Persistent hypertension at 3 months postpartum among women with hypertensive disorders of pregnancy at a tertiary hospital in Southwestern Uganda

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BACKGROUND: Hypertension is a key contributor to the global epidemic of cardiovascular disease and is responsible for more deaths worldwide than any other cardiovascular risk factor. Hypertensive disorders of pregnancy, of which preeclampsia and eclampsia are the most common forms, have been shown to be a female-specific risk factor for chronic hypertension.

OBJECTIVE: This study aimed to determine the proportion and risk factors for persistent hypertension at 3 months after delivery among women with hypertensive disorders of pregnancy in Southwestern Uganda.

STUDY DESIGN: This was a prospective cohort study of pregnant women with hypertensive disorders of pregnancy admitted for delivery at Mbarara Regional Referral Hospital in Southwestern Uganda from January 2019 to December 2019; however, women with chronic hypertension were excluded from the study. The participants were followed up for 3 months after delivery. Participants with a systolic blood pressure of ≥140 mm Hg or a diastolic blood pressure of ≥90 mm Hg or receiving antihypertension therapy at 3 months after delivery were considered to have persistent hypertension. Multivariable logistic regression was used to determine independent risk factors associated with persistent hypertension.

RESULTS: A total of 111 participants with hypertensive disorders of pregnancy diagnosed at hospital admission were enrolled with a follow-up rate of 49% (54/111) at 3 months after delivery. Of these women, 21 of 54 (39%) had persistent hypertension 3 months after delivery. In the adjusted analyses, an elevated serum creatinine level (>106.08 μmol/L [≤1.2 mg/dL]) at admission for delivery was the only independent risk factor for persistent hypertension at 3 months after delivery (adjusted relative risk, 1.93; 95% confidence interval, 1.08–3.46; *P*=.03), controlling for age, gravidity, and eclampsia.

CONCLUSION: Approximately 4 of 10 women presenting with hypertensive disorders of pregnancy at our institution remained hypertensive 3 months after delivery. Innovative strategies are needed to identify these women and provide long-term care to optimize blood pressure control and reduce future cardiovascular disease after hypertensive disorders of pregnancy.

Key words: hypertension, hypertensive disorders of pregnancy, Mbarara, persistent hypertension, postpartum, preeclampsia, Uganda

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Introduction

Hypertension is a key driver of the global epidemic of cardiovascular disease and is responsible for more deaths worldwide than any other cardiovascular risk factor.[1] Globally, 7.6 million premature deaths are attributed to high blood pressure, and 80% of these deaths occurred in low- and middle-income countries (LMICs).[2] Evidence suggests that the burden of disease because of hypertension will increase by 60%, and most of the affected people will be in low-income countries.[2,3]

Hypertensive disorders of pregnancy (HDP), of which preeclampsia and eclampsia are the most common forms, are associated with chronic hypertension.[4] Preeclampsia or eclampsia affects at least 2% to 10% of all pregnant women[5,6] and accounts for the severe complications of pregnancy resulting in more than 70,000 maternal deaths per year, most of which are in LMICs.[7] Moreover, HDP are the second leading cause of mortality at Mbarara Regional Referral Hospital, a tertiary care hospital in Southwestern Uganda.[8]

HDP usually resolve within 3 months after delivery in most women.[9,10] Several studies from high-income countries have followed up women with HDP and demonstrated a long-term risk of developing chronic hypertension, diabetes mellitus, and cardiovascular disease[11,12] in affected women and their offspring.[1] Furthermore, studies[10,13–16] have clarified risk factors for persistent hypertension in women after the immediate postpartum period. However, studies of HDP from Uganda and other sub-Saharan African countries are limited by a short follow-up period of up to 6 weeks[15,17,18] and are lacking in laboratory tests.[14]

Therefore, we sought to describe persistent hypertension in a prospective cohort of women delivering in rural Uganda and determine the proportion of and risk factors for persistent hypertension at 3 months after delivery among women with HDP at Mbarara Regional Referral Hospital.

Materials and Methods

Study design and setting

This was a prospective cohort study of women with HDP admitted for delivery at Mbarara Regional Referral Hospital (MRRH) in Southwestern Uganda from January 2019 to December 2019. MRRH is a government-funded public hospital that performs approximately 9000 deliveries per year and is a teaching hospital for Mbarara University of Science and Technology. MRRH is a tertiary care facility that serves a population of 5 million people from 10 catchment districts in Southwestern Uganda.[19]

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Why was this study conducted?

This study aimed to determine the proportion of and risk factors for persistent hypertension at 3 months after delivery among women whose pregnancies were complicated by hypertensive disorders of pregnancy (HDP) in South-Western Uganda.

Key findings

Approximately 40% of women presenting with HDP remained hypertensive at 3 months after delivery. An elevated serum creatinine level at admission was noted to be an independent risk factor for persistent hypertension 3 months after delivery.

What does this add to what is known?

This study demonstrated that, in South-Western Uganda, a high proportion of women remain hypertensive after pregnancy-induced hypertension and that women with a high creatinine level in pregnancy are at an elevated risk of persistent hypertension after delivery.

Participants

Details of the study cohort have been described in a previous publication.[20] Briefly, our study population included all pregnant women, including those under the age of 18 years, at ≥20 weeks of gestation with new-onset hypertension in pregnancy diagnosed at admission. Normotensive women at admission who later developed elevated blood pressure during their labor course or postpartum course were not included in the study. We defined hypertension as 2 blood pressure readings with either a systolic blood pressure (SBP) of ≥140 mm Hg or a diastolic blood pressure of ≥90 mm Hg measured 4 hours apart. Women reporting a history of hypertension before pregnancy or before 20 weeks of gestation diagnosed by a healthcare provider or taking antihypertensive medication before pregnancy were considered to have chronic hypertension and excluded from participation.

To determine eligibility, all pregnant women admitted to the maternity ward of MRRH for delivery had a screening blood pressure measured by the research staff on admission. Women with elevated blood pressure at admission had a subsequent check 4 hours later. Women who met the inclusion criteria were consented and enrolled in the study, followed up during their delivery and on discharge, and followed up to 3 months after delivery. To obtain information on their sociodemographic background and medical history, the enrolled women were interviewed during their admission and were also invited back to the hospital 3 months after delivery for an interview and blood pressure measurement by trained study staff.

Variables and data sources

We classified enrolled women a priori as those with gestational hypertension, preeclampsia, preeclampsia with severe features, and eclampsia at admission. Gestational hypertension was defined as new-onset hypertension without proteinuria. Preeclampsia was defined as new-onset hypertension with proteinuria. The study team assessed for proteinuria (defined as ≥2+ protein) in all

enrolled women at admission using a dipstick of a midstream urine sample. Severe features of preeclampsia included any of the following: SBP of ≥160 mm Hg or DBP of ≥110 mm Hg, ≥3+ protein by dipstick, persistent epigastric pain, persistent headache, visual changes, or elevated serum creatinine level.[7,21] A blood sample was drawn at recruitment for study purposes and analyzed for renal (serum creatinine and urea levels) function and lipid profile. Women with preeclampsia who presented with, or developed, grand mal seizures and had no known existing or preexisting neurologic condition were defined as having eclampsia.[22]

Outcomes

The primary outcome was persistent hypertension at 3 months after delivery. This was defined as an SBP of ≥140 mm Hg or a DBP of ≥90 mm Hg or receiving antihypertensive medication at 3 months after delivery.

Other covariates of interest included sociodemographic factors: maternal age, marital status, level of education, and referral status (ie, women referred to MRRH from another health center for delivery). Medical history included HIV status (HIV-positive or HIV-negative result done within 3 months), known history of chronic kidney disease, and history of diabetes mellitus. Prepregnancy body mass index (BMI) was not available; however, we measured the weight and height at enrollment to the study and calculated the BMI (weight in kilograms divided by height in meters squared) from this measurement. Obstetrical data collected included gravidity, mode of delivery, gestational age at delivery (determined primarily using the last normal menstrual period [LNMP] or first-trimester obstetrical ultrasound scan if available; however, LNMP was unknown), and history of hypertension in previous pregnancies. This information was obtained using an interviewer-administered questionnaire during participant enrollment and a second questionnaire administered 3 months after delivery. Moreover, we performed the following laboratory tests with the following limits of normal set a priori: serum creatinine level (≤106.08 μmol/L [≤1.2 mg/dL]),[23] triglyceride level (2.48 mmol/L), total cholesterol level (5.89 mmol/L), low-density lipoprotein level (3.62 mmol/L), and high-density lipoprotein (HDL) level (0.91 mmol/L).[24]

Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at Mbarara University of Science and Technology, Department of Obstetrics and Gynecology. REDCap is a secure, Web-based software platform designed to support data capture for research studies.[25]

Data analysis

Maternal sociodemographic, medical, obstetrical, and laboratory tests were presented in frequency tables stratified by the primary outcome. Univariate analysis for the risk of persistent hypertension was performed using the chi-square test. Factors with a P value of ≤.2 in univariate analyses were considered for inclusion in the adjusted analysis. Multivariable logistic regression models were used to determine independent risk factors for persistent hypertension with their corresponding 95% confidence intervals (CIs).[26] A P value of <.05 was considered statistically significant. Data analysis was performed using Stata (version 15; StataCorp, College Station, TX).

Ethical consideration

The study procedures were approved by the Mbarara University Research Ethics Committee (September 7, 2018), Uganda National Council for Science and Technology (HS 2570), and Partners Healthcare Institutional Review Board (2019P001446). All study participants provided written informed consent.

Results

There were 9946 deliveries from January 2019 to December 2019. Of the participants included in the study, 169 presented with HDP, 14 were excluded because they had chronic hypertension, and 44 declined consent. Therefore, we enrolled 111 participants in this study. Of the participants, 5 (4.5%) had gestational hypertension, 2 (1.8%) had preeclampsia without severe features, 79 (71.2%) had preeclampsia with severe features, and 25 (22.5%) had eclampsia. There were 54 participants who attended the study visit 3 months after delivery. The proportion of women who were hypertensive at 3 months after delivery was 39% (21/54).

Most of the participants were <35 years of age (93/111 [84.8%]), had been referred from other health units (71/111 [64%]), and were at ≥34 weeks of gestation at delivery as shown in Table 1. Most of the participants delivered by cesarean delivery (70/111 [63.1%]) and had preeclampsia with severe symptoms (93/111 [83.8%]).

Baseline characteristics for most of the participants who were lost to follow-up at 3 months after delivery were not significantly different from those who attended the follow-up visit except for the district of origin (P<.01), DBP (P=.03), and HDL level (P<.01), as shown in Table 2.

An elevated serum creatinine level at admission was the only independent risk factor for persistent hypertension at 3 months after delivery (adjusted relative risk, 1.93; 95% CI, 1.08−3.46) after controlling for age, gravidity, and eclampsia, as shown in Table 3. No other considered factor was predictive of persistent postpartum hypertension.

Discussion

Principal findings

Our study showed that approximately 40% of women with an HDP admitted to this tertiary care facility in rural Uganda remained hypertensive at 3 months after delivery, which was more likely among women with elevated creatinine levels at admission.

Results

Here, the proportion of women remaining hypertensive at 3 months after delivery was comparable with the proportion of women with preeclampsia delivering at Mulago National Referral Hospital in Uganda (34%).[14] However, the proportion of persistent hypertension was higher than that found in

TABLE 1
Participant characteristics and association with persistent postpartum hypertension

Characteristics		Total (N=111), n (%)	Normotensive at 3 mo (n=33), n (%)	Persistent hypertension at 3 mo (n=21), n (%)	*P* value
Age (y)	<35	93 (83.8)	28 (84.8)	16 (76.2)	.49
	≥35	18 (16.2)	5 (15.2)	5 (23.8)	
Marital status	Single	7 (6.3)	2 (6.1)	1 (4.8)	.84
	Married	104 (93.7)	31 (93.9)	20 (95.2)	
Level of education	Primary and below	55 (49.6)	13 (39.4)	10 (47.6)	.55
	Secondary and above	56 (50.4)	20 (60.6)	11 (52.4)	
Gravidity	Primigravida	40 (36.0)	16 (48.5)	4 (19.1)	.03
	Multigravida	71 (64.0)	17 (51.5)	17 (80.9)	
History of HDP in a previous pregnancy	No	97 (87.4)	31 (93.9)	18 (85.7)	.31
	Yes	14 (12.6)	2 (6.1)	3 (14.3)	
Gestational age at delivery (n=103)	≥34	66 (64.1)	22 (66.7)	12 (57.1)	.48
	<34	37 (35.9)	11 (33.3)	9 (42.9)	
Mode of delivery	Vaginal delivery	41 (36.9)	11 (33.3)	9 (42.9)	.48
	Cesarean delivery	70 (63.1)	22 (66.7)	12 (57.1)	
HIV status	Positive	7 (6.3)	4 (12.1)	1 (4.8)	.36
	Negative	104 (93.7)	29 (87.9)	20 (95.2)	
Body mass index at admission (n=109)	<25	35 (32.1)	10 (30.3)	7 (33.3)	.82
	≥25	74 (67.9)	23 (69.7)	14 (66.7)	
Referral from another facility	Not referred	40 (36.0)	13 (39.4)	8 (38.1)	.92
	Referred	71 (64.0)	20 (60.6)	13 (61.9)	
Preeclampsia with severe features at admission	Asymptomatic	18 (16.2)	4 (12.1)	3 (14.3)	.82
	Symptomatic	93 (83.8)	29 (87.9)	18 (85.7)	
Severe systolic blood pressure at admission (mm Hg)	<160	56 (50.4)	16 (48.5)	7 (33.3)	.27
	≥160	55 (49.6)	17 (51.5)	14 (66.7)	
Severe diastolic blood pressure at admission (mm Hg)	<110	61 (54.9)	16 (48.5)	8 (38.1)	.45
	≥110	50 (45.1)	17 (51.5)	13 (61.9)	
Proteinuria (≥2+ by urine dipstick) at admission	Absent	36 (32.4)	9 (27.3)	8 (38.1)	.40
	Present	75 (67.6)	24 (72.7)	13 (61.9)	
Eclampsia	No	86 (77.5)	24 (72.7)	19 (90.5)	.11
	Yes	25 (22.5)	9 (27.3)	2 (9.5)	
Serum creatinine level at admission (μmol/L)	≤106.08	91 (82.0)	29 (87.9)	14 (66.7)	.06
	>106.08	20 (18.0)	4 (12.1)	7 (33.3)	
Total cholesterol level (mmol/L)	Normal	96 (86.5)	28 (84.9)	18 (85.7)	.93
	Elevated	15 (13.5)	5 (15.1)	3 (14.3)	
Triglyceride level (mmol/L)	Normal	98 (88.3)	28 (84.9)	18 (85.7)	.93
	Elevated	13 (11.7)	5 (15.1)	3 (14.3)	
LDL level (mmol/L)	Normal	104 (93.7)	31 (93.9)	21 (100)	.25
	Elevated	7 (6.3)	2 (6.1)	0 (0)	
HDL level (mmol/L)	Normal	87 (78.4)	30 (90.9)	19 (90.5)	.96
	Low	24 (21.6)	3 (9.1)	2 (9.5)	

HDL, high-density lipoprotein; *HDP*, hypertensive disorders of pregnancy; *LDL*, low-density lipoprotein.

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TABLE 2
Comparison between participants who attended and those who missed the follow-up visit at 3 months after delivery

Characteristics		Total (N=111), n (%)	Attended visit (n=54), n (%)	Missed visit (n=57), n (%)	*P* value
Age (y)	<35	93 (83.8)	44 (81.5)	49 (86.0)	.52
	≥35	18 (16.2)	10 (18.5)	8 (14.0)	
Marital status	Single	7 (6.3)	3 (5.6)	4 (7.0)	.75
	Married	104 (93.7)	51 (94.4)	53 (93.0)	
Level of education	Primary and below	55 (49.6)	23 (42.6)	32 (56.1)	.15
	Secondary and above	56 (50.4)	31 (57.4)	25 (43.9)	
District of origin	Not within Mbarara	48 (43.2)	16 (29.6)	32 (56.1)	<.01
	Within Mbarara	63 (56.8)	38 (70.4)	25 (43.9)	
Gravidity	Primigravida	40 (36.0)	20 (37.0)	20 (35.1)	.83
	Multigravida	71 (64.0)	34 (63.0)	37 (64.9)	
History of HDP in a previous pregnancy	No	97 (87.4)	49 (90.7)	48 (84.2)	.30
	Yes	14 (12.6)	5 (9.3)	9 (15.8)	
Gestational age at delivery (n=103)	≥34	66 (64.1)	34 (63.0)	32 (65.3)	.80
	<34	37 (35.9)	20 (37.0)	17 (34.7)	
Mode of delivery	Vaginal delivery	41 (36.9)	20 (37.0)	21 (36.8)	.98
	Cesarean delivery	70 (63.1)	34 (63.0)	36 (63.2)	
HIV status	Positive	7 (6.3)	5 (9.3)	2 (3.5)	.21
	Negative	104 (93.7)	49 (90.7)	55 (96.5)	
Body mass index at admission (n=109)	<25	35 (32.1)	17 (31.5)	18 (32.7)	.89
	≥25	74 (67.9)	37 (68.5)	37 (67.3)	
Referral from another facility	Not referred	40 (36.0)	21 (38.9)	19 (33.3)	.54
	Referred	71 (64.0)	33 (61.1)	38 (66.7)	
Preeclampsia with severe features at admission	Asymptomatic	18 (16.2)	7 (13.0)	11 (19.3)	.37
	Symptomatic	93 (83.8)	47 (87.0)	46 (80.7)	
Severe systolic blood pressure at admission (mm Hg)	<160	56 (50.4)	23 (42.6)	33 (57.9)	.11
	≥160	55 (49.6)	31 (57.4)	24 (42.1)	
Severe diastolic blood pressure at admission (mm Hg)	<110	61 (54.9)	24 (44.4)	37 (64.9)	.03
	≥110	50 (45.1)	30 (55.6)	20 (35.1)	
Proteinuria (≥2+ by urine dipstick) at admission	Absent	36 (32.4)	17 (31.5)	19 (33.3)	.84
	Present	75 (67.6)	37 (68.5)	38 (66.7)	
Eclampsia	No	86 (77.5)	43 (79.6)	43 (75.4)	.59
	Yes	25 (22.5)	11 (20.4)	14 (24.6)	
Serum creatinine level at admission (μmol/L)	≤106.08	91 (82.0)	43 (79.6)	48 (84.2)	.53
	>106.08	20 (18.0)	11 (20.4)	9 (15.8)	
Total cholesterol level (mmol/L)	Normal	96 (86.5)	46 (85.2)	50 (87.7)	.70
	Elevated	15 (13.5)	8 (14.8)	7 (12.3)	
Triglyceride level (mmol/L)	Normal	98 (88.3)	46 (85.2)	52 (91.2)	.32
	Elevated	13 (11.7)	8 (14.8)	5 (8.8)	
LDL level (mmol/L)	Normal	104 (93.7)	52 (96.3)	52 (91.2)	.27
	Elevated	7 (6.3)	2 (3.7)	5 (8.8)	
HDL level (mmol/L)	Normal	87 (78.4)	49 (90.7)	38 (66.7)	<.01
	Low	24 (21.6)	5 (9.3)	19 (33.3)	

HDL, high-density lipoprotein; *HDP*, hypertensive disorders of pregnancy; *LDL*, low-density lipoprotein.

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TABLE 3
Risk factors for persistent hypertension at 3 months after delivery

Characteristic		Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Age (y)	<35	1		1	
	≥35	1.38 (0.66–2.86)	.42	0.96 (0.45–2.08)	.93
Gravidity	Primigravida	1		1	
	Multigravida	2.50 (1.00–6.39)	.03	2.19 (0.87–5.48)	.09
Eclampsia	No	1		1	
	Yes	0.40 (0.11–1.51)	.11	0.40 (0.11–1.38)	.15
Serum creatinine level at admission (μmol/L)	≤106.08	1		1	
	>106.08	1.95 (1.05–3.63)	.06	1.93 (1.08–3.46)	.03

CI, confidence interval; *OR*, odds ratio.

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Cameroon (28.0%),[13] Cuba (27.8%),[27] or Egypt (12.1%).[28] The differences in study settings and the severity of preeclampsia among the participants studied could, in part, explain our high rate of persistent hypertension.

An elevated serum creatinine level at admission was the only factor associated with persistent hypertension at 3 months after delivery in adjusted models, which is similar to what was found in other studies.[15,23,27] This could be due to endothelin, a potent endogenous vasoconstrictor peptide produced by endothelial cells, which may result in endothelial dysfunction. Persistently elevated endothelin levels are associated with diminished creatinine clearance.[29] The renal insult secondary to vasospasm might lead to ischemic injury to the kidney and triggering of the renin-aldosterone-angiotensin feedback.[30] This might be one of several potential factors involved in the pathogenesis of chronic hypertension among these women with preeclampsia. An elevated creatinine level as a known marker of chronic kidney disease may reflect in women who had undiagnosed asymptomatic kidney disease or chronic hypertension before pregnancy or kidney injury after preeclampsia. In an observational study of women with preeclampsia, women with elevated serum creatinine levels have had hypertension in the previous pregnancy.[31] Therefore, it is not clear whether these are women who could have had undiagnosed hypertension or kidney disease at the start of their current pregnancy that remained hypertensive at follow-up after delivery as chronic hypertension and kidney disease are risk factors for persistent hypertension. Moreover, it is plausible that chronic hypertension and preeclampsia may have similar or related risk factors.

Clinical implications

Our findings have implications for healthcare delivery in this population. The high proportion of women with hypertension at 3 months after delivery indicates a need for new models of care in this region with longer follow-up periods, linkage to long-term hypertension clinics for care, and prenatal care visits before subsequent pregnancies. This linkage to care will be important not only to optimize preconception and prenatal care in subsequent pregnancies, with improved maternal and perinatal outcomes, but also to prevent or mitigate long-term cardiovascular disease. In addition, consideration should be given to measuring serum creatinine levels at admission in women with a hypertensive disorder and longer postpartum follow-up for those with elevated serum creatinine levels. Given the small sample size in this study, further research to understand the risk factors for persistent hypertension and the use of these risk factors in the decision-making for the length of follow-up is needed.

Research implications

Larger prospective and multicenter studies should be conducted to clarify other possible risk factors for persistent hypertension in this setting with attention given to how to implement follow-up of women after delivery and to ensure linkage to long-term care for those with an established diagnosis of chronic hypertension and preventative care for those planning future pregnancies. Moreover, studies should be conducted to determine the barriers and facilitators of postpartum follow-up and interventional studies to enhance postpartum follow-up.

Strengths and limitations

Our study strengths included a prospective study design, a clear assignment of HDP, a follow-up to 3 months after delivery, and the performance of laboratory tests.

However, we had some limitations. Loss to follow-up was high at 12 weeks. We assessed for differences in those lost to follow-up as reported, but there may be other unmeasured systematic differences in those lost to follow-up that may influence the incidence of persistent hypertension found in this study. Our relatively small sample size limited our multivariable analysis; therefore, other risk factors may exist that were

not clarified in this study. We did not measure liver enzymes and platelet counts. Therefore, we were not able to determine whether the condition of hemolysis, elevated liver enzymes, and low platelet count is a risk factor.

Conclusions

Nearly 4 of 10 women with an HDP at delivery remained hypertensive beyond the immediate postpartum period, particularly women admitted with elevated serum creatinine levels. There is a need for longer follow-up of women whose pregnancies have been complicated by hypertension. Larger prospective studies in sub-Saharan Africa should be instituted to understand the long-term cardiovascular health of these women. ■

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