index preeclampsia have been shown to be at a high risk of recurrence. There are associated risk factors that predispose these women to recurrence of PE. These factors entail: preeclampsia in antecedent pregnancy, familial history of preeclampsia, ANC attendance, comorbidities (chronic hypertension, renal failure, systemic lupus erythematous diabetes mellitus and antiphospholipid

antibodysyndrome). Preeclampsia is strongly linked with adverse obstetric and neonatal outcomes such as admission to ICU for the mother and NBU for the neonate and long hospital stay (2–5,17). Early identification and putting in place preventive measures such as counseling of couples, calcium supplementation and use of aspirin have been shown to reduce the rate and or severity of recurrence.

#### 2.2.2. Study justification

This study was therefore done to provide data on prevalence rate of preeclampsia, clinical characteristics that are predictive of patients developing recurrent pre- eclampsia at Kenyatta National Hospital. These findings contribute to epidemiological data and predictive screening check list for triaging antenatal clients for close surveillance and management to prevent maternal and perinatal morbidity and mortality in Kenya. Early identification and establishingpreventive measures such as use of aspirin, antihypertensives, treatmentof comorbidities and counseling of the couples have been shown to reduce the rate andor severity of recurrence.

#### 2.3. Research Question

What is the prevalence, clinical characteristics and outcomes of recurrent preeclampsia among postpartum women in puerperium at Kenyatta National Hospital?

#### 2.4. Research Objectives

#### 2.4.1. Broad objective

To determine the prevalence, clinical characteristic and outcomes of recurrent preeclampsia among postpartum women in puerperium at Kenyatta National Hospital.

#### 2.4.2. Specific objectives

Among postpartum women in puerperium at Kenyatta National Hospital to:

- 1. Calculate the prevalence rate of recurrent preeclampsia
- 2. Describe clinical characteristics of patients with recurrent preeclampsia
- 3. Describe maternal and perinatal outcomes of recurrent preeclampsia

#### CHAPTER THREE: RESEARCH METHODOLOGY 3.1. Study design

This was a cross-sectional study. Women with preeclampsia in at least two gestation receiving care at Kenyatta National Hospital (KNH) were recruited into the study and the prevalence rate, clinical characteristics, maternal and fetal outcomes determined.

#### 3.2. Study site and setting

Kenyatta National Hospital (KNH) is the largest teaching and referral hospital in Kenya and East Africa. It's in close proximity to the Nairobi central business district. It serves residents of the populous Nairobi County as the primary hospital in addition to patients referred patients from different parts of Kenya. The Reproductive Health Department has a capacity of 220 beds and has a wide array of professionals from renown Professors, consultants, senior house officers, nurse's midwives and Interns. The affiliated training institutions like University of Nairobi, Kenya Medical Training College, KEMRI are domiciled within the facility and have turned it into a renowned epicenter of medical training, research and advanced medical services. Kenyatta national Hospital handles over 10000 deliveries per annum and approximately 1000 patients per annum have preeclampsia. It has 2 Maternity theatres that run concurrently 24hrs a day throughout the year. Labour ward has 4 delivery couches and 28 beds. It has 4 wards that deal exclusively with antenatal and postnatal patients. 1 ward with mixed use; caters for oncology, acute gynecology and postnatal patients with complications. In total it has a bed space for over 220 patients.

#### **3.3. Target population**

All postpartum women in puerperium who had preeclampsia in a previous pregnancy and a recurrence in the recent one were recruited into the study.

#### 3.4. Eligibility Criteria

#### **3.4.1.** Inclusion criteria

All postpartum women in puerperium who had Preeclampsia in a previous pregnancy and a recurrence in the recent pregnancy.

#### 3.4.2. Exclusion criteria

Women in puerperium with Recurrent Preeclampsia superimposed on Chronic Hypertension. Postnatal women with preeclampsia superimposed on chronic hypertension.

Chronic hypertension causes target organ damage that manifests with symptoms similar symptoms to Preeclampsia. So, it will not be easy to separate the 2 disease entities. The definition for preeclampsia in this study defines preeclampsia as hypertension with proteinuria and or target organ damage. Chronic hypertension causes renal failure, CNS manifestations such as scotoma, stroke and aneurysms can be confused for pre-eclampsia with severe features. Hence it will not be easy to separate the 2 entities without a baseline clinical workups and examination for chronic hypertension.

#### 3.5. Sampling Technique

This study utilized consecutive sampling techniques.

#### 3.6. Sample Size

According to data from the KNH records department for the last 4 years approximately1000 women are diagnosed with pre-eclampsia at Kenyatta National Hospital.

A study done in 2013 by Mahande Et al in Moshi, Tanzania assessing the prevalence, risk factors and outcomes of recurrent Preeclampsia; 25 % of the patients with pre-eclampsia will have recurrent preeclampsia (15). A study by Van Rijn in Netherland also established that 25% of patients with preeclampsia will have a recurrence, while Bramham in United Kingdom found that 23% of patients

with preeclampsia will have a recurrence (16,23).

Hence the target population was found to be 250 people. Krejcie and Morgan Formula for calculating sample size in a finite population was used.

A population of 152 was established.

Krejcie and Morgan Formula for calculating sample size in a finite population

SIZE = 
$$d^2 (N-1) + X^2 P (1-P)$$

s = required sample size. = 152

X2= the table value of chi-square for 1 degree of freedom at the desired confidence level (3.841). N = the population size=250

P = the population proportion (assumed to be .50 since this would provide the maximum sample size).

d = the degree of accuracy expressed as a proportion (.05). How the Prevalence rate will be answered

#### 3.7. Sampling procedure

Study participants were recruited from postnatal wards. Questionnaires were administered at first contact after informed consent was sought and given by the patient.

The questionnaires were issued by the principal investigator and the research assistants. More data was

extracted from the patient's file.

Patient subsequently received routine care.



Figure 2: Flow diagram of patient's selection

#### 3.8. Recruitment of research assistants

Two research assistants were recruited to help in the data collection process. The research assistants were qualified clinical officers who understand the KNH set up for ease of access to the targeted patients. The research assistants underwent rigorous training. The first day involved familiarization of the study tool and sampling procedure while the second day involved visiting the study setting to interact with patients while identifying key approach to be used in obtaining accurate and complete data from the selected participants.

#### 3.9. Pretest

The study pretest was conducted at Mbagathi County hospital reproductive health department. This aided in ensuring that the questions included in the questionnaire are understood and respondents understand the study objectives with ease. Mbagathi has been selected for pre-test because they handle same patients as Kenyatta National Hospital in their obstetric wards.

#### 3.10. Validity and Reliability

Internal validity of the study was achieved by severally reviewing the information collected and recorded during the interviews and also from administered questionnaire. External validity was achieved through the use of a randomly selected participants and verifying the accuracy of the data collected. The research was audited by frequently checking that interpretations are transferable, credible, confirmable and above all dependable. Reliability will also be achieved by ensuring that experts in the field cross check the data collection tool for completeness, accuracy and efficacy. An expert statistician was employed to review the data collection tool and ensure that the objectives are achievable.

#### 3.11. Data collection

Data collection process commenced after approval from KNH-UoN Ethics Committee and Kenyatta National Hospital Administration.

#### 3.11.1. Screening of participants

Inclusion and exclusion criteria was used in screening of the participants in the study. The study utilized consecutive sampling. Thus, patients with previous history of preeclampsia were screened those with recurrent preeclampsia were recruited until the sample size was attained. The prevalence was calculated based on recruited patients with recurrent preeclampsia (n = 152) divided by the number of patients screened.

#### **3.11.2. Data collection procedure**

Only patients with recurrent preeclampsia were recruited in the study. Questionnaire were administered for primary data collection. Primary data was included: bio-data, risk factors and clinical presentation and pregnancy outcome (maternal and fetal), additional information like birth weight, apgar score were obtained from patients files.

Research assistants were trained on how to administer the questionnaire to minimize questionnaire and interpretational bias. Questionnaire were printed in both English and Swahili (official languages) for ease of communication.

#### 3.12. Study variables

#### 3.12.1. Independent Variables

Sociodemographic characteristics; Age. Marital status education and income

**Clinical Characteristics;** Gestational age of onset, Number of pregnancies affected by Preeclampsia, Parity, Diabetes mellitus, antiphospholipid syndrome. Systemic Lupus Erythematosus Antenatal clinic attendance

Use of Low dose Aspirin Use of Calcium Supplementation

#### 3.12.2. Dependent Variables

#### Maternal outcomes

Acute Kidney Injury, Mode of Delivery, Cerebral Vascular Accident, Placenta Abruptio, Post-Partum Hemorrhage, Preterm delivery and ICU admission.

#### **Fetal outcomes**

Low birth weight, Perinatal death, Admission to NBU, Apgar score, Foetal growth restriction

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Objective	Formula
Prevalence	total number of recurrent preeclampsia during the study period × 100
	total number of preeclampsia during the study period

The records of the total number of preeclampsia patients and those with recurrent preeclampsia during the study period was assessed by analyzing KNH records.

#### 3.13. Quality assurance

The data collection using questionnaire allowed interaction between researcher and respondent hence researchers were able to interpret and explain effectively about the purpose of the study as well as the questions that might not be clear. The questionnaires used in data collection were serialized to control any form of duplication. Respondents were given unique identities to ensure that they are not enrolled twice into the study. During data collection process, a sample of questionnaires were randomly selected and checked for completeness. A qualified statistician was contracted to carry out data entry and analysis.

#### 3.14. Data Management and Analysis

Material used for this study including stationery, questionnaire, registries, hard drives, password protected computers and iCloud.

Data remained confidential and restricted access only to the principal investigator and the research assistants. Questionnaires were kept in safe data cabinets with lock and key. The computer database was password protected to restrict access to unauthorized individuals. Filled questionnaires will be destroyed by shredding after successful defense of the study findings or publication of study results, whichever

comes first and computer databases and USBs will be deleted after 10 years.

Data entry was done on EXCEL and STATA. Results were presented in tables, chart, and graphs and as measures of central tendencies.

Descriptive statistics were presented in the tables and charts. Proportions were calculated for recurrent preeclampsia then compared using chi square for statistical significance. Descriptive statistics for instance measures of central tendency and dispersion such as the mean and the standard deviation were used to summarize continuous variables such as age, and Apgar score if normality assumptions will be satisfied.

Categorical variables such as admission to the new born unit (NBU), preterm birth, or stillbirth were evaluated using frequencies and the corresponding percentages. Continuous variables such as age, gestational age, weight among others were evaluated using mean and the corresponding standard deviation.

Maternal outcomes among the women with preeclampsia were summarized using the descriptive statistics for the measures of central tendency and dispersion. Frequencies and the corresponding percentages were used to summarize categorical variables specific maternal outcomes include: eclampsia, acute kidney injury, stroke and target organ damage.

Neonatal outcomes for women with preeclampsia were summarized using the descriptive statistics. Continuous variables such as birth weight, Apgar score among others were summarized using mean and standard. Frequencies and the corresponding percentages were used to summarize categorical variables such as admission to the newborn unit (NBU), preterm birth, or stillbirth among others.

#### 3.15. Ethical considerations

Approval to conduct the study was sought from KNH-UoN Ethics and Research Committee. We also sought authorization to compile and evaluate data from the following departments of Kenyatta National

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Hospital respectively; reproductive health services, departments of research and clinical services, health information and records. KNH ethics approval number; P644/08/2018

Ensuring the security of the physical copy of documents and the data storage devices such as USB and external hard disk was paramount. This helped maintain confidentiality and security of data. Information collected remains confidential and willbe used exclusively for the study.

The study adhered to the highest ethical standards based on globally recognized guidelines and conventions such as the Belmont principles and the KNH / UON ethical Guidelines.

Researchers were trained in ethical standards, study protocols and should have good clinical practice (GCP) certification.

The patient autonomously opted in or out of the study without being coerced. Truthful and candid information about the study was shared before getting informed consent.

The patient got the required care regardless of whether they opt in or out of the study. If the patient needed further management based on the information from the interview. The recommendation was relayed to the caregivers and the patient to ensure the patient is assisted.

Due to the presence of Covid 19; Researchers strictly adhered to the KNH and Ministry of health guidelines to mitigate spread of Covid. Sanitizing, social distancing and use of masks and protective gear was adhered to. Regular checking of temperature and if a member has symptoms of Covid he / she was given ample timeto recuperate, get proper care to mitigate risk of spread. A patient found or suspected to have Covid was guided on how and where to get proper care.

#### 3.16. Study limitations

We anticipated encountering files with missing or incomplete data. However, this will be vercome by corroborating the information with the participants themselves.

Recall bias. Patients might not recall some information accurately hence more information will be acquired from records such as file and antenatal book.

#### 3.17. Dissemination of study findings

The findings were presented in Obstetrics and Gynecology department of UoN. The findings will also be shared with Kenyatta National Hospital to aid in policy review in a bid to control recurrent preeclampsia. The results will also be published in a peer reviewed journal like JOGECA and East African Medical Journal.

#### **CHAPTER FOUR: RESULTS**

#### 4.1. Introduction

The study sought to determine the prevalence, clinical characteristics, maternal and perinatal outcomes of patients with recurrent preeclampsia at Kenyatta National Hospital from October 11 th 2021 to March 31<sup>st</sup> 2022. A total sample of 152 participants were recruited into the study.

#### Study flow chart



Figure 3Recruitment scheme of patients with Recurrent Preeclampsia at KNH between Oct 2021 and March2022

#### 4.2. Demographic characteristics

#### 4.2.1. Socio-demographic characteristics of patients with recurrent preeclampsia

The mean age of the participants was 32.41 (SD $\pm 5.03$ ) years and most of the participants were 32 years old. The youngest was 19 years old and the eldest 45 years old. Majority of the women (92.8%) were married with over 80% of them having post primary education. Fifty four percent of the women were unemployed hence no stable source of income. Majority of them 99.3% attended ANC clinics with 77% having attended more than four times. The prevalence of recurrent preeclampsia at KNH during the study period was 27.5%.

Table 1: Socio-demographic characteristics of patients with recurrent preeclampsia

Variable	Ν		Frequency (n)	Percent (%)
Age (Mean ±SD)		152	32±5.03	
19 -35 years			104	68.4
>35 years			48	31.6
Marital status				
Single/Divorced			11	7.2
Married			141	92.8
Education		152		
None/Primary			27	17.8
Secondary			72	47.4
Tertiary			53	34.9
Occupation		152		
Unemployed			82	53.9
Employed			70	46.1
ANC attendance		152		
No			1	0.7
Yes			151	99.3
ANC Visits		152		
>4 visits			35	23.0
$\geq$ 4 visits			117	77.0
#### 4.2.2. Clinical characteristics of patients with recurrent pre-eclampsia

Majority of the women recruited in the study 113 (74.3%) were Para 3 and below with 14 (9.2%) of them having pre-existing medical conditions which included diabetes mellitus, chronic kidney disease, deep vein thrombosis, HIV, epilepsy, fibroids, systemic lupus erythematous, p and tuberculosis. The mean inter pregnancy interval was 5.89 with a standard deviation of 3.07, majority of the women 26 (17.7%) had a pregnancy interval of 5 years. Sixty nine Percent of the women had a gestation age of more than 34 weeks, with 140 having date certainty. Majority of the women 94 (61.8%) also had late onset of preeclampsia. One hundred and seven women 70.4% did not receive any calcium supplements, similarly 121 (79.6%) did not use aspirin.

Variable	N	Frequency	Percent
variable	IN	(n)	(%)
Parity			
Para 2 -3	152	113	74.3
≥para 4		39	25.7
Preexisting Medical conditions			
No		138	90.8
Yes	152	14	9.2
History of smoking			
No	152	152	100
Yes		0	0
HIV Status	152		
Positive		1	0.7
Negative		151	99.3
Mode of Conception	152		
Normal		152	100
Assisted		0	0
Inter Pregnancy Interval (Mean ±SD)	152	$5.89 \pm 3.7$	
Date certainty	152		
No		12	7.9
Yes		140	92.1
Onset of Pre-eclampsia	152		
Early		58	38.2
Late		94	61.8
Calcium Supplement	152		
No		107	70.4
Yes		45	29.6
Aspirin Use	152		
No		121	79.6
Yes		31	20.4
Gestational age at diagnosis	152		
Preterm		80	52.6
Term		72	47.4

## Table 2: Clinical characteristics of patients with recurrent pre-eclampsia

## 4.2. Maternal outcomes of patients with recurrent pre-eclampsia

The findings revealed that 119(78.3%) delivered via CS, 65(42.8%) developed pregnancy complications which included abruption placenta, HELLP syndrome, Intra Uterine Fetal Death, PPH, PROM, NRFS and twin gestation while 2(1.4%) were admitted to the ICU as shown in Table 4.4.

	Frequency	Percent
Mode of delivery		
CS	119	78.3
SVD	33	21.7
Pregnancy complications		
Yes	65	42.8
No	87	57.2
ICU admission		
Yes	2	1.4
No	150	98.6

## Table 3: Maternal outcomes of patients with recurrent pre-eclampsia

## 4.3. Fetal outcomes of patients with recurrent pre-eclampsia

Thirty-nine (25.7%) of the babies born had an Apgar score of less than seven at 5<sup>th</sup> minute, 82(53.9%) of the newborns had a birth weight of below 2500 grams. With regards to birth outcomes there were 19(12.5%) stillbirths and 87(57.2%) of the babies were admitted into NBU as shown in Table 4.5. The indications for NBU admission included Low birth weight prematurity and respiratory distress syndrome.

## Table 4: Fetal outcomes of patients with recurrent pre-eclampsia

	Frequency	Percent
Apgar score at 5th minute		
<7	39	25.7
>=7	113	74.3
Birthweight		
<2500g	82	53.9
<=2500g	70	46.1
Stillbirth		
Yes	19	12.5
No	133	87.5
NBU admission		
No	87	57.2
Yes	65	42.8
Foetal Growth Restriction		
Yes	26	17.1
No	126	82.9

## 4.4. Factors associated with maternal outcomes among women with recurrent preeclampsia

## 4.4.1. Factors associated with mode of delivery among women with preeclampsia

Factors associated with mode of delivery among women with preeclampsia were investigated as shown in Table 5. Education level (p = 0.016), occupation (p = 0.031) and parity (p = 0.037) were significantly associated with mode of delivery among women with recurrent preeclampsia.

	Mode of Delivery		
	CS n (%)	SVD n(%)	<b>P-value</b>
Age of patient			
19 - 35 years	80(76.9)	24(23.1)	0.353
Above 35 years	39(81.3)	9(18.8)	
Education level			
None/Primary	16(59.3)	11(40.7)	
Secondary	58(80.6)	14(19.4)	0.016
Tertiary	45(84.9)	8(15.1)	
Occupation			
Unemployed	59(72.0)	23(28.0)	0.031
Employed	60(85.7)	10(14.3)	
Marital status			
Single	9(90)	1(10)	
Married	110(78.0)	31(22.0)	0.11
Divorced/Separated	0	1(100)	
ANC visits			
>4 visits	28(80.0)	7(20.0)	0.491
=>4 visits	91(77.8)	26(22.2)	
Parity			
Para 2 - 3	93(82.3)	20(17.7)	0.037
=>Para 4	26(66.7)	13(33.3)	
Comorbidities			
Yes	11(78.6)	3(21.4)	0.641
No	108(78.3)	30(21.7)	
Date certainty			
Yes	110(78.6)	30(21.4)	0.506
No	9(75.0)	3(25.0)	
Calcium supplements			
No	85(79.4)	22(20.6)	0.371
Yes	34(75.6)	11(24.4)	
Aspirin use			
No	93(76.9)	28(23.1)	0.281
Yes	26(83.9)	5(16.1)	
Onset of pre-eclampsia			
Early	47(81.0)	11(19.0)	0.332
Late	72(76.6)	22(23.4)	
Gestational age at delivery			
Preterm	66(82.5)	14(17.5)	0.132
Term	53(73.6)	19(26.4)	

Table 5: Factors associated with mode of delivery among women with preeclampsia

### 4.4.2. Factors associated with pregnancy complications among women with recurrent

## preeclampsia

Factors associated with pregnancy complications among women with recurrent preeclampsia were investigated as shown in Table 4.7. Number of ANC visits (p<0.001), calcium supplement use (p=0.001), onset of preeclampsia (p=0.005) and gestational age at delivery (p<0.001) were significantly associated with pregnancy complications.

Table 6: Factors associated with pregnancy complications among women with recurrentpreeclampsia

	Pregnancy complication		
			P-
	Yes n (%)	No n (%)	value
Age of patient			
19 - 35 years	44(42.3)	60(57.7)	0.502
Above 35 years	21(43.8)	27(56.3)	
Level of education			
None/Primary	14(51.9)	13(48.1)	
Secondary	32(44.4)	40(55.6)	0.362
Tertiary	19(35.8)	34(64.2)	
Occupation			
Unemployed	36(43.9)	46(56.1)	0.759
Employed	29(41.4)	41(58.6)	
Marital Status			
Single	6(60)	4(40.0)	
Married	59(41.8)	82(58.2)	0.366
Divorced/Separated	Û	1(100)	
Number of ANC visits			
>4 visits	25(71.4)	10(28.6)	<0.001
=>4 visits	40(34.2)	77(65.8)	
Parity			
Para 2 - 3	50(44.2)	63(55.8)	0.331
=>Para 4	15(38.5)	24(61.5)	
Comorbidities			
Yes	6(42.9)	8(57.1)	0.604
No	59(42.8)	79(57.2)	
Date certainty			
Yes	60(42.9)	80(57.1)	0.593
No	5(41.7)	7(58.3)	
Calcium Supplement			
No	55(51.4)	52(48.6)	0.001
Yes	10(22.2)	35(77.8)	
Aspirin Use			
No	55(45.5)	66(54.5)	0.131
Yes	10(32.3)	21(67.7)	
Onset of Pre-eclampsia			
Early	33(56.9)	25(43.1)	0.005
Late	32(34.0)	62(66.0)	
Gestational age at	· · /	. ,	
delivery			
Preterm	46(57.5)	34(42.5)	<0.001
Term	19(26.4)	53(73.6)	

# 4.4.3. Independent factors associated with maternal outcomes among patient's recurrent preeclampsia

Bivariate analysis revealed that secondary level education (OR =3.87, 95%CI: 1.32 - 11.33, p =0.014), being employed (OR =2.34, 95%CI: 1.03 - 5.34, p =0.043), and being para 2-3 (OR =2.33, 95%CI: 1.02 - 5.29, p =0.044), were associated with increased risk of CS among women with recurrent preeclampsia. Multivariate analysis found that women with recurrent preeclampsia and parity of between 2 and 3 were 1.98 times more likely to have CS delivery.

The findings also showed that, ANC visits less than 4 (OR =4.81, 95%CI: 2.11 - 11.0, p <0.001), lack of calcium supplements (OR =3.7, 95%CI: 1.67 - 8.23, p =0.001), early onset of preeclampsia (OR =2.56, 95%CI: 1.31 - 5.01, p =0.006) and gestational age at delivery (OR =3.7, 95%CI: 1.9 - 7.5, p <0.001) were associated with increased risk of pregnancy complication among women with recurrent preeclampsia. Multivariate analysis established that ANC visits less than 4 (AOR =4.78, 95%CI: 1.94 - 11.79, p =0.001), lack of calcium supplements (AOR =3.72, 95%CI: 1.55 - 8.97, p=0.003) and gestational age at delivery (AOR =3.62, 95%CI: 1.21 - 10.86, p=0.021) were independent factors associated with increased risk of pregnancy complication as shown in Table 4.8.

Table 7: Independent factors associated with maternal adverse outcomes among patient's recurrent

preeclampsia

	COR(95%CI)	<b>P-value</b>	AOR(95%CI)	P-value
Mode of delivery (CS)				
Education				
None/Primary	Ref		Ref	
Secondary	3.87(1.32 - 11.33)	0.014	2.47(0.69 - 8.88)	0.166
Tertiary	1.36(0.52 - 3.52)	0.529	1.09(0.38 - 3.17)	0.871
Occupation				
Employed	2.34(1.03 - 5.34)	0.043	1.64(0.61 - 4.44)	0.331
Unemployed	Ref		Ref	
Parity				
Para 2 - 3	2.33(1.02 - 5.29)	0.044	1.98(1.13 - 4.64)	0.017
>=para 4	Ref		Ref	
Pregnancy complications				
ANC visits				
Less than 4	4.81(2.11 - 11.0)	< 0.001	4.78(1.94 - 11.79)	0.001
4 or more visits	Ref		Ref	
Calcium supplements				
No	3.7(1.67 - 8.23)	0.001	3.72(1.55 - 8.97)	0.003
Yes	Ref		Ref	
Onset of Pre-eclampsia				
Late	Ref		Ref	
Early	2.56(1.31 - 5.01)	0.006	0.88(0.29 - 2.64)	0.821
Gestational age at delivery				
Less than 37 weeks	3.77(1.9 - 7.5)	< 0.001	3.62(1.21 - 10.86)	0.021
37 or more weeks	Ref		Ref	

## 4.5. Factors associated with fetal outcomes among women with recurrent pre-eclampsia

## 4.5.1. Factors associated with fetal growth restriction among patients with recurrent pre-

## eclampsia

The results as presented in Table 4.9 revealed that onset of preeclampsia (p<0.001) and gestational age (p<0.001) at diagnosis were significantly associated with FGR.

	FGR		
	Yes n (%)	No n(%)	<b>P-value</b>
Age of patient			
21-35	19(18.3)	85(81.7)	0.378
Above 35	7(14.6)	41(85.4)	
Education			
None/Primary	1(3.7)	26(96.3)	
Secondary	14(19.4)	58(80.6)	0.091
Tertiary	11(20.8)	42(79.2)	
Occupation			
Unemployed	10(12.2)	72(87.8)	0.064
Employed	16(22.9)	54(77.1)	
Marital status			
Single	2(20.0)	9(80.0)	0.87
Married	24(17.0)	117(83.0)	
Parity			
Para 2 - 3	22(19.5)	91(80.5)	0.141
=>Para 4	4(10.3)	35(89.7)	
ANC Visits			
>4 visits	6(17.1)	29(82.9)	587
=>4 visits	20(17.1)	97(82.9)	
Comorbidities			
Yes	2(14.3)	12(85.7)	0.559
No	24(17.4)	114(82.6)	
Date certainty			
Yes	25(17.9)	115(82.1)	0.355
No	1(8.3)	11(91.7)	
Calcium supplements			
No	19(17.8)	88(82.2)	0.472
Yes	7(15.6)	38(84.4)	
Aspirin use			
No	23(19.0)	98(81.0)	0.131
Yes	3(9.7)	28(90.3)	
Onset of Pre-eclampsia			
Early	18(31.0)	40(69.0)	<0.001
Late	8(8.5)	86(91.5)	
Gestation age at delivery			
Preterm	24(30.0)	56(70.0)	<0.001
Term	2(2.8)	70(97.2)	

Table 8: Factors associated with fetal outcomes among women with recurrent pre-eclampsia

## 4.5.2. Factors associated with NBU admission among women with recurrent pre-eclampsia

Factors associated with NBU admission among women with recurrent preeclampsia were investigated as shown in Table 4.9. Onset of preeclampsia (p<0.001) and gestational age at diagnosis (p<0.001).

Table 9: Factors associated with NBU admission among women with recurrent pre-ecla	mpsia
------------------------------------------------------------------------------------	-------

	NICU		
	No	Yes	<b>P-value</b>
Age of patient			
21-35	60(57.7)	44(42.3)	0.502
Above 35	27(56.3)	21(43.8)	
Highest education level			
None/Primary	18(66.7)	9(33.3)	
Secondary	41(56.9)	31(43.1)	0.258
Tertiary	28(52.8)	25(47.2)	
Occupation			
Unemployed	52(63.4)	30(36.6)	0.064
Employed	35(50)	35(50)	
Marital status			
Single	8(72.7)	3(329.3)	0.473
Married	79(56)	62(44)	
Parity			
Para 2 - 3	65(57.5)	48(42.5)	0.525
=>Para 4	22(56.4)	17(43.6)	
Comorbidities			
Yes	7(50)	7(50)	0.611
No	80(58)	58(42)	
Date certainty			
Yes	79(56.4)	61(43.6)	0.355
No	8(66.7)	4(33.3)	
ANC visits			
>4 visits	19(54.3)	16(45.7)	0.416
=>4 visits	68(58.1)	49(41.9)	
Calcium supplements			
No	59(55.1)	48(44.9)	0.266
Yes	28(62.2)	17(37.8)	
Aspirin use			
No	66(54.5)	55(45.5)	0.131
Yes	21(67.7)	10(32.3)	
Onset of Pre-eclampsia			
Early	16(27.6)	42(72.4)	<0.001
Late	71(75.5)	23(24.5)	
Gestational age at birth	· · ·	. /	
Preterm	24(30.0)	56(70.0)	<0.001
Term	63(87.5)	9(12.5)	

#### 4.5.3. Independent factors associated with fetal outcomes among patient's recurrent

#### preeclampsia

Bivariate analysis found that early onset of preeclampsia (OR =4.84, 95%CI: 1.94 - 12.06, p =0.001) and gestational age at birth (OR =15.0, 95%CI: 3.40 - 55.2, p<0.001), were associated with increased risk of FGR among infants born of mothers with recurrent preeclampsia. Multivariate analysis established that babies born of women with recurrent preeclampsia were 13 times more likely to have FGR (AOR =13.13, 95%CI: 2.42 - 71.13, p =0.003).

In investigating factors associated with NBU admission, bivariate analysis found that early onset of preeclampsia (OR =8.1, 95%CI: 3.85 - 17.04, p <0.001), and preterm delivery (OR =16.33, 95%CI: 7.01 - 38.09, p <0.001), were associated with increased risk of NBU admission. Multivariate analysis found that preterm babies born of women with recurrent preeclampsia were 12 times more likely to have NBU admission as shown in Table 4.11.

Table 10: Independent factors associated with fetal outcomes among patient's recurrent preeclampsia

	COR (95%CI)	<b>P-value</b>	AOR (95%CI)	<b>P-value</b>
FGR				
Onset of Pre-eclampsia				
Early	4.84(1.94 - 12.06)	0.001	1.2(0.4 - 3.57)	0.743
Late	Ref			
Gestational age at birth				
Preterm	15(3.40 - 55.2)	< 0.001	13.13(2.42 - 71.13)	0.003
Term	Ref			
NBU admission				
Onset of Pre-eclampsia				
Early	8.1(3.85 - 17.04)	< 0.001	1.5(0.53 - 4.25)	0.446
Late				
Gestational age at birth				
Preterm	16.33(7.01 - 38.09)	< 0.001	12.25(4.02 - 37.34)	<0.001
Term				

#### **CHAPTER FIVE: DISCUSSION**

The prevalence of pre-eclampsia in the present study (27%) is comparable with findings from a study done in Tanzania by Mahande which found the prevalence rate at 25 % (15). Another study done by Emmanuel and Butt also found the same prevalence rate (42). Both studies had a similar study design, comparable study population and settings both being in Low- and middle-income countries.

In contrast to this, the incidence rates of recurrent pre-eclampsia reported by Mostello et al at 14.7%, was lower than the current study. This difference could be due to strict criteria for defining pre-eclampsia are adhered to and when under-reporting of pre-eclampsia cases occurs (22). The difference could also be attributed to the study being done in St. Louis, Missouri- a high-income setting. The population-based cohort study might have had a high attrition rate of study participants thus resulting in a smaller percentage of the population having recurrent pre-eclampsia.

The clinical characteristics, associated risk factors for pre-eclampsia ascertained in this study are similar to those have been described in other studies conducted in different countries. Most of the studies showed that the risk of recurrent pre-eclampsia increases with age supporting this, our study indicates that pregnant women who were 35 years old had more than 3 times higher odds of redeveloping pre-eclampsia compared to the women who were under 20. This could be because of aging of uterine blood vessels and increased arterial stiffness leads to gradual loss of compliance of the cardiovascular vessels causing endothelial dysfunction. Our study also found that women aged below 20 years' old were less likely to develop recurrent pre-eclampsia relative to the above 35 age group which is in contrast to the studies conducted in Indonesia and India. This might be due to the effects of confounders, type of study design and studied population diversity.

This study found a significant association between aspirin use and the reduction of recurrent preeclampsia these sentiments were echoed in a study done by Barton 2008 also had the same findings in which they suggested supplementation of low dose aspirin to be offered in an individual basis (43). Low dose aspirin plays a key role in preventing preeclampsia, foetal growth restriction and thus is

essential in improving the outcomes. The rationale is that pre-eclampsia reduces thromboxane synthesis while maintaining prostacyclin synthesis a 1993 study by Sibai Et Al ,1993 (44).

A vast majority 99.3% of patients attended antenatal which is commendable. W.H.O recommends that patients attend at least 4 only 47 % of the patients did. This is important for screening, evaluating risk factors and preventive measures.

This study evaluated key aspects in the prevention of preeclampsia in the antenatal clinic.

This study showed a significant association between calcium supplementation and good maternal and fetal outcomes the results are supported by several studies done in different parts of the world.

It was observed that Mayan women in Guatemala had a low incidence of hypertensive disorders. They have a low milk intake but soak their maize in lime which provides calcium. Studies mentioned below have shown the benefits of calcium in preventing preeclampsia. It's also beneficial for gravid and lactating women. W.H.O has released guidelines recommending the use of calcium in populations with low intake.

Average daily dietary calcium intake in a nationally representative Kenyan sample was 511 mg/day with standard deviation 281 mg/day, in an analysis reports submitted by Healthbridge to Micronutrient Initiatives in the Kenya National Micronutrient Survey 2011and 2016 (45).

The minimal amount of Ca intake needed to prevent pre-eclampsia is yet to be determined. The WHO recommends 1.5 to 2.0 g/day of supplemental Ca based on meta-analysis of randomized trials; however, comparable benefit has been reported in meta-analysis of studies administering dosages below 1.0 g/day, but the primary studies were of poor quality and relevance (Hofmeyr, Lawrie, Atallah, Duley, & Torloni, 2014) A cochrane review analysing 27 Randomized controlled trials in 2018 by Hofmey Et al showed reduced risk of Preeclampsia significantly, relative risk of 0.42 amongst patients who got 1gm of calcium (36).

This study was done at Kenyatta national hospital practices in various hospitals only 30 % of the patients got calcium supplements. Being a referral facility, it shows the practices across various facilities in the region There is paucity of data to show adherence to the W.H.O guidelines in Kenya hence it's a first.

This study provides a baseline data for future comparison.

A study done by Omotayo Et Al and Z Qureshi Et Al did a study to show the feasibility of integrating calcium and iron–folate supplementation to prevent preeclampsia and anemia in pregnancy in primary healthcare facilities in Malava, Western Kenya (46). It demonstrated that with training of healthcare workers, setting up programs to provide free or subsidized supplements 98% of patients would adhere to the use of the calcium supplements.

Our study demonstrates that gestational age below 34 weeks is significantly associated with preeclampsia. However, women with pre-eclampsia have a higher probability of giving pre-term birth compared to women without pre-eclampsia. Hence, preterm delivery is the consequence of recurrent preeclampsia.

Underlying medical conditions such as gestational diabetes, urinary tract infection and CKD are found to be associated with increased risk of recurrent pre-eclampsia. Our study found that underlying medical conditions had nearly higher odds of recurrent pre-eclampsia, which is in line with studies conducted in India, Yemen, Ethiopia, Jordan, Uganda in the WHO Global Survey on Maternal and Perinatal Health study.

Gestational diabetes patients had higher odds of pre-eclampsia and this is supported by the other studies. This is biologically plausible because insulin resistance and high levels of insulin cause increased sympathetic activity and abnormal tubular sodium absorption, which eventually lead to endothelial cell damage and thus increased risk of pre-eclampsia. Some studies reported that the pre-eclampsia is more common in women who have urinary tract infection, and thus our observation concurs. It has been suggested that this impact may be due to the increased inflammatory response during infectious diseases. Our study found out that our participants had more preterm births than term these results are supported with a study done by Hnat et al which also found at that women with recurrent preeclampsia were more likely to deliver preterm with a statistically significant value of 0.004 (47).

Our study found out that (53.9%) of the newborns had a birth weight of below 2500 grams. These results are similar to a study done in Taiwan which also found out that the majority of women with recurrent

preeclampsia delivered newborns with low birth weight and were more likely to be admitted to the newborn unit.

#### CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

#### 6.1. Conclusion

This study showed that there are various risk factors associated with recurrent pre-eclampsia, such as advanced maternal age, parity, gestational and preexisting comorbidities. It demonstrated poor use of preventive strategies such as calcium and aspirin amongst patients at risk of recurrence despite a high attendance of antenatal clinic Therefore, the result of this study will be useful for policy and clinical purposes, as understanding the determinants of recurrent pre-eclampsia will facilitate the prioritization of interventions and thus resource allocations. Prevention, screening and follow up will avert the adverse outcomes associated with pre-eclampsia.

#### **6.2. Recommendations**

With the findings on prevalence:

- Counselling patients on the risks of recurrence and possible outcomes is vital.
- Optimization on quality of antenatal care by offering calcium supplements to patients in the subsequent pregnancies.
- Need to create local guidelines, sensitize HCWs on the benefits of giving low dose aspirin to those at risk.
- Improve the proportion of at-risk patients getting aspirin from 20%.
- There is need for more studies to investigate adherence to guidelines FIGO / WHO on prevention of preeclampsia /recurrence and establish S.O.P.s / Kenyan guidelines for the same.
- Patients should be followed up in centres able to manage possible outcomes and should be prepared in terms of personnel and facilities in order to handle foetal growth restriction, preterm birth, conduct caesarian sections and offer newborn care.

## REFERENCES

- Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Karumanchi SA, et al. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. Pregnancy Hypertens. 2022 Mar 1;27:148–69.
- 2. Myers JE, Baker PN. Hypertensive diseases and eclampsia. Curr Opin Obstet Gynecol. 2002 Apr;14(2):119–25.
- 3. 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 Health. 2014 Jun;2(6):e323-333.
- 4. Wagner LK. Diagnosis and management of preeclampsia. Am Fam Physician. 2004 Dec 15;70(12):2317–24.
- 5. World Health Organization, Fund UNP, Disability MS of PHAMD and, Fund (UNICEF) UNC. Monitoring emergency obstetric care : a handbook [Internet]. World Health Organization; 2009 [cited 2023 Sep 6]. Available from: https://apps.who.int/iris/handle/10665/44121
- 6. Alkema L, Chou D, Hogan D, Zhang S, Moller AB, Gemmill A, et al. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. Lancet Lond Engl. 2016 Jan 30;387(10017):462–74.
- 7. Stern JE, Luke B, Tobias M, Gopal D, Hornstein MD, Diop H. ADVERSE PREGNANCY AND BIRTH OUTCOMES ASSOCIATED WITH UNDERLYING DIAGNOSIS WITH AND WITHOUT ART TREATMENT. Fertil Steril. 2015 Jun;103(6):1438–45.
- 8. Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of preeclampsia and eclampsia: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2013 Sep;170(1):1–7.
- 9. The World Health Report 2005. Make every mother and child count [Internet]. [cited 2023 Sep 6]. Available from: https://www.who.int/publications-detail-redirect/9241562900
- 10. Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: current concepts. Am J Obstet Gynecol. 1998 Nov;179(5):1359–75.
- 11. Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol. 2009 Jun;33(3):130–7.
- 12. Campbell DM, MacGillivray I, Carr-Hill R. Pre-eclampsia in second pregnancy. Br J Obstet Gynaecol. 1985 Feb;92(2):131–40.
- Sibai BM, el-Nazer A, Gonzalez-Ruiz A. Severe preeclampsia-eclampsia in young primigravid women: subsequent pregnancy outcome and remote prognosis. Am J Obstet Gynecol. 1986 Nov;155(5):1011–6.
- Lie RT, Rasmussen S, Brunborg H, Gjessing HK, Lie-Nielsen E, Irgens LM. Fetal and maternal contributions to risk of pre-eclampsia: population based study. BMJ. 1998 May 2;316(7141):1343–7.
- 15. Kalengo NH, Sanga LA, Philemon RN, Obure J, Mahande MJ. Recurrence rate of preterm birth

and associated factors among women who delivered at Kilimanjaro Christian Medical Centre in Northern Tanzania: A registry based cohort study. PLoS ONE. 2020 Sep 14;15(9):e0239037.

- van Rijn BB, Hoeks LB, Bots ML, Franx A, Bruinse HW. Outcomes of subsequent pregnancy after first pregnancy with early-onset preeclampsia. Am J Obstet Gynecol. 2006 Sep;195(3):723– 8.
- 17. Firoz T, Sanghvi H, Merialdi M, von Dadelszen P. Pre-eclampsia in low and middle income countries. Best Pract Res Clin Obstet Gynaecol. 2011 Aug;25(4):537–48.
- von Dadelszen P, Ansermino JM, Dumont G, Hofmeyr GJ, Magee LA, Mathai M, et al. Improving maternal and perinatal outcomes in the hypertensive disorders of pregnancy: A vision of a community-focused approach. Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet. 2012 Oct;119 Suppl 1:S30–4.
- 19. North RA, McCowan LME, Dekker GA, Poston L, Chan EHY, Stewart AW, et al. Clinical risk prediction for pre-eclampsia in nulliparous women: development of model in international prospective cohort. BMJ. 2011 Apr 7;342:d1875.
- 20. Sibai BM, Gordon T, Thom E, Caritis SN, Klebanoff M, McNellis D, et al. Risk factors for preeclampsia in healthy nulliparous women: a prospective multicenter study. The National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. Am J Obstet Gynecol. 1995 Feb;172(2 Pt 1):642–8.
- 21. van Oostwaard MF, Langenveld J, Schuit E, Papatsonis DNM, Brown MA, Byaruhanga RN, et al. Recurrence of hypertensive disorders of pregnancy: an individual patient data metaanalysis. Am J Obstet Gynecol. 2015 May;212(5):624.e1-17.
- 22. Mostello D, Kallogjeri D, Tungsiripat R, Leet T. Recurrence of preeclampsia: effects of gestational age at delivery of the first pregnancy, body mass index, paternity, and interval between births. Am J Obstet Gynecol. 2008 Jul;199(1):55.e1-7.
- 23. Bramham K, Briley AL, Seed P, Poston L, Shennan AH, Chappell LC. Adverse maternal and perinatal outcomes in women with previous preeclampsia: a prospective study. Am J Obstet Gynecol. 2011 Jun;204(6):512.e1-9.
- 24. Poon LCY, Kametas NA, Chelemen T, Leal A, Nicolaides KH. Maternal risk factors for hypertensive disorders in pregnancy: a multivariate approach. J Hum Hypertens. 2010 Feb;24(2):104–10.
- 25. Meazaw MW, Chojenta C, Muluneh MD, Loxton D. Systematic and meta-analysis of factors associated with preeclampsia and eclampsia in sub-Saharan Africa. PloS One. 2020;15(8):e0237600.
- 26. Bartsch E, Medcalf KE, Park AL, Ray JG, High Risk of Pre-eclampsia Identification Group. Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and metaanalysis of large cohort studies. BMJ. 2016 Apr 19;353:i1753.
- 27. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. BMJ. 2005 Mar 12;330(7491):565.
- 28. 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. Paediatr Perinat Epidemiol. 2007

Jul;21 Suppl 1:36-45.

- 29. Odegård RA, Vatten LJ, Nilsen ST, Salvesen KA, Austgulen R. Risk factors and clinical manifestations of pre-eclampsia. BJOG Int J Obstet Gynaecol. 2000 Nov;107(11):1410–6.
- 30. Hernández-Díaz S, Toh S, Cnattingius S. Risk of pre-eclampsia in first and subsequent pregnancies: prospective cohort study. BMJ. 2009 Jun 18;338:b2255.
- 31. Langenveld J, Jansen S, van der Post J, Wolf H, Mol BW, Ganzevoort W. Recurrence risk of a delivery before 34 weeks of pregnancy due to an early onset hypertensive disorder: a systematic review. Am J Perinatol. 2010 Aug;27(7):565–71.
- 32. Ronsmans C, Graham WJ, Lancet Maternal Survival Series steering group. Maternal mortality: who, when, where, and why. Lancet Lond Engl. 2006 Sep 30;368(9542):1189–200.
- 33. Boyd HA, Tahir H, Wohlfahrt J, Melbye M. Associations of personal and family preeclampsia history with the risk of early-, intermediate- and late-onset preeclampsia. Am J Epidemiol. 2013 Dec 1;178(11):1611–9.
- 34. WHO Recommendations for Prevention and Treatment of Pre-Eclampsia and Eclampsia [Internet]. Geneva: World Health Organization; 2011 [cited 2023 Sep 6]. (WHO Guidelines Approved by the Guidelines Review Committee). Available from: http://www.ncbi.nlm.nih.gov/books/NBK140561/
- 35. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol. 2020 Jun;135(6):e237–60.
- 36. Hofmeyr GJ, Lawrie TA, Atallah ÁN, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2018 Oct 1;10(10):CD001059.
- 37. Duley L, Henderson-Smart DJ, Meher S, King JF. Antiplatelet agents for preventing preeclampsia and its complications. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD004659.
- 38. Van Doorn R, Mukhtarova N, Flyke IP, Lasarev M, Kim K, Hennekens CH, et al. Dose of aspirin to prevent preterm preeclampsia in women with moderate or high-risk factors: A systematic review and meta-analysis. PLoS ONE. 2021 Mar 9;16(3):e0247782.
- 39. Alasztics B, Kukor Z, Pánczél Z, Valent S. [The pathophysiology of preeclampsia in view of the two-stage model]. Orv Hetil. 2012 Jul 29;153(30):1167–76.
- 40. Staff AC. The two-stage placental model of preeclampsia: An update. J Reprod Immunol. 2019 Sep;134–135:1–10.
- 41. Roberts JM, Hubel CA. The two stage model of preeclampsia: variations on the theme. Placenta. 2009 Mar;30 Suppl A(Suppl A):S32-37.
- 42. Emanuel M, Butt S. Frequency and factors leading to recurrent pre-eclampsia. JPMA J Pak Med Assoc. 2015 Nov;65(11):1173–7.
- 43. Barton JR, Sibai BM. Prediction and prevention of recurrent preeclampsia. Obstet Gynecol. 2008 Aug;112(2 Pt 1):359–72.

- 44. Sibai BM, Caritis SN, Thom E, Klebanoff M, McNellis D, Rocco L, et al. Prevention of preeclampsia with low-dose aspirin in healthy, nulliparous pregnant women. The National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. N Engl J Med. 1993 Oct 21;329(17):1213–8.
- 45. The Kenya National Micronutrient Survey 2011.pdf [Internet]. [cited 2023 Sep 6]. Available from: https://www.nutritionhealth.or.ke/wp-content/uploads/Downloads/The%20Kenya%20National%20Micronutrient%20Survey%202011.p df
- 46. Omotayo MO, Dickin KL, Pelletier DL, Martin SL, Kung'u JK, Stoltzfus RJ. Feasibility of integrating calcium and iron–folate supplementation to prevent preeclampsia and anemia in pregnancy in primary healthcare facilities in Kenya. Matern Child Nutr [Internet]. 2018 Feb [cited 2023 Sep 6];14(Suppl 1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6866141/
- 47. Hnat MD, Sibai BM, Caritis S, Hauth J, Lindheimer MD, MacPherson C, et al. Perinatal outcome in women with recurrent preeclampsia compared with women who develop preeclampsia as nulliparas. Am J Obstet Gynecol. 2002 Mar 1;186(3):422–6.

## ANNEXES

## Annex 1: Study time frame

# Table 11: Study Timeline

The proposed timeline for the research including dissemination of the study results is as follows:

		2021			
	January - March	April	May - August	October 2021to March 2022	June/ 2022
Proposal development					
Proposal presentation					
Ethical approval submission					
Data collection/analysis					
Result presentation to the department					

# Annex 2: Study budget

# Table 12: Study budget

TEST	COST IN KSH	TOTAL
PROPOSAL WRITING		
Typing/Typesetting Printing and	d	
Photocopying	5,000	5,000
	5,000	5,000
DATA COLLECTION	-	
Assistants Data Entry		
	30,000	30,000
	20,000	20,000
Data Analysis	40,000	40,000
FINAL THESIS	10,000	10,000
MISCELANEOUS	5000	5000
TOTAL	115,000	115,000

#### **Annex 3: Participant's Informed Consent Form**

Study Title: Prevalence, Risk Factors and Outcomes of Recurrent Preeclampsia at Kenyatta National Hospital. A Cross-Sectional Study.

#### Introduction

This Study is being conducted by Dr Zephania Ashira Student pursuing Masters in medicine in Obstetrics and Gynecology at the University of Nairobi, under the guidanceand supervision of the Reproductive Health Department

Hypertensive disorders in pregnancy is a common problem that that tends to occur andto recur amongst gravid women. It has a negative risk effect on the maternal and fetal outcome.

**Objective:** This study aims to establish the prevalence, risk factors associated with it and the outcomes. **Study procedure:** 

The study will involve a brief interview of patients who have had preeclampsia in more than one pregnancy. The participant can choose to voluntarily participate or not participate in the study without fear of any discrimination. The participant will still access routine medical care even if they opt not to participate in the study.

#### **Benefits of the study:**

The main benefit will be to contribute to knowledge about the disease and thus improve the prevention and management strategies.

**Risks, stress and discomfort:** There are no direct foreseen risks in you participating in this study. However, the study will require you to spare at most 10 minutes of yourtime and fill the questionnaire. If there are any questions you do not want to answer, you are obliged to skip. In addition, you have the right to decline giving information.

Cost and risk of loss of Confidentiality: There will be no direct cost incurred by youneither will you

receive any money for participating in this study. Data includingquestionnaires and file from the study will be kept locked in a cabinet during the studyperiod. Your data will be labelled with your unique identity and your name concealed to maintain confidentiality when taking part in the study. Furthermore, your name willnot appear in any report or publication of the research and all your personal information will be handled with a high level of confidentiality.

**Voluntary Participation and withdrawal:** Remember, your participation is entirely voluntarily. Should you consider changing your mind midway, you have the right to doso and you shall not suffer any consequence whatsoever.

**Sharing of results:** The results of this study may be presented during scientific and academic forums and may be published in scientific medical journals and academic papers.

#### **Contact information:**

The patient should feel free to ask any get clarification from the interviewer or evencontact the principal investigator. Principal investigator; Dr Ashira Zephania Ayaya Phone number 0726637227 Email; <u>Zephashy@gmail.com</u> .The study is regulated by the KNH/UON ethics committee in case of complaints on unethical behavior or breech of participants rights please contact them via Email: uonknh\_erc@uonbi.ac.ke <u>Participants consent</u>

I confirm that the researcher has explained fully the nature of the study and the extent of activities which I will be asked to undertake. I confirm that I have had adequate opportunity to evaluate and ask questions about this study. I understand that my participation is voluntary and that I may withdraw at any time during the study, withouthaving to give a reason. I agree to take part in this study by filling in the questionnaire.Signed by participant...... Date......

#### **Researcher's statement**

**Interviewer**: I certify that the purpose, potential benefits and possible risks associated with participating in this research have been explained to the above participant and the individual has consented to participate.

Signature	Date

#### Kiambatisho 4: Fomu ya ridhara ya mshiriki ya mtuhusiwa

#### Utangulizi

Utafiti huu unafanywa na Daktari Zephania Ashira Mwanafunzi anayefuata Shahada ya Uzamili katika utabibu katika somo la Afya ya Uzazi katika Chuo Kikuu cha Nairobi, chini ya mwongozo na usimamizi wa Idara ya Afya ya Uzazi .

Shida za shinikizo la damu (ugonjwa wa presha )wakati wa ujauzito ni shida ya kawaidaambayo huelekea kutokea na kujirudia kati ya wanawake wenye nguvu. Inayo athari mbaya ya hatari kwa matokeo ya mama na fetusi. Utafiti huu unakusudia kuanzisha kuenea, sababu za hatari zinazohusiana na hilo na matokeo.

Utafiti huo utahusisha mahojiano mafupi ya wagonjwa ambao wamekuwa na ugonjwawa presha / shinikizo la damu katika uja uzito katika zaidi ya uja uzito mmoja. Mshirikianaweza kuchagua kushiriki kwa hiari au asishiriki katika utafiti bila hofu ya ubaguzi wowote. Mshiriki bado atapata huduma ya kawaida ya matibabu hata ikiwa watachaguakutoshiriki katika utafiti

Faida kuu itakuwa kuchangia maarifa juu ya ugonjwa na hivyo kuboresha mikakati ya kuzuia na usimamizi.

Mgonjwa anapaswa kujisikia huru kuuliza yoyote kupata ufafanuzi kutoka kwa mhojiwa au hata wasiliana na mchunguzi mkuu.

Mchunguzi mkuu; Dk Ashira Zephania Ayaya

Namba ya simu 0726637227 Barua pepe; Zephashy@gmail.com

Utafiti huo unasimamiwa na kamati ya maadili ya KNH / UON ikiwa kuna malalamikojuu ya tabia isiyo ya maadili au upunguzaji wa haki za washiriki tafadhali wasiliana nao kupiti Barua pepe : uonknh\_erc@uonbi.ac.ke

Wasaini wanakubali kushiriki katika utafiti, asili na malengo ambayo nimeelezewa kwaufasaha.

Ninakubali kwamba habari iliyopatikana itatumika tu kwa madhumuni ya utafiti naitahifadhiwa kwa siri kabisa.

Nilipewa nafasi ya kuuliza maswali juu ya utafiti huo, na nikafanya hivyo.

Ninajua kuwa nina chaguo la kujiondoa kwenye utafiti na kwamba ikiwa nitafanyahivyo sitapoteza haki yoyote au kupata huduma ya matibabu ambayo ninastahili.

Jina la mshiriki:	Saini:
Taraha	
1 arene:	—
Jina la Mtafiti:	
Sahihi	
Tarehe:	

## **Annex 5: Questionnaire**

Study number..... OP number..... Date.....

## **Socio Demographic Characteristics**

## Age

- a. 18-20
- b. 21-35
- c. Above 35

## LEVEL OF EDUCATION

- a. None/Primary
- b. Secondary
- c. Tertiary/University

## **OCCUPATION**

- a. Unemployed
- b. Self employed
- c. Formally employed

## MARITAL STATUS

- a. Single
- b. Married
- c. Divorced/Separated

## **CLINICAL/OBSTETRIC CHARACTERISTICS**

## <u>Parity</u>

- a. 1
- b. 2
- c. 3
- d. 4+

## Gravidity

- a. 1
- b. 2
- c. 3
- d. 4+

Gestational age: (weeks).....

## **History of previous pregnancy**

- 1. How many pregnancies have you had?
  - a. 1
  - b. 2
  - c. 3
  - $d. \ \geq 4$
- 2. In your previous pregnancy/pregnancies did you have preeclampsia?
  - a. Yes
  - b. No
- 3. If yes, did you receive treatment for the same?
  - a. Yes
  - b. No
- 4. If yes, what was the outcome of the pregnancy?

## Birth outcome

a. Liv	ve birth
--------	----------

- b. Still birth
- c. Prematurity

#### NBU admission

- a. Yes
- b. No

Long hospital stay

a. Yes

b. No

Maternal admission to ICU

a. Yes

b. No

Any other specify:

5. If yes, do you have any medical documentations of the previous pregnancy/pregnancies?

- a. Yes
- b. No
- 6. If yes, do you have ANC profile/book of the previous pregnancy/pregnancies?
  - a. Yes
  - b. No
- 7. In this present/last pregnancy have you had preeclampsia?
  - a. Yes
  - b. No

8. If yes, what is the outcome of this present/last pregnancy?

Birth outcome

- a. Live birth
- b. Still birth

## c. Prematurity

NBU admission

a. Yes b. No Long hospital stay a. Yes b. No Maternal admission to ICU a. Yes b. No Any other specify:..... 9. If yes, do you have any medical documentations of the present/last pregnancy? a. Yes b. No 10. If yes, do you have ANC profile/book of the present/last pregnancy? a. Yes b. No 11. Do you have any of the following chronic medical conditions? a. DM/ Diabetes mellitus b. Chronic hypertension c. Family history of preeclampsia d. SLE /Systemic lupus erythematosus e. HIV Human immunodeficiency syndrome

Any other: \_\_\_\_\_

12. History of smoking

- a. Yes
- b. No

#### Recent attendance

13. Last normal menstrual period in the recent pregnancy?

Date.....

#### Can't recall date?

14. Factor that could have caused uncertainty about dates

- a. Irregular periods
- b. Use of contraceptive around the time of conception?
- c. Interval between last and recent pregnancy (months).....
- 15. If uncertain earliest ultrasound scan, first trimester scan?

#### Antenatal attendance

16. Number of times she attended ANC clinic

- a. 1
- b. 2
- c. 3
- d. 4+

17. When did she start attending ANC clinic (gestational date) .....

18. Which facility did she attended? Level of Facility.....

### 19. Medication given

- a. Calcium supplementation in the antenatal period?
- b. Dosage / No of tabs in a day? .....
- 20. Time of the day she used the aspirin .....
- 21. Medical reason she didn't use aspirin.....
- 22. Presence of comorbidities

- a. Gestational Diabetes
- b. HIV

23. Onset of preeclampsia; Gestational date Less than or greater than 34 weeks

## 24. Severity of Preeclampsia

Blood pressure

BP .....

a) >160/110 b) <160/110

## Laboratory values

Haemoglobin.....

Platelets count.....

## **Renal functions**

Urea.....

Creatine .....

## **Liver Function Test**

Alkaline Phosphatase.....

Aspartate Phosphatase.....

Lactate dehydrogenase (LDH).....

## Urinalysis

Proteinuria.....

## Ultrasonography

Foetal growth restriction

a. Yes

b. No

## Early Onset Preeclampsia <34 weeks

- c. Yes
- d. No

Late Onset Preeclampsia > 34 weeks

- a. Yes
- b. No

Preeclampsia with Severe Features

- c. Yes
- d. No

25. Specific signs and symptoms alluding to severe features

- b. Headache
- c. Visual disturbance
- d. Seizures

26. G.I and genitourinary system

- a. Epigastric pain
- b. Reduced urine output

27. No of times admitted in the current pregnancy?.....

28. Preeclampsia related reason or any other?.....

29. Gestational age at time of delivery

30. Mode of delivery

- a. Vaginal Delivery
- b. Caesarean section
| 31. Indication for C/S                 |
|----------------------------------------|
|                                        |
| 32. Indication for Induction of labour |
| 33. Spontaneous labour                 |
| a. Yes                                 |
| b. No                                  |
| 34. Duration of stay                   |
| 35. Specific reason for                |
| admission,                             |
|                                        |
| 36. If referred; reason for            |
| referral                               |
|                                        |
| 37. Days prior delivery                |
| 38. Days after delivery                |
| 39. Total duration                     |
| NEONATAL OUTCOME                       |
| 40. Birth weight                       |
| a. Below 2500                          |
| b. Above 2500                          |
| 41. Apgar score at 1 minute            |
| 42. Apgar score at 5 minutes           |
| 43. Apgar score at 10 minutes          |
| 44. Admission to NBU                   |
| a. Yes                                 |

b. No

45. Indication for admission.....

..,....

46. Duration (days).....

## Annex 6: Kiambatisho 6: Maswali ya data ya damografia ya jamii

Kichwa cha Utafiti: Kiwango cha Kuenea, Sababu za Hatari na Matokeo ya Kurudia kwa Shinikizo la damu/ Ugonjwa wa Presha katika uja uzito katika Hospitali ya Kitaifaya Kenyatta. Utafiti wa Sehemu Zote.

Nambari ya masomo
Nambari ya OP
Tarehe

### Sifa za Demografia ya Kijamii

Umri

a. 18-20

b. 21-35

c. Juu ya 35

### NGAZI YA ELIMU

a. Hakuna/Msingi

b. Sekondari

c. Elimu ya Juu/Chuo Kikuu

### KAZI

a. Wasio na kazi

b. Kazi binafsi

c. Kuajiriwa rasmi

#### HALI YA NDOA

# a. Mtu mmoja

## b. Ndoa

c. Kuachwa/Kutengana

# TABIA ZA Kliniki/Uzazi

Usawa

a. 1

b. 2

c. 3

d. 4+

## Mvuto

a. 1

b. 2

c. 3

d. 4+

Umri wa ujauzito: (wiki).....

Historia ya ujauzito uliopita

1. Umewahi kupata mimba ngapi?

a. 1

b. 2

c. 3

d. ≥4

2. Je, katika ujauzito/ujauzito wako uliopita ulikuwa na preeclampsia? 77

- a. Ndiyo
- b. Hapana
- 3. Ikiwa ndio, je, ulipokea matibabu sawa?
- a. Ndiyo
- b. Hapana
- 4. Ikiwa ndio, matokeo ya ujauzito yalikuwaje?
- Matokeo ya kuzaliwa
- a. Kuzaliwa hai
- b. Bado kuzaliwa
- c. Kabla ya wakati

Kiingilio cha NBU

- a. Ndiyo
- b. Hapana

Kukaa hospitalini kwa muda mrefu

- a.Ndiyo
- b.Hapana

Kulazwa kwa mama katika ICU

- a. Ndiyo
- b. Hapana
- Taja nyingine yoyote: \_\_\_\_\_

5. Kama ndiyo, una nyaraka zozote za matibabu za ujauzito/mimba za awali?

a. Ndiyo

b. Hapana

6. Kama ndiyo, je, una wasifu/kitabu cha ANC cha ujauzito/mimba zilizopita?

a. Ndiyo

b. Hapana

7. Je, katika ujauzito huu wa sasa/mwisho umewahi kupata preeclampsia?

a. Ndiyo

b. Hapana

### 8. Kama ndiyo, matokeo ya ujauzito huu wa sasa/mwisho ni nini?

Matokeo ya kuzaliwa

a. Kuzaliwa hai

b. Bado kuzaliwa

c. Kabla ya wakati

Kiingilio cha NBU

a. Ndiyo

b. Hapana

### Kukaa hospitalini kwa muda mrefu

a. Ndiyo

b. Hapana

Kulazwa kwa mama katika ICU

a. Ndiyo

b. Hapana

Taja nyingine yoyote:.....

9. Kama ndiyo, una nyaraka zozote za matibabu kuhusu ujauzito wa sasa/wa mwisho?

a. Ndiyo

b. Hapana

10. Kama ndiyo, je, una wasifu/kitabu cha ANC kuhusu ujauzito wa sasa/wa mwisho?

a. Ndiyo

b. Hapana

- 11. Je, una mojawapo ya magonjwa sugu yafuatayo?
- a. DM/ Ugonjwa wa kisukari
- b. Shinikizo la damu sugu
- c. Historia ya familia ya preeclampsia
- d. SLE /System lupus erythematosus
- e. HIV/ Ugonjwa wa Upungufu wa Kinga ya binadamu

Nyingine yoyote:\_\_\_\_\_

12. Historia ya kuvuta sigara

a. Ndiyo

b. Hapana

Mahudhurio ya hivi majuzi

13. Hedhi ya mwisho ya kawaida katika ujauzito wa hivi karibuni?

Tarehe.....

Huwezi kukumbuka tarehe?

- 14. Sababu ambayo inaweza kusababisha kutokuwa na uhakika kuhusu tarehe
- a. Vipindi visivyo vya kawaida
- b. Matumizi ya uzazi wa mpango karibu na wakati wa mimba?
- c. Muda kati ya mimba ya mwisho na ya hivi karibuni (miezi).....

15. Ikiwa hakuna uhakika wa uchunguzi wa mapema zaidi wa ultrasound, skani katika miezi mitatu ya kwanza?

-----

Kuhudhuria katika ujauzito

#### 16. Idadi ya mara alihudhuria kliniki ya ANC

a. 1

b. 2

c. 3

d. 4+

17. Alianza lini kuhudhuria kliniki ya ANC (tarehe ya ujauzito) .....

18. Alihudhuria kituo gani? Kiwango cha Kituo .....

19. Dawa iliyotolewa

- a. Kuongezewa kalsiamu katika kipindi cha ujauzito?
- b. Kipimo / Idadi ya vichupo kwa siku? .....

20. Wakati wa siku alitumia aspirin ......

21. Sababu ya kimatibabu hakutumia aspirini .....

22. Uwepo wa magonjwa yanayofanana

a. Kisukari cha ujauzito

b. VVU

23. Mwanzo wa preeclampsia; Tarehe ya ujauzito Chini ya au zaidi ya wiki 34

24. Ukali wa Preeclampsia
Shinikizo la damu
BP
a) >160/110 b) <160/110
Maadili ya maabara
Hemoglobin
Idadi ya chembechembe za damu
Kazi za figo
Urea
Creatine
Mtihani wa Kazi ya Ini
Alkaline Phosphatase
Aspartate Phosphatase
Lactate dehydrogenase (LDH)
Uchambuzi wa mkojo

Proteinuria			
Ultrasonografia			
Kizuizi cha ukuaji wa fetasi			
a. Ndiyo			
b. Hapana			
Preeclampsia ya Mapema chini ya wiki 34			
c. Ndiyo			
d. Hapana			
Kuchelewa Kuanza Preeclampsia> Wiki 34			
a. Ndiyo			
b. Hapana			
Preeclampsia yenye Vipengele Vikali			
c. Ndiyo			
d. Hapana			
25. Dalili na dalili mahususi zinazodokeza sifa kali			
b. Maumivu ya kichwa			
c. Usumbufu wa kuona			
d. Mishtuko ya moyo			
26. G.I na mfumo wa genitourinary			
a. Maumivu ya Epigastric			
b. Kupungua kwa pato la mkojo			

27. Idadi ya nyakati zilizokubaliwa katika ujauzito wa sasa?.....

28. Sababu inayohusiana na Preeclampsia au nyingine				
yoyote?				
29. Umri wa ujauzito wakati wa kujifun	ngua			
	6			
20 Nilia va utacii				
a. Kujifungua kwa Uke				
b. Sehemu ya Kaisaria				
31. Maagizo ya C/S				
32. Dalili ya Kuanzishwa kwa leba				
33 Kazi ya pekee				
a Ndiva				
b. Hapana				
34. Muda wa kukaa				
35. Sababu	mahususi	ya		
kuandikishwa		,		
36 Ikitaiwa: sababu ya rufaa				
37. Siku zilizopita kabla ya kujifungua				

38. Siku baada ya kujifungua .....

39. Jumla ya muda .....

### MATOKEO YA NEONATALI

40. Uzito wa kuzaliwa

a. Chini ya gramu 2500

b. Zaidi ya gramu2500

41. Apgar alama kwa dakika 1.....

42. Apgar alama kwa dakika 5.....

43. Apgar alama kwa dakika 10.....

44. Kuingia kwa NBU

a. Ndiyo

b. Hapana

45. Dalili ya kuingia .....

..,....

46. Muda (siku).....