Incidence of Postpartum Hypertension Among Kenyan Women With Preeclampsia: a Prospective Cohort Study

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Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in the Duke Global Health Institute in the Graduate School
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ABSTRACT

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Abstract

Background: The burden of cardiovascular disease (CVD) is rising in sub-Saharan Africa (SSA). Preeclampsia, a type of hypertensive disorder of pregnancy, is a unique risk factor for CVD among women, yet little is known about the postpartum cardiovascular risk among women with preeclampsia in SSA. Objective: To determine the incidence of hypertension, a major risk factor for CVD, at 6-months postpartum among Kenyan women with preeclampsia. Methods: This prospective cohort study included all pregnant or recently postpartum women with preeclampsia who were admitted to a national, referral hospital in western Kenya from January 20, 2020 - March 19, 2020, when the study was unexpectedly paused due to the COVID-19 pandemic. Using home blood pressure monitoring technique, we described the trajectory of blood pressure after delivery. Bivariate and multivariable regression analyses were performed to investigate for risk factors associated with hypertension at 6-month follow-up. Results**:** Eight-six women with preeclampsia were enrolled prior to March 19, 2020, when the study was unexpected paused due to the COVID-19 pandemic. Among the 50 women who completed follow up, 38% (n=19) had hypertension. Blood pressure normalized for all women by 6 weeks after delivery but rose again beyond 12 weeks among those with hypertension at follow up. Maternal age, parity and history of preeclampsia in prior pregnancy or a previous pregnancy complication (preterm delivery or stillbirth) were

associated with hypertension at follow up. Overall, rates of routine, postpartum clinic follow up were low (64%) among women despite nearly all (97%) attending clinic for infant immunizations following delivery. Conclusion: There is a high incidence of hypertension at 6-months postpartum among Kenyan women with preeclampsia, though low rates of postpartum follow up care indicate a potential missed opportunity for early CVD identification and prevention among this high risk-population.

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1. Introduction

1.1 Background of cardiovascular disease in sub-Saharan Africa

Cardiovascular disease (CVD) is the leading cause of death worldwide, with 80% of deaths occurring in low and middle income countries (1). Reducing this burden is a global priority. In 2013 the Global CVD Task Force of the World Health Organization (WHO) set a target to reduce global CVD mortality by 25% by 2025 (2). In sub-Saharan Africa (SSA), where rates of CVD are rising, current efforts are focused on early detection and treatment of CVD risk factors, such as hypertension (3-6). The WHO estimates that the African continent has the highest number of people living with hypertension globally, with a disproportionate burden on young people and women. Nearly half of all adults over the age of 25 and up to 20% of those under 25 in SSA have hypertension (4, 5). Further, this growing burden has disproportionate effects on women, with women having a higher age-standardized mortality rate due to CVD compared to men in SSA (5). As such, hypertension poses a significant economic threat to the continent as prevalence of cardiovascular risk factors rise among young people and has been described as one of the continent's greatest health challenges after HIV/AIDS (4, 7).

However, lack of awareness of hypertension diagnosis and low rates of treatment are barriers to CVD prevention in the region, with less than half of people aware of their diagnosis (3, 8). A national, cross-sectional survey of households in Kenya conducted in 2015 estimated that 25% of all adults had hypertension but only 15% of those were aware of their diagnosis and only one-quarter of those were on treatment (8). Thus, strategies to identify groups at high risk of CVD for screening and early disease identification are critical to improving hypertension awareness, increasing treatment, and ultimately reducing overall CVD-related morbidity and mortality across the region.

1.2 Preeclampsia: an overview

Women with preeclampsia, a type of hypertensive disorder of pregnancy, are at significantly increased risk of hypertension and CVD later in life. Preeclampsia is a complex pregnancy condition characterized by new onset high blood pressure that develops in pregnancy after 20 weeks gestation and accompanied by signs of end-organ-damage, most often to the kidney, liver, or brain (9, 10). Diagnosis is made by an elevated blood pressure reading (systolic blood pressure (SBP) > 140mmHg *or* diastolic blood pressure (DBP) > 90mmHg) on two, separate occasions, at least 4 hours apart, together with evidence of proteinuria, derangements in kidney function, liver function

and/or platelets, or typical symptoms, including headache, vision changes, or right upper quadrant abdominal pain (9, 11).

The underlying cause of preeclampsia is unclear. Leading hypotheses suggest it stems from abnormal implantation of the placenta in the uterus early in pregnancy. This results in decreased blood flow to the developing fetus, which in turns stimulates a cascade of changes in maternal circulation to increase blood flow to the developing fetus (12). These changes ultimately lead to systemic vascular dysfunction in the mother, resulting in hypertension and damage to other body systems (13, 14). Vascular, environmental, immunological, and genetic risk factors all appear to play a role (14, 15).

There is a wide spectrum of preeclampsia severity, ranging from mild elevations in blood pressure to the most severe forms of eclampsia (seizures), HELLP syndrome (a disorder marked by destruction of blood cells, liver damage and bleeding), and can even result in maternal death (13). Further, decreased blood flow to the fetus can lead to neonatal complications, including intrauterine growth restriction, premature delivery and stillbirth (11, 13).

While the underlying etiology of disease is still unknown, many risk factors have been associated with preeclampsia. Major risk factors for the development of preeclampsia include maternal age (both young and older), first pregnancy, multiple

gestations (twins, triplets), maternal obesity, diabetes or hypertension prior to pregnancy, and certain autoimmune disorders (16). Family history of preeclampsia in a sister, mother or aunt and preeclampsia in a previous pregnancy may also increase risk. Other risk factors vary by global region; in LMICs in particular, severe anemia and HIV have been associated with preeclampsia (17-20). In line with international guidelines, the WHO recommends that all women at risk for developing preeclampsia should be started on low-dose aspirin in the second trimester to prevent or delay the onset of preeclampsia in pregnancy (21). Once preeclampsia develops, management in pregnancy focuses on blood pressure control with anti-hypertensive medications and close monitoring to determine the timing of delivery (11).

1.3 Preeclampsia as a risk factor for cardiovascular disease

Historically, delivery was thought to "cure" the disease, however, more recent evidence suggests that underlying vascular dysfunction persists, thus increasing the risk of future CVD among these women (22-25). Women with preeclampsia have a 3-5-fold increased risk of CVD, including hypertension, stroke, and heart disease after pregnancy (24-26). As such, having preeclampsia in pregnancy can be considered an early predictor for impending cardiovascular disease for women, and should be considered similar to a failed cardiac stress test (27).

Early epidemiologic studies initially established a link between preeclampsia and increased cardiovascular disease among women later in life, more than 10-years following their pregnancy (13, 28). However, more recent data suggest that these complications occur much sooner after delivery (29, 30). Large cohort studies from high income countries found that 25-40% of women with preeclampsia develop chronic hypertension within 1-3 years postpartum, with even higher rates among those who have 'preterm preeclampsia' (preeclampsia occurring before 37 weeks gestational age) (29, 31-33). A small cohort study from Cameroon, the only study of cardiovascular effects among women with preeclampsia from SSA, found that 28% of women had hypertension as early as 12-weeks after delivery (34).

The blood pressure trajectory following delivery among women with preeclampsia is relatively unknown. In normal pregnancies, fluid shifts and hemodynamic changes in cardiac output, vascular resistance following delivery lead to a progressive rise in blood pressure during the first week postpartum, with blood pressure typically peaks on day 3-6 after delivery (35). However, women with preeclampsia have higher rates of elevated blood pressure up to 6-12 weeks postpartum; it remains unclear whether blood pressure normalizes immediately postpartum then increases again later, or whether there is a slower time to normalization over the first

three months postpartum (29, 31). Spikes in blood pressure after the first postnatal week can lead to hypertensive heart failure, which has been more commonly observed in African populations, in particular (36).

Further, the incidence of heart failure is increased among women with preeclampsia. While the underlying pathogenesis remains unknown, preeclampsia has been associated with increased rates of both heart failure with reduced left ventricular function (commonly referred to as 'systolic heart failure') and heart failure with preserved left ventricular heart failure (or 'diastolic heart failure') as well as peripartum cardiomyopathy, a type of idiopathic heart failure that occurs around the time of pregnancy in women (23, 37, 38). A longitudinal, prospective cohort study of U.S. women with preeclampsia found that roughly 15% of women with preeclampsia had evidence of asymptomatic heart failure (with reduced left ventricular ejection fraction) on echocardiogram at 1-year following delivery (37, 39, 40). Both structural and functional cardiac changes can been on echocardiogram among pregnant women with preeclampsia, and persistent changes in left ventricular geometry on echocardiograms ≥4 months after delivery may be an early indicator of future hypertension among women with preeclampsia (39, 40).

1.4 Epidemiology of preeclampsia in sub-Saharan Africa

It is estimated that 10-15% of all pregnancies worldwide are complicated by preeclampsia, with a higher burden in SSA (36, 41, 42). Despite this, little is known about the longitudinal, postpartum cardiovascular risk associated with preeclampsia in SSA. Additionally, unique risk factors for both preeclampsia and CVD exist in this region; high rates of human immunodeficiency virus (HIV), indoor air pollution, high elevation/altitude and underlying genetic factors compound the CVD risk in women with preeclampsia (16, 18, 34, 43). However, rates of routine, postpartum follow up care among women in SSA are low, which may result in a missed opportunity for early CVD prevention (26, 36, 44).

1.5 Preeclampsia and cardiovascular disease in Kenya

The national prevalence of preeclampsia in Kenya is unknown, but unpublished data from a large national referral hospital in western Kenya found around 6% of all admission to the maternity ward were complicated by preeclampsia (45). Simultaneously, eclampsia, the most severe form of preeclampsia, was the leading cause of maternal mortality and accounted for 22% of all maternal deaths between 2004-2011 at the same hospital (46, 47). Therefore, better understanding the postpartum

cardiovascular risk among women with preeclampsia is critical to developing interventions to help prevent early CVD among this potentially high-risk population.

We designed a prospective, cohort study of pregnant women with preeclampsia who were admitted to a national referral hospital in western Kenya and aimed to determine the incidence of hypertension at six months postpartum. We used an innovative approach of home blood pressure monitoring to describe the postpartum BP trajectory over the first three months. We aimed to describe the health-seeking behavior among postpartum women, to identify gaps in care for this at-risk population. We hypothesized that mothers with preeclampsia in Kenya will have high rates of postpartum hypertension, and thus represent a high-risk population to target for early prevention and treatment strategies and ultimately reduce CVD-related morbidity and mortality among women in SSA.

2. Methods

2.1 Study design

This is a prospective cohort study of pregnant or recently postpartum women admitted to the inpatient wards of Moi Teaching and Referral Hospital with a confirmed diagnosis of preeclampsia and followed for six months postpartum. Study approval was obtained from the Institutional Research and Ethics Committee (IREC) of Moi University (Eldoret, Kenya) and IRB of Duke University (Durham, NC, USA).

2.1.1 Study site

Moi Teaching and Referral Hospital (MTRH) is one of two national, referral hospitals in Kenya, located about 300 kilometers northwest of the capital city, Nairobi, in Eldoret town in western Kenya. MTRH provides both high-risk obstetric services and subspecialized cardiovascular care to a catchment area of over 13 million people throughout the region (48). Its standalone maternity hospital, Riley Mother Baby Hospital, performs roughly 12,000 deliveries annually from referrals throughout western Kenya.

2.1.2. Study population

All women admitted to the inpatient antenatal or postnatal wards of Riley Mother Baby Hospital and gynecologic wards of MTRH were screened for study

inclusion from the admission and nursing logs on each ward. We included all women admitted with a clinically confirmed diagnosis of preeclampsia who were >14 years old, ≥20 weeks pregnant and underwent labor, delivery or termination, or postpartum women who were admitted <2 weeks postpartum. Preeclampsia was defined by the International Society for the Study of Hypertension in Pregnancy (ISSHP) guidelines (49), as : 1) systolic BP >140 or diastolic BP >90 mmHg on at least two occasions, and 2) at least one of the following: a) ≥1+ protein on urinalysis or b) signs of end-organ damage: AST or ALT >40 IU/L; serum creatinine >90 μmol/L, platelets <150,000/μL, eclampsia (seizure) or stillbirth (fetal death >20 weeks gestational age without any signs of life at delivery). Women who were admitted antepartum and discharged before delivery were not enrolled. Women were excluded if <14 years old, pregnancy <20 weeks, had a known history of hypertension prior to pregnancy, had a known history of kidney disease prior to pregnancy, or had a reported history of preeclampsia but without confirmed, clinical documentation of inclusion criteria as described above.

Study enrollment began on January 20, 2020; recruitment and follow up were unexpectedly paused as a result of the COVID-19 pandemic on March 19, 2020 and resumed again on August 1, 2020 after approval by the hospital and local ethics board

(IREC). After the re-initiation of the study, women on isolation precautions for suspected or confirmed SARS-CoV-2 infection/COVID-19 syndrome were also excluded.

2.2 Data collection

Women who met inclusion criteria and were interested in participation in the study provided informed consent. Baseline data about demographics, social history, family history, past medical and obstetric histories, and antenatal care (number of visits, place of visits) and medication use during pregnancy were collected by participant self-report. Vital signs on admission to MTRH were recorded, which included the first blood pressure, heart rate, oxygen saturation recorded on arrival. Maternal lab results (urinalysis, hemoglobin, platelets, liver function tests, uric acid), delivery type (vaginal vs. C-section), place of delivery (hospital vs. home), gestational age at delivery, delivery complications (eclampsia, presence of HELLP syndrome, heart failure, need for ICU admission), and delivery outcomes (live birth vs. stillbirth vs. termination of pregnancy, infant APGAR scores and infant weight if live birth) were collected from the paper medical chart. If more than one set of lab results were obtained, the results from the time of preeclampsia diagnosis, or from admission to MTRH if diagnosis occurred at outside facility, were recorded. All data were collected on paper data collection forms then entered into Redcap database by a research assistant.

A baseline echocardiogram was performed on all women after delivery/termination or enrollment (for postpartum women) to assess for cardiac geometry, ventricular function, and hemodynamics. Measurements included: left ventricular systolic ejection fraction (LVEF), left ventricular hypertrophy, left ventricular diastolic function, chamber sizes, right ventricular function, pulmonary pressure, and gross valvular function. LVEF was reported as a continuous variable and also categorized into the following groups based on clinical relevance: LVEF >55%, LVEF 40-55, LVEF <40%.

To measure blood pressure trajectories, participants were taught to use automated BP machine (Omron M2) for home use prior to hospital discharge. Participant technique was observed by the study research assistant; three separate BP measurements were obtained by both participant and research assistant prior to discharge to ensure concordance. Participants were given a notebook to log their BPs twice weekly at home, starting from hospital discharge through 12 weeks postpartum. A research assistant called each participant weekly to obtain recorded BP values and ask if women were taking any medications, and whether they had any follow up or hospitalizations since the last call. A referral protocol was followed for women who

were noted to have blood pressure >140 mmHg / >90mmHg, per international guidelines for postpartum hypertension (Appendix A).

Participants returned for an in-person follow-up visit at MTRH 6 (+/-2) months postpartum. An earlier version of the protocol included follow up at 3-months (after 12 weeks of home BP monitoring). However, due to unexpected interruptions in the study resulting from the COVID-19 pandemic, in-person follow up was rescheduled for 6 months postpartum (+/-2 months). At the follow-up visit, maternal height, weight and oxygen saturation were measured. BP was measured using validated Omron M2 automated machine, with three separate measurements taken 1-minute apart, then averaged (50, 51). Women completed a follow-up survey to collect information about postpartum care, including current medication use, heart failure symptoms, frequency and type of follow up in the postpartum period, factors affecting follow up, knowledge of preeclampsia, and use of home BP monitoring (ease of use, acceptability, adherence, reporting preferences, etc.).

2.3 Sample size

The sample size needed to estimate a proportion (prevalence) with a specified level of precision was calculated for the intended primary outcome of incidence of hypertension at 3-months postpartum. The reported prevalence of hypertension in the

postpartum period among women with preeclampsia varies significantly, ranging from 19-50% in the early postpartum period (29, 31, 33, 34). Using a conservative estimate of 25% prevalence of hypertension at 3-months and a precision level of 7% around the estimate, we needed a sample size of 159 (34). Assuming a loss to follow up rate of 25%, the target sample size for enrollment was 199 participants.

Due to unexpected disruptions in study enrollment and follow-up related to the COVID-19 pandemic, our data collection is ongoing. This analysis focuses on the study subset of those who were enrolled prior to March 19, 2020 (when research activities were paused due to the COVID-19 pandemic).

2.4 Statistical analyses

The primary outcome of the study was hypertension at six months postpartum. Hypertension was defined as an average SBP >130mmHg or DBP >90mmHg of the three blood pressure values checked during the 6-month follow up visits or use of anti-hypertensive medication at follow up. Hypertension was treated as a binary variable (yes/no). Analyses were done using STATA (version 15.0); figures (scatterplots and time-to-event graph) were created in SAS (Cary, NC) and R studio.

Descriptive analyses were done comparing baseline demographic, past medical and family history, as well as index pregnancy history, including access to antenatal

care, medication use in pregnancy, timing and type of delivery, laboratory findings on hospital admission, length of hospitalization. Baseline characteristics were compared between the total enrolled study population enrolled as of March 19, 2020, those with hypertension at follow-up and those without hypertension at follow-up. Median, interquartile range (25^{th}-75^{th} percentile), and max values were reported for continuous variables, and counts and proportions were reported for categorical variables.

Similarly, postpartum healthcare utilization was compared between those with hypertension at follow up and those without. The proportion hospitalized after delivery, average number of clinics follow up appointments attended in the postpartum period, type/location of clinic attended, reason for attending that clinic, whether the hospital provider recommended follow-up, and health-seeking behavior for childhood vaccination, and participant experience regarding the use of home BP monitoring were collected by participant self-report at the 6-month follow-up visits and reported using numbers/proportions and mean/ranges.

2.4.1. Bivariate and multivariable analyses

Bivariate analysis was performed to determine differences in baseline characteristics between those who had the outcome (hypertension at 6-month follow up) and those who did not; to test statistical significance, the Kruskal-Wallis test for

continuous variables and Fisher's exact for categorical variables were used due to small sample size. Statistical significance was defined as a p-value <0.05.

Multivariable logistic regression models were fit to determine factors associated with increased odds of hypertension at 6-months. First, a model was run using variables identified *a priori* to be associated with hypertension at follow up. These included: age, parity (0 vs. >0), history of preeclampsia (yes/no), severity of preeclampsia (severe vs. not severe), aspirin use during pregnancy, and left ventricular ejection fraction on echocardiogram (>55% vs. 40-55% vs. <40%). Some of these *a priori* variables were not statistically significantly associated with the outcome in bivariate analysis and therefore were not included in the regression. A second model was run using variables of significance from the bivariate analysis (defined as p-value <0.2); these included: age; parity (0 vs. >0); education level (none vs. primary school vs. secondary school or greater); history of previous pregnancy complication (including: history of previous preeclampsia, previous preterm delivery, or previous IUFD/stillbirth); use of aspirin during pregnancy; proteinuria on U/A (yes/no); elevated liver function tests on admission (yes/no), use of oxytocin during labor and delivery (yes/no); and use of misoprostol during labor and delivery (yes/no). Variables with small cell counts (<5) were removed from the model.

2.4.2 Longitudinal blood pressure measurements: Loess models

Scatterplots were generated to visualize the longitudinal BP trend over the 12-week postpartum period using the home BP data. Systolic and diastolic blood pressure values on the date of hospital admission, hospital discharge, and all available home BP reading values collected biweekly for week 1-12 postpartum were plotted for each participant over time in weeks. Locally weighted smoothing models (LOESS) were used to create a smooth line through the scatterplot, using weight of 0.3. Three separate plots were generated to show the longitudinal BP trends compared among the following groups: 1) those with incident hypertension at 6-months; 2) those without hypertension at 6-months; 3) those who did not have a 6-month follow-up.

2.4.3 Loss to follow up: time-to-event analysis

Time to loss to follow up was estimated using time-to-event analysis for all participants eligible for 6-month follow up. Loss to follow up was defined as the event of not completing the full 12 weeks of home BP monitoring. Participants who did not have any blood pressure values recorded during the week 12 home BP call were considered loss to follow up, regardless of the 6-month follow up status. The date of lost to follow up was recorded as the date of the last recorded BP value before the first missed value. From this measure, the follow-up time was defined as time from delivery to date of loss

to follow-up. Proportions of patients who were not lost to follow-up were reported at the following postpartum times: 1 week, 2 weeks, 4 weeks, 6 weeks, and 12 weeks.

3. Results

Between January 20, 2020 and March 19, 2020 (date of study pause due to COVID-19), a total of 216 women admitted to MTRH had a recorded diagnosis of preeclampsia, of which 108 met inclusion criteria (Figure 1). Of those, a total of 86 were enrolled before March 19, 2020. Four were excluded or withdrew during the study follow up period, leaving a total of 82 eligible for 6-month follow-up. Among these, only 61% (n=50) returned for 6-month follow up visit. The most common reason for loss to follow up was being unable to reach the participant by phone, followed by participants being too far away or having relocated to the village and unable to return to MTRH; one reported anxiety about returning to the hospital due to COVID-19 and four were scheduled by did not show up.

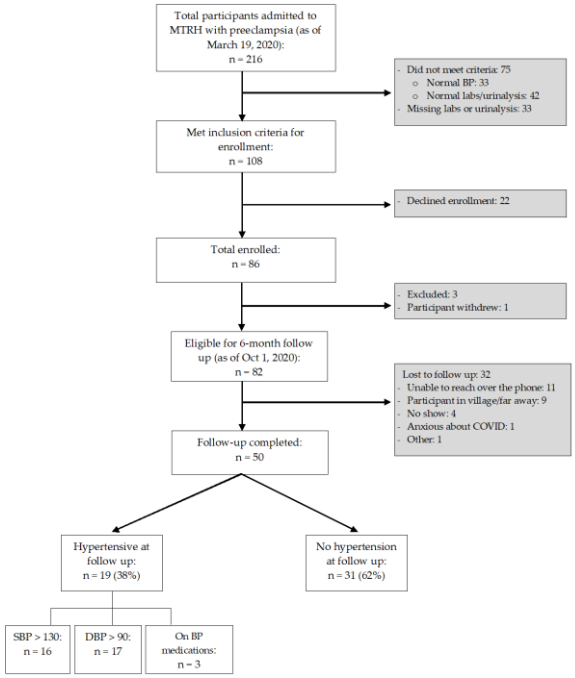


Figure 1. Strobe diagram of participant enrollment and inclusion

3.1 Characteristics of the study population

Baseline characteristics for all participants are summarized in Table 1. The median age among all women enrolled was 24 years. Most women were nulliparous (parity=0), indicating their first delivery, though parity ranged up between 0-7 in the sample. Nearly all (95%) of women were admitted to hospital prior to delivery, with only 4 admitted in the postpartum period. Most participants (78%) lived in Uasin Gishu, the county within which MTRH is located. Roughly one quarter (26%) of women had only a primary school education level, while one-third (37%) completed secondary

school and another one-third (37%) had a college or university degree. Less than half (41%) were enrolled in the National Health Insurance Fund (NHIF) and had public health insurance coverage. Despite this, most (99%) received antenatal care during pregnancy, with over half of women (54%) having 3-4 visits during pregnancy and 79% reported taking prenatal vitamins during pregnancy. One-quarter (24%) were managed on anti-hypertensive medication during pregnancy, while only 3% were taking baby aspirin, a guideline-directed therapy for prevention of preeclampsia and associated complications (21).

Table 1. Baseline characteristics of study participants by outcome

Characteristic	Total Enrolled (n = 86)	**Hypertension at Follow-up (n = 19)**	**No hypertension at follow-up (n = 31)**
Demographics			
Age, median (IQR)	24 (22 – 32)	32 (26 – 35)	24 (21 – 26)
Parity, median (IQR, max)	0 (0 – 2, 7)	2 (0 - 4, 5)	0 (0-1, 3)
Residence in Uasin Gishu county, n (%)	67 (77.9)	15 (79.0)	25 (80.7)
Highest education level completed, n (%)			
Primary school	22 (26.2)	5 (26.3)	3 (9.7)
Secondary school	31 (36.9)	10 (52.6)	13 (41.9)
University / college	31 (36.9)	4 (21.1)	15 (48.4)
NHIF enrolled, n (%)	34 (41.0)	9 (47.4)	12 (36.4)
Past medical / pregnancy history			
Previous preeclampsia	9 (10.5)	5 (26.3)	2 (6.5)
Previous preterm delivery	9 (10.5)	5 (26.3)	0 (0.0)
Previous stillbirth	5 (5.8)	4 (21.1)	0 (0.0)
Family History			
Preeclampsia	9 (10.5)	3 (15.8)	3 (9.7)
CVD	25 (29.1)	6 (31.6)	7 (22.6)
Current pregnancy			
Received antenatal care, n (%) *	82 (98.8)	19 (100)	30 (100)
1-2 visits	18 (22.0)	4 (21.1)	7 (21.2)

3-4 visits	44 (53.7)	8 (42.1)	20 (60.6)
≥5 visits	20 (24.4)	7 (36.8)	6 (18.2)
Antenatal clinic visits, mean (SD)	3.5 (1.4)	3.9 (1.5)	3.6 (1.5)
Medication use during pregnancy, n (%)	74 (88.1)	17 (89.5)	25 (80.7)
Prenatal vitamins	68 (79.1)	16 (84.2)	24 (77.4)
Anti-hypertensives	21 (24.4)	6 (31.6)	5 (16.1)
Baby aspirin	3 (3.5)	2 (10.6)	0 (0)
Delivery & Hospitalization			
Gestational age at delivery, weeks, median (range)	35 (22 – 44.4)	36 (23.4 – 40.6)	37 (22-42.3)
Preterm delivery, n (%)	46 (57.5)	11 (57.9)	15 (50.0)
Low birth weight, n (%)	15 (39.5)	6 (42.9)	9 (37.5)
C-section delivery, n (%)	36 (42.4)	10 (52.6)	12 (38.7)
Birth outcome, n (%)			
Live birth	71 (83.5)	14 (73.7)	27 (87.1)
Stillbirth	8 (9.4)	3 (15.8)	0 (0)
Termination of pregnancy	6 (7.1)	2 (10.5)	4 (12.9)
Labs at admission, n (%)			
Anemia (n=85)	8 (9.4)	2 (10.5)	2 (6.5)
Thrombocytopenia (n=85)	11 (12.9)	3 (15.8)	5 (16.1)
Proteinuria on U/A (n=70)	66 (94.3)	13 (86.7)	28 (100)
Acute kidney injury (n=82)	17 (20.7)	3 (16.7)	7 (24.1)
Elevated liver function tests (n=78)	25 (32.1)	3 (17.7)	11 (40.7)
Severe PET, n (%)	51 (61.5)	12 (63.2)	17 (56.7)
SBP ≥160mmHg or DBP ≥110mmHg	32 (37.2)	9 (47.4)	10 (32.3)
Eclampsia	8 (9.3)	1 (5.3)	4 (12.9)
HELLP syndrome	12 (14.0)	2 (10.5)	5 (16.1)
Medication use during hospital stay, n (%)			
Beta blockers	9 (10.5)	1 (5.3)	5 (16.1)
Calcium-channel blockers	80 (93.0)	18 (94.7)	31 (100)
Methyldopa	8 (9.3)	1 (5.3)	2 (6.4)
Magnesium	68 (79.1)	13 (68.4)	26 (83.9)
Oxytocin	37 (43.0)	6 (31.6)	17 (54.8)
Misoprostol	24 (27.9)	10 (52.6)	7 (22.6)

Most (84%) women had a live birth, though nearly 10% had stillbirth (or intrauterine fetal demise) and 7% had a termination. The median gestational age at

delivery was 36 weeks, though over half of all pregnancies (58%) had a preterm delivery (<37 weeks). The average gestational age at delivery was lower for those with a stillbirth (32.1 weeks) and those who had a termination of pregnancy (24 weeks). Nearly half of all deliveries (42%) were via C-section, while 40% underwent induction of labor with oxytocin and/or misoprostol. Over half (62%) of women included had severe preeclampsia, with over one third (37%) having severe-range blood pressure (systolic BP ≥ 160mmHg or a diastolic BP ≥ 110mmHg), 9% with eclampsia and 14% with HELLP syndrome. Overall, though, 79% of all women received magnesium sulfate, a medication used to prevent and treat eclampsia in those with severe preeclampsia (11). Calcium-channel blockers were the most common medication used to manage hypertension during hospitalization (90%), followed by 11% on a beta-blocker and 9% on methyldopa.

3.2 Incidence of hypertension at 6-month follow up: primary outcome

Overall, loss to follow-up was relatively high among postpartum women, with only 61% of 82 eligible participants returning for the 6-month study visit (n=50). The median time to 6-month follow-up was 6.6 months postpartum and ranged from 6 – 8.4 months postpartum. The point incidence of hypertension at follow-up was 38%, with 19 of the 50 participants who followed up having hypertension. Of these, 16 (98.2%) had systolic hypertension (SBP >130mmHg), 17 (89.5%) had a diastolic hypertension (DBP

>90mmHg). The median systolic BP was 142mmHg (interquartile range: 134 – 150mmHg, max: 174mmHg) and median diastolic BP 96mmHg (92 – 103mmHg, max: 129mmHg). Only 3 participants were on anti-hypertensive medications at the postpartum follow up.

3.3 Factors associated with hypertension at follow up: bivariate analysis and multivariable regression

Those with hypertension at follow up were significantly older (32 years vs. 24 years, p<0.01) and had a higher parity than those without hypertension at follow up (2 vs. 0, p<0.01, Table 2). Women with hypertension at follow up had a lower level of education overall, with a smaller proportion having completed a university or college degree and a higher proportion having completed only primary school compared to women with normal BP (21% vs. 48% and 26.3% vs. 9.7%, respectively). Less than half of each group had public health insurance through NHIF.

Table 2. Bivariate analysis of factors associated with incident hypertension at 6-month follow-up

Characteristic	Total completed follow-up (n =50)	Hypertension at Follow-up (n = 19)	No hypertension at follow-up (n=31)	p-value
Demographics				
Age, median (IQR)	25 (22 – 32)	32 (26 – 35)	24 (21 – 26)	<0.001
Parity, median (IQR, max)	0 (0 – 2, 5)	2 (0 - 4, 5)	0 (0-1, 3)	0.002
Residence in Uasin Gishu county, n (%)	40 (80.0)	15 (79.0)	25 (80.7)	1.000
Education level, n (%)				0.105
Primary school	8 (16.0)	5 (26.3)	3 (9.7)	

Secondary school	23 (46.0)	10 (52.6)	13 (41.9)	
University / college	19 (38.0)	4 (21.1)	15 (48.4)	
NHIF enrolled, n (%)	22 (44.0)	9 (47.4)	13 (41.9)	0.774
Past medical / pregnancy history				
Previous preeclampsia	7 (14.0)	5 (26.3)	2 (6.5)	0.089
Previous preterm delivery	5 (10.0)	5 (26.3)	0 (0.0)	0.005
Previous IUFD / stillbirth	4 (8.0)	4 (21.1)	0 (0.0)	0.017
Family History				
Preeclampsia	6 (12.0)	3 (15.8)	3 (9.7)	0.661
CVD*	13 (26.0)	6 (31.6)	7 (22.6)	0.521
During index pregnancy				
Received antenatal care, n (%)*	49 (98.0)	19 (100)	30 (96.8)	0.645
1-2 visits	11 (22.5)	4 (21.1)	7 (21.2)	n/a
3-4 visits	24 (49.0)	8 (42.1)	20 (60.6)	n/a
≥5 visits	14 (28.6)	7 (36.8)	6 (18.2)	n/a
Medications during pregnancy, n (%)				
Prenatal vitamins	40 (80.0)	16 (84.2)	24 (77.4)	0.722
Anti-hypertensive	11 (22.0)	6 (31.6)	5 (16.1)	0.293
Aspirin use	2 (4.0)	2 (10.6)	0 (0)	0.140
Delivery & Hospitalization				
GA at delivery, wks, median (range)	34.4 (22 – 42.3)	36 (23.4 – 40.6)	37 (22-42.3)	0.886
Preterm, n (%)	26 (53.1)	11 (57.9)	15 (50.0)	0.770
Low birth weight (<2500g), n (%)	15 (39.5)	6 (42.9)	9 (37.5)	1.000
C-section, n (%)	22 (44.0)	10 (52.6)	12 (38.7)	0.725
Birth outcome, n (%)				0.096
Live birth	41 (82.0)	14 (73.7)	27 (87.1)	n/a
Stillbirth	3 (6.0)	3 (15.8)	0 (0)	n/a
Termination	6 (12.0)	2 (10.5)	4 (12.9)	n/a
Severe PET, n (%)	29 (59.2)	12 (63.2)	17 (56.7)	0.769
Medications during hospitalization, n (%)				
Magnesium	39 (78.0)	13 (68.4)	26 (83.9)	0.293
Diuretics	1 (2.0)	1 (5.3)	0 (0)	0.380
Beta blockers	6 (12.0)	1 (5.3)	5 (16.1)	0.387
Calcium channel blockers	49 (98.0)	18 (94.7)	31 (100)	0.380
Methyldopa	3 (6.0)	1 (5.3)	2 (6.4)	1.000
Oxytocin	23 (46.0)	6 (31.6)	17 (54.8)	0.148

Misoprostol	17 (34.0)	10 (52.6)	7 (22.6)	0.037
Length of hospital stay (days), median (IQR, max)	6.5 (3-10, 49)	7 (3 – 10, 18)	6 (2-10, 49)	0.665
Echocardiogram measures				
LV ejection fraction at delivery	n = 33	n = 15	n = 18	0.722
>55%, n (%)	23 (69.7)	11 (73.3)	12 (66.7)	n/a
40-55%, n (%)	10 (30.3)	4 (26.7)	6 (33.3)	n/a

There were significantly higher rates of hypertension at follow up among women with a previous preterm delivery (26% vs. 0%, $p<0.01$), previous stillbirth (21% vs. 0%, $p=0.02$) as well as a non-significantly higher proportion who had a history of previous preeclampsia compared to women with normal BP (26% vs. 7%, $p=0.09$). Similarly, more women with hypertension at follow up had a family history of CVD, with nearly one-third (32%) of women with hypertension at follow up reporting a family history of CVD, compared to only 23% of those without hypertension. Interestingly, no women reported family history of stroke or heart failure. Rates of preterm delivery and low birth weight infants were similarly high between those who had hypertension at follow up and those without (58% vs. 50% and 43% vs. 38% respectively); however, 16% of women with hypertension at follow up had a stillbirth while none of those with normal BP did (Table 1).

There was no significant difference in rates of severe preeclampsia between those with hypertension at follow up and those without, with over half of both groups having

severe preeclampsia prior to delivery (63% of those with hypertension at follow up vs. 57% of those without, p=0.77). While almost half (47%) of women with hypertension at follow up had severe-range BP with SBP ≥160mmHg or DBP ≥110mmmHg on admission, compared to only one-third (32%) of those without hypertension, although this difference was not statistically significant in bivariate analysis. Interestingly, women without hypertension at follow up had a higher proportion of eclampsia and/or HELLP syndrome than those with hypertension at follow up. There were no differences between groups in the rates of anemia, thrombocytopenia, acute kidney injury, elevated liver function tests, or uric acid levels, and nearly all women in both groups had proteinuria on urinalysis at admission. Of the 63 baseline echocardiograms reported to date, most women (70%) had a normal left ventricular ejection fraction (LVEF >55%) at the time of delivery, but over one-quarter (30%) of all women had a slightly reduced LVEF (40-55%); no women had a severely reduced LVEF <40%. While there was a slightly higher rate of reduced LVEF (<55%) among women without hypertension at follow up compared to those with hypertension (33% vs. 27%), this was not statistically significant (p=0.722).

Results from the multivariable regression model showed that increased age was the only variable associated with increased odds of hypertension at follow up among

those women with follow up to date (Table 3). When regression was run using *a priori* selected variables, only 33 observations were included in the model (Table 3, model 3a). There was no significant association between severe preeclampsia (OR 0.46, 95% CI 0.07-3.14) or baseline LVEF (0.35, 95% CI 0.01-1.27) and odds of hypertension at follow up. However, when the model was run using variables with p-value < 0.2 from the bivariate analysis, 43 observations were included. There was a trend for parity (parity > 0) and birth outcome (stillbirth) and increased odds of hypertension at follow up, though the confidence intervals were large and non-significant. Education level and proteinuria on urinalysis were not found to be associated with hypertension at follow up (Table 3, model 3b).

Table 3. Multivariable regression of factors associated with hypertension at 6-months postpartum

3a. Variables selected *a priori*

Risk Factor	Hypertensive at 6-months (OR)	95% CI
Age	1.37	1.07 – 1.74
Parity	1.12	0.13 – 9.46
Severe preeclampsia	0.46	0.07 – 3.14
LVEF < 55%	0.35	0.01 – 1.27

n = 33 with residual df = 37

3b. Variables selected from results of bivariate analysis

Risk Factor	Hypertensive at 6-months (OR)	95% CI
Age	1.33	1.03 – 1.73
Parity	1.74	0.15 – 19.78
Education level	0.61	0.16 – 2.27
Birth outcome	3.94	0.25 – 61.73
Proteinuria on urinalysis at hospital admission	0.66	0.15 – 2.85

n = 43 with residual df = 28

3.4 Trends in blood pressure following delivery

There were no apparent differences in the systolic or diastolic BP at hospital admission or discharge between those with hypertension at follow up versus those without (Table 4). Median BP on hospital admission was 158 / 105mmHg among those with hypertension at follow up (IQR SBP: 152-164mmHg, IQR DBP: 99-113mmHg) compared to 154 / 99mmHg in those without hypertension at follow up (IQR SBP: 145-162mmHg, IQR DBP: 99-109mmHg). While the systolic blood pressure at discharge was slightly higher among those with hypertension at follow up (median 137mmHg, IQR 128-142mmHg vs. 130mmHg, IQR 125-139mmHg), fewer were discharged on anti-hypertensive medications compared to those without hypertension at follow up (74% vs 87%). The median length of hospitalization overall was 5.5 days (IQR 3 – 10) and was similar between groups (7 days (IQR 3- 10) among those with hypertension at follow up compared to 6 days (IQR 2-10) among those without hypertension at follow up).

Table 4. Blood pressure at hospital admission, discharge and follow-up by outcome

BP measurements	Total enrolled (n=86)	Hypertension at follow-up (n = 19)	No hypertension at follow up (n=31)	No follow-up (n = 36)
At hospital admission				
SBP (mmHg), median (IQR, max)	155 (147-164, 219)	158 (152 – 164, 213)	154 (145 – 162, 202)	153 (147-168, 219)
DBP (mmHg), median (IQR, max)	103 (94-108, 160)	105 (99-113, 155)	99 (93-108, 132)	102 (93-109, 160)
On BP medications, n (%)	34 (40.0)	7 (36.8)	11 (35.5)	16 (45.7)

At hospital discharge				
SBP (mmHg), median (IQR, max)	132 (125-143, 170)	137 (128-142, 157)	130 (125-139, 161)	132 (125-144, 170)
DBP (mmHg), median (IQR, max)	88 (79-94, 122)	88 (84-95, 107)	87 (80-94, 109)	87 (78-91, 122)
On anti-hypertensive medications, n (%)	71 (85.5)	14 (73.7)	26 (86.7)	31 (91.2)
Calcium-channel blockers	68 (79.1)	13 (68.4)	25 (80.7)	30 (83.3)
Beta-blockers	2 (2.3)	0 (0)	1 (3.2)	1 (2.8)
Diuretic	2 (2.3)	1 (5.3)	0	1 (2.8)
Methyldopa	4 (4.7)	1 (5.3)	0 (0)	3 (8.3)
Length of hospital stay (days), median (IQR, max)	5.5 (3 – 10, 49)	7 (3 – 10, 18)	6 (2-10, 49)	5 (3 – 9, 42)
At follow-up*				
SBP (mmHg), median (IQR, max)	122 (115-136, 174)	142 (134-150, 174)	116 (111-122, 129)	n/a
DBP (mmHg), median (IQR, max)	83 (78-94, 129)	96 (92-103, 129)	81 (74-83, 89)	n/a
On anti-hypertensive medications, n (%)	3 (6.0)	3 (15.8)	0 (0)	n/a

*Includes n=50

Figure 2 shows the longitudinal trends in home BP over 12 weeks postpartum by those with hypertension at follow up, those with normal BP and those with incomplete follow up at 6-months. The loess curve of smoothness shows that in general, there is a dramatic decrease in blood pressure at time of delivery (time 0), and both systolic and diastolic blood pressure rapidly returns to normal (≤130mmHg / ≤90mmHg) within the two weeks after delivery for most women. However, among women with hypertension

at follow up, blood pressure initially normalizes following delivery but then begins to rise again after 3 months postpartum.

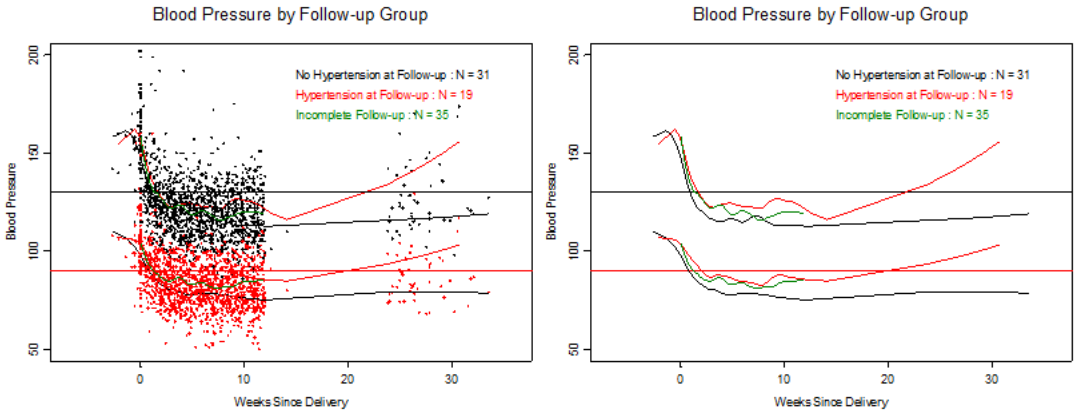


Figure 2. Trends in postpartum BP between those with incident hypertension and those without over 6 months postpartum. Loess curves showing trends in postpartum blood pressure after delivery (top line: systolic BP; bottom line: diastolic BP) among women with incident hypertension (red), women with normal BP at 6-month follow up (black), and women who did not complete 6-month follow-up (green). The left graph shows scatter plot of all blood pressure values collected for each participant with superimposed loess curves, while the right graph shows only the loess curves.

3.5 Postpartum healthcare utilization

Of the 50 women who completed a 6-month follow up visit, only 2 were hospitalized postpartum, both for high blood pressure. Postpartum clinic attendance for women was low, with less than two-thirds of women (64%) having attended any clinic for follow up after delivery, though, only half (50%) reported being told to follow up in clinic by a provider at the time of hospital discharge (Table 5). Interestingly though, most women (97%) took their infants to clinic for routine immunizations, with over half

(60%) having 3-4 immunization visits and 41% with more than 5 visits for childhood immunizations.

Table 5. Healthcare utilization in the postpartum period by outcome

	Total completed follow up (n = 50)	Hypertension at follow up (n= 19)	No hypertension at follow up (n = 31)	p-value
Hospitalized after delivery, n (%)	2 (4.0)	1 (5.3)	1 (3.2)	1.000
Clinic follow-up in postpartum period, n (%)	32 (64.0)	13 (68.4)	19 (61.3)	0.764
1-2 visits, n (%)	23 (46.0)	9 (47.4)	14 (45.2)	n/a
3-4 visits, n (%)	8 (16.0)	3 (15.8)	5 (16.1)	n/a
≥ 5 visits, n (%)	1 (2.0)	1 (5.3)	0 (0)	n/a
Type of clinic				
Postpartum (OB/Gyn)	17 (34.0)	8 (42.1)	9 (29.0)	0.373
MCH	12 (24.0)	3 (15.8)	9 (29.0)	0.332
Specialty	1 (2.0)	0 (0)	1 (3.2)	1.000
Clinic Location				<0.001
MTRH	6 (18.8)	0 (0)	6 (31.6)	n/a
Local clinic	13 (40.6)	2 (15.4)	11 (57.9)	n/a
Dispensary	5 (15.6)	3 (23.1)	2 (10.5)	n/a
Other	9 (25.0)	8 (61.5)	0 (0)	n/a
Why did you choose this clinic?				
Closest to home	22 (44.0)	10 (52.6)	12 (38.7)	0.398
Been there before	6 (12.0)	2 (10.5)	4 (12.9)	1.000
Child gets care there	1 (2.0)	0 (0)	1 (3.2)	1.000
I was told to go there	7 (14.0)	2 (10.5)	5 (16.1)	0.695

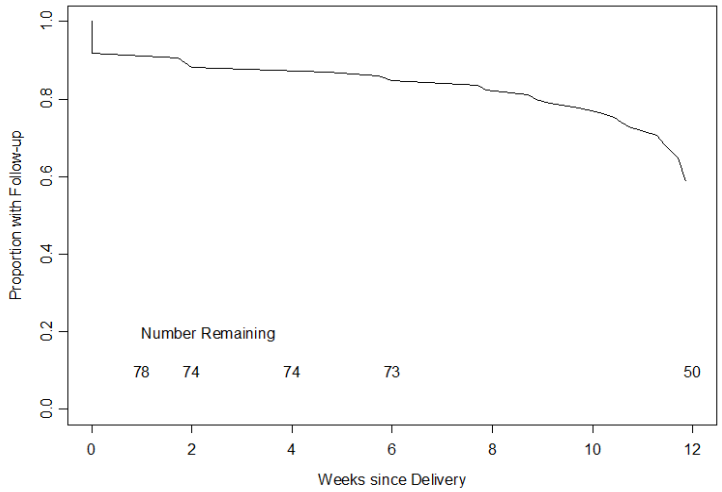
There was no difference in rates of clinic follow up between those with hypertension at follow up and those without. However, there was a significant difference in the location of clinic follow up between those with hypertension at follow up and those without; among women with hypertension at 6-months, a higher

proportion had follow up care at a dispensary (a lower tier medical clinic in the public health system), as compared to women without hypertension who had higher rates of follow up at MTRH or a local, outpatient clinic. Despite, the high rate of infant follow up care, only 1 woman sought follow up at the same clinic where her child also received care.

While 85% of all women were discharged on anti-hypertensive medications, only 6% remained on medications at 6-months follow up. Running out of medications was the most common reason for stopping, as reported by 68% of women overall at follow up and 63% of those with hypertension at follow up who would qualify for continued medication use.

3.6 Loss to follow up: Time-to-event analysis

Figure 3 shows time-to-event analysis of when loss to follow up occurred. Of all participants, 8% were lost to follow up within the first week after delivery, 13% by the end of week 2. There was very little additional loss to follow up between week 2 and week 6 postpartum, with 86% of all participants completed BP checks at 6 weeks postpartum. The largest loss to follow up occurred between week 6 and week 12 postpartum, though, with only 59% of participants completing the full 12 weeks home BP monitoring.



Weeks from Delivery	Number remaing	Survival Proportion
0	85	1.0
1	78	0.92
2	74	0.87
4	74	0.87
6	73	0.86
12	50	0.59

Figure 3. Time-to-loss to follow up after delivery on weekly home blood pressure monitoring calls

4. Discussion

This prospective cohort study investigated the incidence of chronic hypertension among Kenyan women at 6-months postpartum after a pregnancy complicated by preeclampsia. We sought to describe the characteristics associated with hypertension at follow up and the postpartum healthcare utilization in this population. Data collection is still ongoing for this study due to unexpected pauses in study enrollment and follow-up related to the COVID-19 pandemic, but preliminary results analyzed here found that more than one-third (38%) of women with preeclampsia had hypertension at 6-months postpartum. While severe preeclampsia and associated complications were common in pregnancy, there was no difference in rates of hypertension at follow up among women with severe preeclampsia compared to those with preeclampsia without severe features. Half of all women had a preterm delivery and over one-third of infants were low birth weight, both independent risk factors themselves for CVD in women. Women with hypertension at follow up were older and had higher rates of previous pregnancy complications, including a history of preeclampsia, preterm delivery or previous stillbirth, though multivariable analysis did not show any specific risk factors associated with hypertension at follow up. Most women were discharged on anti-hypertensive medications, yet less than three-quarters of women had any follow-up visits in the

postpartum period. Loss to follow-up was highest between 6 and 12 weeks after delivery. These results illustrate that women with preeclampsia in Kenya represent a high-risk population for early CV disease, though high loss to follow-up rates in the postpartum period result in a missed opportunity for early CVD prevention.

This study found a higher than expected rate of hypertension 6-months following delivery, when the effects of preeclampsia should have resolved, suggesting that women with preeclampsia in pregnancy in Kenya are a particularly high-risk group for the development of chronic hypertension at a young age. Over one-third of women in our study had hypertension at 6-months, a rate twice as high as previous cohort studies have reported. A small, retrospective study of U.S. women with preeclampsia found 19% had hypertension at 6-months postpartum (52); notably, women in that study were much older (over half over the age of 40) compared to our study where the median age of women overall was 24. The only other study published from sub-Saharan Africa that has explored trends in postpartum hypertension among women with preeclampsia, found even lower rates of hypertension at 6-months among women in Cameroon with only 15% having hypertension at 6-months following delivery, as compared to the 38% in our sample (34). These findings suggest that women with preeclampsia in Kenya represent a high-risk group for development of hypertension after delivery. Given

chronic hypertension is also a risk factor for future pregnancy complications, early identification of chronic hypertension following preeclampsia is critical to not only improving CVD in women but may also impact future maternal health outcomes for these young women.

Despite the overall high rate of hypertension seen 6-months postpartum, we did not find any clear actionable risk factors associated with hypertension at follow up. While there was a trend towards increased odds of hypertension at follow up and maternal age and stillbirth, the small sample size included in this preliminary analysis limited the findings from our multivariable analysis. Importantly, though, we did find a high prevalence of factors that have been previously associated with increased odds of chronic hypertension. Maternal age, severity of preeclampsia, preterm delivery, and early changes in left ventricular size have previously been associated with chronic hypertension following pregnancy (34, 39, 52, 53). Severe preeclampsia, defined by systolic BP ≥ 160mmHg and/or diastolic BP ≥ 110mmHg with specific signs of significant end-organ dysfunction, including liver damage, kidney damage or low platelets, occurred in 62% of all participants, with a slighter higher proportion in those with hypertension at follow up. Interestingly, women without hypertension at 6-months had higher proportions of low birth weight infants and proteinuria on urinalysis at hospital

admission, both of which have been associated increased risk of hypertension in the postpartum period (31). This suggests that women without hypertension at follow up still have underlying risk factors for the development of hypertension following their preeclampsia, and therefore remain at high risk of CVD going forward.

We did find a trend, though, between having a previous pregnancy-related complication (preterm delivery, previous stillbirth, history of preeclampsia) and hypertension at follow up, with a disproportionately higher rate among women with hypertension at follow up than those without. One-quarter of all women with hypertension at follow up had a history of preeclampsia in a previous pregnancy. This is consistent with results from a recent systematic review and meta-analysis of 22 studies that found that women with recurrent preeclampsia in multiple pregnancies had high risk of cardiovascular disease (including hypertension, ischemic heart disease, heart failure and strokes), though there was notable variation in lengths of follow up among studies (54). Despite the high rate seen in our study, only 10% of these women were on guideline-directed therapy for preeclampsia prevention during their pregnancy. The WHO recommends that all pregnant women with a history of preeclampsia be started on low-dose aspirin in pregnancy to prevent or delay the onset of recurrent preeclampsia (21, 55). Given our data suggest a possible link between recurrent

preeclampsia hypertension at 6-months postpartum, promotion of aspirin use in pregnancy may be a critical, not only to prevent recurrent preeclampsia but also to indirectly reduce rates of chronic hypertension following delivery in these women. More research is needed to better understand the effects of aspirin use in pregnancy on postpartum cardiovascular risk.

We explored the longitudinal blood pressure trajectory over the first 12 weeks following delivery and found that blood pressure appeared to normalized between 2-4 weeks postpartum for all women, but then rises after 8-12 weeks following delivery among women with hypertension at follow up. In women who did not have hypertension prior to delivery, international guidelines suggest that blood pressure should return to normal by 6-12 weeks following delivery, and thus, hypertension after 12 weeks may be considered and treated as chronic hypertension (52, 56). Previous cohort studies of U.S. women with preeclampsia have reported the time-to-normalization of postpartum BP ranges from 16 days to 9 weeks postpartum, with mean-time-to-normalization of 5 weeks (31, 52). This trend was similar in our cohort, with blood pressure normalizing between 2-4 weeks postpartum for all women in our study. Importantly, most women were taking anti-hypertensive medications during this period following discharge. However, among those who had hypertension at 6-month

follow up, blood pressure was found to rise again in the later postpartum period, beyond 8-12 weeks following delivery; over half (68%) of these women reported running out of anti-hypertensive medications by the time. Overall, though, this uptrend suggests that normal blood pressure at the standard 6-week postpartum clinic follow up visit may be falsely reassuring and more longitudinal follow up may instead be necessary for the early detection of hypertension.

However, rates of postpartum healthcare utilization are low resulting in a missed opportunity for early disease detection. Only 64% of women had a postpartum clinic follow up visit by 6-months. While postpartum care utilization may have been negatively impacted due to the COVID-19 pandemic and disruption to local clinic access and availability, similarly low rates of postpartum follow up are seen among women with preeclampsia in high income countries indicates this is a universally challenging period for women (57-59). Frequent well-baby and routine immunization visits for the infant are often prioritized over maternal health, and stress having to navigate transportation with an infant or finding a caregiver and long clinic wait times are often deterrents for women to seek postpartum care. Thus, novel healthcare delivery models that incorporate women's follow up into well-baby visits, or non-clinic based follow up strategies (ie. mHealth vs. community health worker models) are needed to engage and

retain this high-risk population in longitudinal care for early identification and management of hypertension.

Feasibility studies from high income countries have showed home BP monitoring to be a potential, promising telehealth strategy for hypertension monitoring in the early postpartum period. Home BP monitoring has shown to increase adherence to BP checks within the very early postpartum period; a randomized controlled trial of U.S. women with preeclampsia found women doing home BP monitoring were twice as likely to have their BP checked within 10 days postpartum compared to women with clinic follow up (60). While a much higher proportion of women completed home blood pressure monitoring in the early postpartum period (86% up to 6 weeks), similarly high rates of loss to follow up occurred after 8 weeks postpartum. Overall, a similar rate of women completed the 12-weeks of home blood pressure monitoring compared to the number who attended clinic follow up.

Unique barriers to postpartum care exist in Kenya and throughout SSA that compound these challenges. Only half of women in our study reported being told by their medical provider to follow-up after hospital discharge, indicating a large gap in provider-patient communication. Of those who did attend clinic, there was considerable variation in the type of clinic that women went to for postpartum care, with some

seeking care at OB/Gyn postpartum clinic, some seeing a nurse at maternal-child-health clinic. Proximity of clinic to the home was the largest determinant for place of follow up. Interestingly, though, nearly all women (97%) took their infants to clinic for routine vaccination, with all attending at least 3-4 appointments, suggesting that there may be opportunity to link maternal follow up with routine well-childcare going forward.

4.1 Strategies for improved retention with integration of care

In Kenya, where high rates of hypertension are largely underdiagnosed in the general population, identification of particularly high-risk groups to target for screening and early intervention may be an important population-level strategy to reduce the overall burden of hypertension. Pregnancy provides unique foreshadowing into the future cardiovascular health of a woman. Given the high incidence of hypertension found just 6-months following delivery in young women with preeclampsia in Kenya, targeted strategies focused on linking and retaining these women in follow up care will be critical to prevent premature morbidity and mortality due to cardiovascular disease among women in this population.

Both reproductive health care and prevention of CVD have been identified by the Kenyan government as top health priorities. As Kenya moves towards developing a universal healthcare model, strategies to link these care delivery systems need to be

considered. In 2013, the Kenyan government passed the Free Maternity Service policy that abolished all fees for maternity care services in public facilities, which resulted in a brisk increase in the number of deliveries happening in healthcare facilities, and thus represented a unique opportunity to identify and engage with high-risk women (61). As our results showed, nearly all women received antenatal care during pregnancy and brought their infants to clinic for routine immunizations after delivery, indicating a high level of engagement with the health system in the peripartum period among Kenyan women. Thus, integrating postpartum follow up for women with hypertension screening and management protocols into this existing maternal-child-health infrastructure could lead to earlier identification and treatment of hypertension.

Similar integrated care strategies have proved successful in decreasing disease rates among high-risk groups. The design of prevention-of-mother-to-child-transmission (PMTCT) programs aimed to decrease the rate of HIV spread across sub-Saharan Africa through the integration of HIV care services into the existing maternal-child health infrastructure. This model of care delivery has proved to be hugely successful in not only decreasing rates of vertically transmitted HIV infection, but has more broadly impacted primary care delivery for women and children (62, 63). Similar strategies aimed at leveraging the existing HIV clinic network for delivery of non-communicable

and chronic disease care to people living with HIV seem feasible (64, 65). In fact, the Pan African Society of Cardiology (PASCAR) has proposed integration of hypertension detection and treatment programs within existing vertical programs for HIV and TB, as part of their strategic map for achieving 25% hypertension control in Africa by 2025 (4). However, given the impending burden of cardiovascular disease among young women in Kenya, this proposed strategy needs to also include integration of hypertension care into maternal-child-health networks.

4.2 Limitations

While this study offers insights into the relationship between preeclampsia and hypertension among Kenyan women in the postpartum period, there are some limitations to consider in interpreting our results. First and foremost, this is a preliminary analysis using an incomplete dataset, as enrollment and data collection is still ongoing for our study. As such, the sample size included in this analysis was smaller than needed to make statistically significant inferences from our data. Loss to follow up rates were higher than anticipated, possibly in part due to effects of the COVID-19 pandemic, as many women returned to their rural village homes; further, anxiety about interaction with the health care system could have contributed more globally to lower than usual postpartum clinic follow up and possible undertreatment of

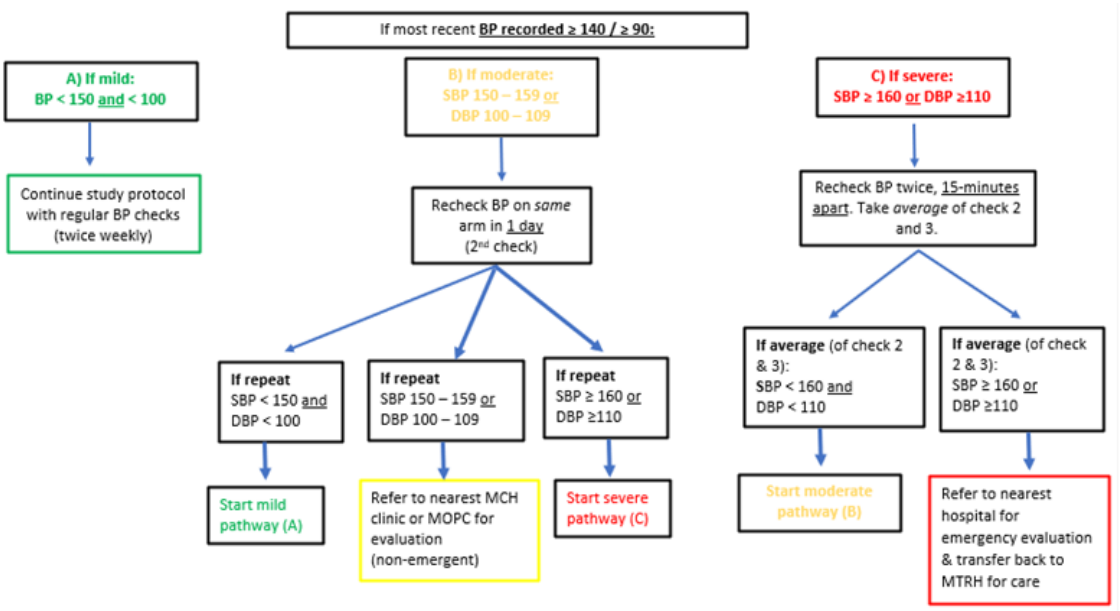
blood pressure, resulting in higher rates of hypertension at 6-month follow up. Beyond these unexpected challenges, we used a broad case definition to define preeclampsia, as established by the International Society for the Study of Hypertension in Pregnancy (ISSHP); while this definition provides a standard to make comparable between research studies, it differs from clinical definitions used by other societies (e.g. the American College of Gynecology). This broader classification could have included some participants who would not have otherwise been considered to have preeclampsia clinically, which would have biased towards the null.

Selection bias and recall bias also could have affected our results, given we relied on participant self-report for some demographic factors, past medical and obstetric history and health care utilization; in particular, lack of reliable gestational age ascertainment could have resulted in misclassification of variables such as preterm delivery. Similarly, it is possible that some women included may have had undiagnosed, chronic hypertension prior to pregnancy that went reported by participants, thus elevating rates of hypertension attributed to preeclampsia. Lastly, it is also possible that observer bias affected the fidelity and reporting of the values reported from the home blood pressure monitoring.

6. Conclusions

Despite these limitations, this is the first study to explore the relationship between preeclampsia and postpartum hypertension among women in Kenya. Our results illustrate that a high rate of women with preeclampsia develop chronic hypertension at 6-months following delivery, despite initial normalization of blood pressure within the first 6 weeks postpartum. Yet low rates of postpartum follow up care contribute to underdiagnosis and treatment of hypertension among this high-risk population. Further research is needed to explore effective strategies to link and retain women to longitudinal postpartum follow up care for early identification and management of chronic hypertension, to ultimately improve maternal health outcomes and prevent cardiovascular disease among women in SSA.

Appendix A. Clinical algorithm for postpartum blood pressure monitoring – study safety protocol



This algorithm was used by the research assistant (RA) to assess and guide need for referral to clinical care based on weekly home BP recordings. This algorithm was devised using a combination of international guidelines and recommendations for management of postpartum hypertension. This algorithm was followed if the *most recent* BP reported by the participant during weekly home BP calls was > 140mmHg / >90mmHg.

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