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Cardiovascular Outcome Related to Pregnancies Complicated by Preeclampsia in Three Hospitals in Yaounde

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Abstract

Introduction: Preeclampsia is associated with an increased lifetime-risk of cardiovascular disease, possibly through the occurrence of persistent hypertension, renal diseases, heart failure, and other cardiovascular events shortly or years after preeclampsia. The main aim of this study was to evaluate the cardiovascular outcome related to pregnancies complicated by preeclampsia in Yaounde (Cameroon). We conducted a cross-sectional analytical study with prospective and retrospective collection of data over a period of seven months (November 18, 2021 to June 01, 2022) of women with a pregnancy complicated by preeclampsia between January 2015 and June 2021 in three hospitals in Yaounde. We included all women with a confirmed history of preeclampsia and having given their consent for the study whereas, women with pre-pregnancy cardiovascular comorbidities (chronic hypertension, cardiac disease, chronic kidney disease or diabetes mellitus), those pregnant during our study period and those less than 6months postpartum were excluded. Hypertension on Ambulatory Blood Pressure Monitoring (ABPM) was considered the dependent variable. Descriptive statistics were performed to express participant's characteristics. Univariate and multivariate logistic regressions were conducted and odds ratio calculated with their 95% confidence interval to identify independent associated risk factors. Potential confounding factors were identified using chi-square tests of Pearson. We included 113 women, with 46 (40.7%) having persistent hypertension, with the most represented hypertensive phenotypes being sustained hypertension 30 (26.5%) and 77 (68.1%) had a disadvantageous dipping pattern. Factors found to be associated

to persistent hypertension were: family history of hypertension (OR = 5.33 (1.20 - 23.60); p = 0.03), severe PE at diagnosis (OR = 13.19 (1.67 - 104.28); p = 0.01) and preeclampsia in prior pregnancies (OR = 4.99 (1.11 - 22.36); p = 0.04). The cardiovascular outcomes related to preeclampsia in our study were; Persistent hypertension (about two in five women), left ventricular hypertrophy and heart failure. Ultimately, women with history of preeclampsia should be screened for cardiovascular risk factors and offered treatment in order to reduce cardiovascular morbidity and mortality.

Keywords

Cardiovascular Disease, Outcomes, Preeclampsia, Yaounde

1. Introduction

Cardiovascular disease (CVD) is currently the main cause of death among men and women worldwide [1]. Although women develop CVD on average 10 - 15 years later than men, some cardiovascular risks factors (CVRF) are already present at younger age [1]. One of these CVRF is a hypertensive disease in pregnancy (HDP) such as preeclampsia (PE). PE is defined as the presence of new-onset hypertension (≥140 mmHg/90 mmHg) appearing after 20 weeks gestation in previously normotensive women and resolving completely by the 6th week of postpartum associated with proteinuria and/or other end-organ damage [2]. Hence Preeclampsia is a life-threatening multi-system disorder of pregnancy that generally affects all systems particularly the cardiovascular system. Preeclampsia occurs in approximately 2% - 8% of pregnancies and is one of the leading cause of maternal morbidity and mortality worldwide; responsible for about 50 000 maternal death each year [3]. According to the World Health Organization (WHO), 16% of maternal deaths in sub-Saharan Africa are attributable to HDP, with PE being the leading cause with an incidence ranging from 5% to 10% [4]. A hospital-based study in Cameroon revealed HDP being the top two (21.2%) cause of maternal death after hemorrhage with preeclampsia and Eclampsia predominantly representing 11.1% [4]. Current estimate of preeclampsia reports a prevalence of 3.8% in the United State of America (USA) [5]. Not surprisingly, the rate of PE is high in developing countries due to lack of prenatal care, in sub-Saharan Africa, preeclampsia's prevalence is 25%, making it a real public health problem [3]. An in-hospital study reported by Nkwabong *et al.* in 2021 in Cameroon reveals a prevalence of 7% [6]. Even though delivery of the placenta is considered the cure for preeclampsia, the traditional expectation is that hypertension resolves by the end of the puerperium, a period generally defined as 6 weeks after delivery [7]. However, emerging evidence suggests that hypertension may persist beyond 6 weeks postpartum which is considered as persistent hypertension [8]. This is due to a combination of two factors. Firstly, women with preeclampsia have a lifetime in-

creased risk of future chronic hypertension, cardiovascular disease risk factors and cardiovascular diseases due to underlying vascular (re) constitution or preeclampsia related vascular damage [7]. Secondly, women with previous undiagnosed chronic hypertension are misclassified during pregnancy as gestational hypertension, and their persisting hypertension beyond the postpartum erroneously considered as new onset chronic hypertension following preeclampsia [7]. Although blood pressure in patients with preeclampsia return to normal values in the months following delivery, women with a history of preeclampsia experiences twice the rate of CVD events, a two-to four- fold increase risk of chronic hypertension, 80% increased rate of type 2 diabetes, 30% increased rate of elevated cholesterol and 30% increased rate of renal disturbance compared to women with normotensive pregnancies [9]. Two hospital base studies in Cameroon revealed the prevalence of persistent hypertension at 32.6% and 23.53% [3] [10] respectively. Previous studies have identified a number of associated factors for persistent hypertension after preeclampsia and these include; severe hypertension and/or early onset preeclampsia, recurrent preeclampsia and advance maternal age [3] [10] [11]. In order to improve the quality of life of women with a history of preeclampsia and understand the other possible comorbidities they can develop, we decided to study the cardiovascular outcome related to pregnancies complicated by preeclampsia in three hospitals in Yaounde (Cameroon).

2. Methods

2.1. Study Design and Setting

This was a cross-sectional analytical study with retrospective and prospective collection of data including women with a history of preeclampsia between January 2015 and June 2021 with a written consent form of participation and a complete medical file. We excluded Women with a cardiovascular comorbidity before pregnancy (chronic hypertension, cardiopathy, kidney disease, diabetes), Women pregnant during our study period or on postpartum less than 6 months.

The study was conducted in three main obstetrical and gynecologic units of Yaounde; The Yaounde Central Hospital, the Yaounde Gyneco-Obstetric and Pediatric Hospital and the Yaounde University Teaching Hospital. Participants were recruited from the 18th of November 2021 to the 1st of June 2022.

2.2. Sample Size Estimation

The sample size was estimated to 90 using the Fleiss formula, the expected prevalence of family history of hypertension among women with persistent hypertension (80%) and among normotensive women to be (61.3%) [3].

2.3. Data Collection

Ethical approvals were obtained from the institutional committee review board of the Faculty of Medicine and Biomedical Sciences of the University of Yaounde I,

and administrative authorizations were obtained from all participating hospitals. Participants were identified through their medical records; we identified 714 cases of women with preeclampsia. 378 records were complete, and only 321 had available addresses of these patients, 229 responded favorably to our call, we contacted them by phone and invited them to participate in the study, 163 were included and only 113 were retained. Informed consent was obtained from each participant before inclusion. Data were collected using a data collection sheet.

It was first an interview to collect information on the past medical history, including cardiovascular risk factors (preeclampsia/eclampsia, hypertension, diabetes), obstetrical history (past history of; miscarriage, preeclampsia/Eclampsia, number of years of postpartum, gravidity, parity, new paternity). Afterward, we performed a physical examination to measure weight and height for body mass index (BMI) calculation, blood pressure (measured according to European Society of Hypertension guidelines using a validated automated device (OMRON®MX2 Basic, OMRON HEALTHCARE, INC. Bannockburn, Illinois 60015.CHINA), We considered the average of the last two values of each occasion), and a complete physical exam, Waist circumference, SPO2 (%), pulse rate (bpm), respiratory rate (cpm), headache, visual impairment, chest pain, dyspnea.

ABPM (Ambulatory Measure of Blood Pressure) was performed using a validated automated oscillometric device (OSCAR 2; SunTech Medical; Morrisville NC, USA). Recordings were obtained over a minimum 24-hour period, with measurements taken every 20 minutes during daytime (06:00-22:00) and every 30 minutes during night-time (22:00-06:00). A recording was considered valid if at least 70% of scheduled measurements were successful, including a minimum of 14 valid daytime readings and 7 valid night-time readings, in accordance with the 2018 ESC/ESH Guidelines. Persistent hypertension was defined as a 24-hour mean ≥130/80 mmHg, a daytime mean ≥135/85 mmHg, or a night-time mean ≥120/70 mmHg. The nocturnal dipping pattern was classified as: dipper (10% - 20% nocturnal fall in BP), extreme dipper (>20% fall), non-dipper (<10% fall), and riser (higher night-time than daytime BP).

Echocardiography and electrocardiography were performed and Heart failure was diagnosed according to the 2016 ESC Heart Failure Guidelines, requiring: 1- symptoms and/or signs of heart failure (dyspnoea, fatigue, ankle oedema); 2- structural and/or functional cardiac abnormality on echocardiography; and 3- elevated natriuretic peptides where available. Most cases identified in this study had heart failure with preserved ejection fraction (HFpEF), defined as left ventricular ejection fraction ≥50% with evidence of diastolic dysfunction or elevated filling pressures.

At the end of the interview, blood sampling was collected for lipid profile, serum creatinine, fasting glucose level and uric acid levels.

To address the heterogeneity introduced by the wide range of time elapsed since index delivery (6 months to 7 years), a sensitivity analysis was performed stratifying participants into two groups: those assessed ≤2 years postpartum and those

assessed >2 years postpartum. The prevalence of persistent hypertension was compared between these groups using Pearson's chi-square test.

2.4. Operational Terms

Hypertension on ABPM is ≥130/80 mmHg over 24 hours, ≥135/85 mmHg for daytime average and ≥120/70 mmHg for the night-time average。

Left Ventricular Hypertrophy was considered if Left Ventricular Mass index > 95 g/m^2.

The criteria for left ventricular hypertrophy (LVH) was any Cornel voltage (Sv3 + Ravl) ≥ 20 mm which is an indirect electrocardiographic sign of chronic hypertension.

2.5. Statistical Analysis

All the data collected were analyzed using the software SPSS version 23.0. Quantitative variables are presented with their mean and standard deviation (SD). Qualitative variables were expressed as counts and proportions. The comparison of means was made using the Student's T-test. Fisher's test was used to compare proportions. Multivariable logistic regression was performed to identify independent factors associated with persistent hypertension. Variables entered into the model were those with $p < 0.20$ on univariable analysis and those considered clinically relevant a priori, including: age ≥ 35 years, family history of hypertension, prior preeclampsia, severity of PE at diagnosis, multiparity, BMI, and LVH on ECG. To maintain parsimony given the 46 hypertensive cases (approximately 1 variable per 10 events), a stepwise backward elimination procedure was used, retaining only variables that remained significant at $p < 0.05$ after adjustment. Adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) are reported.

Serum creatinine and eGFR were not entered simultaneously into the regression model due to collinearity.

3. Results

During this study, we identified 714 cases of women with prior preeclampsia. 378 records were complete, and only 321 had available addresses of these patients. We successfully contacted 229 women, of whom 34 refused to participate in the study, 28 travelled and 4 had died (three strokes and one unknown cause). Of the 163 women included, 50 were excluded of whom 7 with superimposed preeclampsia, 31 pregnant women and 12 on postpartum less than 6 months. Finally, 113 women were retained for our study (**Figure 1**).

3.1. Baseline Characteristics of the Study Population

Distribution of study population according to hospitals

The distribution of the study population by hospitals in which they were enrolled is displayed in the figure below. Most of the participants were enrolled from the YCH (39.8%) and YGOPH (35.4%) (**Figure 2**).

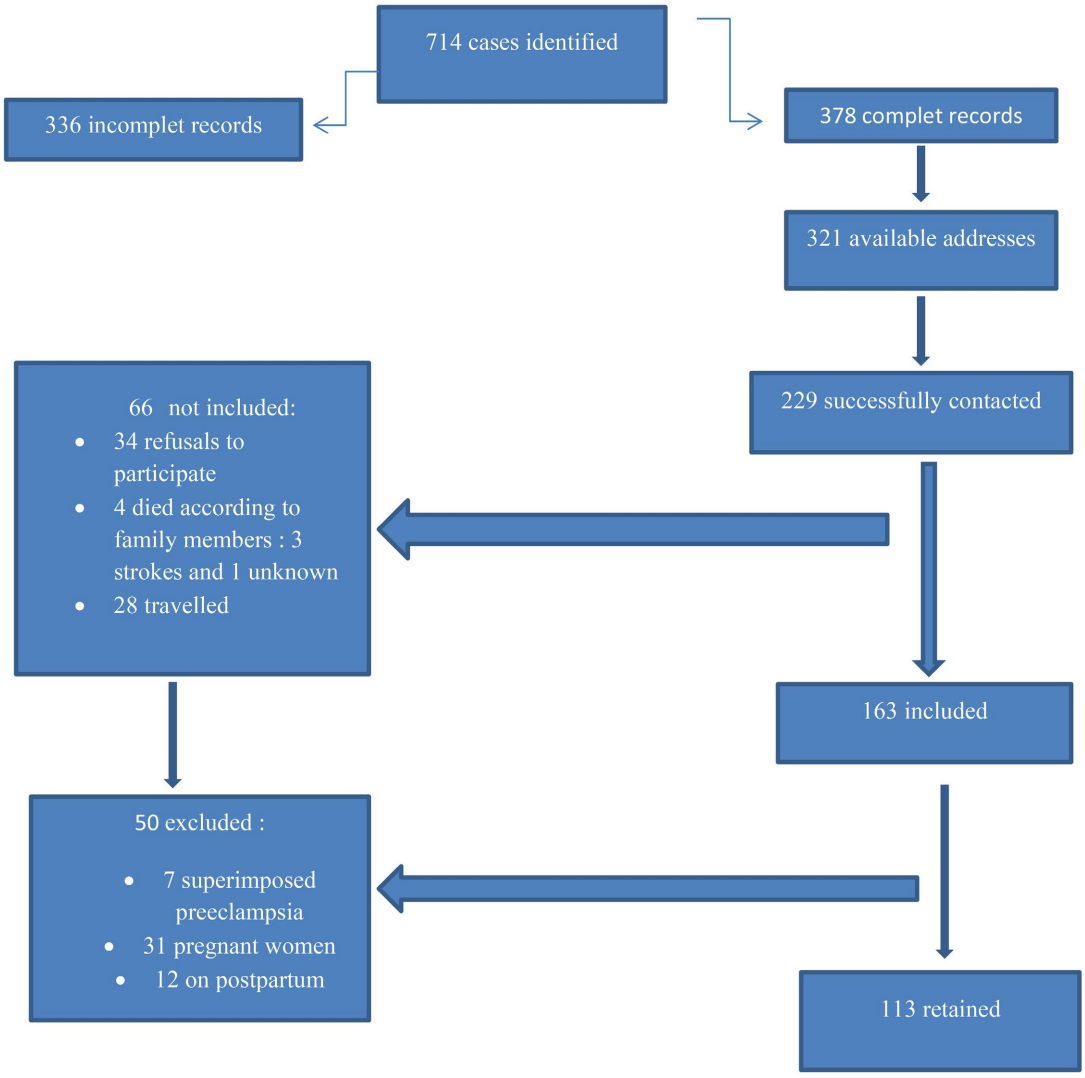

Figure 1. Flow chart of the study population.

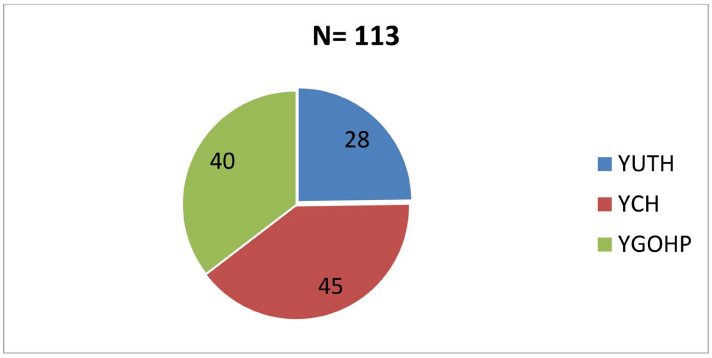

Figure 2. Distribution of study population according to hospitals.

Sociodemographic characteristic of the study population

Table 1 below shows that, in our study population, ages ranged from 17 to 43 years. The mean age was 29.78 ± 6.19 years. The most represented age group was

that of 26 to 35 years. Thirty-four-point five percent (34.5%) of our participant were from the centre region. Sixty-one point one (61.1%) were married; almost all lived in urban areas (86.7%). Majority were schooled (higher: 43.4% and secondary: 38.9%). Forty-seven point eight (47.8%) were workers and 71.7% earned a low monthly revenue.

Table 1. Sociodemographic characteristics of women after preeclampsia in Yaounde.

Variables (N = 113)	Frequency (n)	Percentage (%)
Age group		
[15 - 25[	29	25.7
[25 - 35[	65	57.5
[35 - 45[	19	16.5
≥ 45	-	-
Region of origin		
Adamawa	14	12.4
Center	39	34.5
Others*	31	27.4
West	29	25.7
Marital status		
Divorced	2	1.8
Married	69	61.1
Single	42	37.2
Residence		
Rural	10	8.9
Semi-urban	5	4.4
Urban	98	86.7
Occupation		
Housewives	40	35.4
Student	19	16.8
Workers	54	47.8
Education		
Higher	49	43.4
Primary	20	17.7
Secondary	44	38.9
Religion		
Christian	78	69
Muslim	35	31
Monthly revenue		
High	9	8
Low	81	71.7
Medium	23	20.4

Others*: north, far north, North West, south, south west, littoral and east.

Proportion of persistent hypertension after preeclampsia

We had 113 women who had pregnancies complicated by preeclampsia in our different hospital giving us a total proportion of 31% for office blood pressure measurement and 40.7% at ABPM (Table 2).

Table 2. Proportion of persistent hypertension after preeclampsia in Yaounde.

Variable (N = 113)	Frequency (n)	Percentage (%)
Office BP	35	31%
ABPM	46	40.7%

BP: blood pressure ABPM: ambulatory blood pressure monitoring

The mean interval between index preeclampsia and study inclusion was 2.25 ± 1.48 years (range: 0.5 - 7.0 years). In the sensitivity analysis stratifying by time since delivery, the prevalence of persistent hypertension was 43.8% in women assessed ≤2 years postpartum and 36.7% in those assessed >2 years postpartum (p = 0.45), suggesting that the pooled prevalence estimate was not substantially driven by time since delivery.

3.2. Blood Pressure Profile of Women after Preeclampsia

Blood pressure phenotypes at ABPM

The most represented hypertensive phenotypes were sustained hypertension 30 (26.5%) followed by masked hypertension 16 (14.2%) (Table 3).

Table 3. Blood pressure phenotypes of women after preeclampsia in Yaounde.

Variable (N = 113)	Frequency (n)	Percentage (%)
Phenotypes		
Sustained hypertension	30	26.5
Masked hypertension	16	14.2
White-coat hypertension	03	2.7

Frequency of hypertension

Hypertension was most of the time permanent 29 (63%) (Table 4).

Table 4. Frequency of hypertension in women after preeclampsia at Yaounde

Variable (N = 46)	Frequency (n)	Percentage (%)
Frequency		
Permanent	29	63
Paroxystic	17	37

Type of hypertension in women after preeclampsia in Yaounde

More than half of the hypertensive women had both type of hypertension 38

(82.6%) (Table 5).

Table 5. Type of hypertension in women after preeclampsia at Yaounde.

Variable (N = 46)	Frequency (n)	Percentage (%)
Type		
Both	38	82.6
Diurnal	6	13
Nocturnal	2	4.4

Dipping pattern, adrenergic component and pulse pressure of our study population

Majority of women (61.9%) in our study population had an adrenergic component involved at ABPM. Almost all had a normal pulse pressure (Table 6).

Table 6. Adrenergic component and pulse pressure of our study population.

Variable (N = 113)	Frequency (n)	Percentage (%)
Adrenergic component		
Yes	43	38.1
No	70	61.9
Pulse Pressure		
High	16	14.2
Normal	97	85.8

Table 7 below shows that, more than half of our study population were non-dipper (68.1%), and followed by dipper (31%).

Table 7. Dipping pattern of women after preeclampsia in Yaounde.

Variable (N = 113)	Frequency (n)	Percentage (%)
Dipping pattern		
Dipper	35	31
Extreme dipper	1	0.9
Non-dipper	77	68.1

3.3. Comparison of the Socio-Demographic Profile of Women with Persistent Hypertension vs Normotensive Women after Preeclampsia in Yaounde

Comparison between ages

In our study population, ages ranged from 17 to 43 years. The mean age was 29.78 ± 6.19 years (32.37 ± 5.63 for hypertensive women and 28 ± 5.95 for nor-

motensive women). The most represented age group was that of 26 to 35 years (Table 8).

Table 8. Age comparison between hypertensive and normotensive women afterpreeclampsia.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%s)	No n (%)	Total N (%)	
Age groups				**0.002**
[15 - 25[	5 (10.9)	24 (35.8)	29 (25.7)	
[25 - 35[	26 (56.5)	39 (58.2)	65 (57.5)	
[35 - 45[	15 (32.6)	4 (6)	19 (16.8)	
≥ 45	-	-	-	

Comparison between region of origin, residence and marital status among hypertensive and normotensive women

The region of origin and the marital status were significant with persistent hypertension (Table 9).

Table 9. Comparison between region of origin, residence and marital status among hypertensive and normotensive women.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%s)	No n (%)	Total N (%)	
Region of origin				**0.048**
Adamawa	5 (10.9)	9 (13.4)	14 (12.4)	
Center	10 (21.7)	29 (43.3)	39 (34.5)	
Others	14 (12.4)	17 (25.4)	31 (27.4)	
West	17 (37.0)	9 (13.4)	29 (25.7)	
Marital status				
Divorced	0 (0.0)	2 (3.0)	2 (1.8)	**0.019**
Married	35 (76.1)	34 (50.7)	69 (61.1)	
Single	11 (23.9)	31 (46.3)	42 (37.2)	
Residence				
Rural	4 (8.7)	6 (8.9)	10 (8.8)	0.187
Semi-urban	4 (8.7)	1 (1.5)	5 (4.4)	
Urban	38 (82.6)	60 (89.6)	98 (86.7)	

Comparison between educational level, monthly revenue and religion among hypertensive and normotensive women

Other characteristics like educational level, monthly revenue and religion were distributed in a homogenic manner, hence not significant.

Hypertensive and normotensive women (Table 10)

Table 10. Comparison between educational level, monthly revenue and religion among hypertensive and normotensive women.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%s)	No n (%)	Total N (%)	
Occupation				0.053
Housewives	18 (39.1)	22 (32.8)	40 (35.4)	
Student	3 (6.5)	16 (23.9)	19 (16.8)	
Workers	25 (54.3)	29 (43.3)	54 (47.8)	
Educational level				0.747
Higher	18 (39.1)	31 (46.3)	49 (43.3)	
Primary	9 (19.6)	11 (16.4)	20 (17.7)	
Secondary	19 (41.3)	25 (37.3)	44 (38.9)	
Religion				0.605
Christian	33 (71.7)	45 (67.2)	78 (69.0)	
Muslim	13 (28.3)	22 (32.8)	35 (31.0)	
Monthly revenue				0.198
High	4 (8.7)	5 (7.5)	9 (8.0)	
Low	29 (63.0)	52 (77.6)	81 (71.7)	
Medium	13 (28.3)	10 (14.9)	21 (18.6)	

Comparison of the reproductive characteristics among hypertensive and normotensive women

Table 11. Comparison of the reproductive characteristics among hypertensive and normotensive women.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%s)	No n (%)	Total N (%)	
Parity				**<0.001**
Multiparous	20 (45.5)	4 (6.0)	24 (21.2)	
Nulliparous	10 (21.7)	31 (46.3)	41 (36.3)	
Pauciparous	8 (17.4)	21 (31.3)	29 (25.7)	
Primiparous	8 (17.4)	11 (9.7)	19 (16.8)	
Miscarriage				0.202
Yes	22 (47.8)	24 (35.8)	46 (40.7)	
No	24 (52.2)	43 (64.2)	67 (59.3)	
Prematurity				0.515
Yes	1 (2.2)	3 (4.5)	4 (3.5)	
No	45 (97.8)	64 (95.5)	109 (96.5)	
Prior preeclampsia				**<0.001**
Yes	26 (56.5)	5 (7.5)	31 (27.4)	
No	20 (43.5)	62 (92.5)	82 (72.6)	

Table 11 above shows that gestation (p = 0.025), parity (p < 0.001) and prior preeclampsia (p < 0.001), were significantly associated with persistent hypertension. The mean parity was 1.81 ± 1.87 weeks (2.52 ± 1.918 for hypertensive women and 1.31 ± 1.68 for normotensive women). Parity ranged from zero to eight.

3.4. Comparison of Past History among Hypertensive and Normotensive Women

Comparison of personal past history among hypertensive and normotensive women

Table 12 below shows that medical and environmental past history variables are evenly distributed among the population. Hence not significantly associated to persistent hypertension.

Table 12. Comparison of personal past history among hypertensive and normotensive women. Hypertensive and normotensive women.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%s)	No n (%)	Total N (%)	
Occupation				
Housewives	18 (39.1)	22 (32.8)	40 (35.4)	0.053
Student	3 (6.5)	16 (23.9)	19 (16.8)	
Workers	25 (54.3)	29 (43.3)	54 (47.8)	
Educational level				
Higher	18 (39.1)	31 (46.3)	49 (43.3)	0.747
Primary	9 (19.6)	11 (16.4)	20 (17.7)	
Secondary	19 (41.3)	25 (37.3)	44 (38.9)	
Religion				
Christian	33 (71.7)	45 (67.2)	78 (69.0)	0.605
Muslim	13 (28.3)	22 (32.8)	35 (31.0)	
Monthly revenue				
High	4 (8.7)	5 (7.5)	9 (8.0)	0.198
Low	29 (63.0)	52 (77.6)	81 (71.7)	
Medium	13 (28.3)	10 (14.9)	21 (18.6)	

HTN: hypertension.

Comparison of family past history among hypertensive and normotensive women

Table 13 below shows that having a family of hypertension (p = 0.001) in the first degree was significantly associated with persistent hypertension.

Table 13. Comparison of frequencies of clinical symptoms between women with and without persistent hypertension following preeclampsia

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%)	No n (%)	Total N (%)	
Preeclampsia				
Yes	8 (17.4)	6 (9.0)	14 (12.4)	0.181
No	38 (82.6)	61 (91.0)	99 (87.6)	
Hypertension				
Yes	36 (78.3)	32 (47.8)	68 (60.2)	**0.001**
No	10 (21.7)	35 (52.2)	45 (39.8)	
Diabetes				
Yes	25 (54.3)	44 (65.7)	44 (38.9)	0.225
No	21 (18.6)	23 (34.3)	69 (61.1)	
New paternity				
Yes	4 (8.7)	1 (1.5)	5 (4.4)	0.067
No	42 (91.3)	66 (98.5)	108 (95.6)	

3.5. Comparison of the Information on Labor and Delivery among Hypertensive and Normotensive Women

Table 14 below shows that GA at delivery (P = 0.014), severity of preeclampsia (p ≤ 0.001) and mode of delivery (p = 0.026) were significantly associated with persistent hypertension.

Table 14. Comparison of the information on labor and delivery among hypertensive and normotensive women.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%)	No n (%)	Total N (%)	
GA at delivery (weeks)				**0.014**
<37	16 (34.8)	10 (14.9)	26 (23.0)	
≥37	30 (65.2)	57 (85.1)	87 (77.0)	
Severity of PE				**<0.001**
mild to moderate	2 (4.3)	27 (40.3)	29 (25.7)	
Severe	44 (95.7)	30 (59.7)	84 (74.3)	
Mode of delivery				**0.026**
Cesarean	33 (71.7)	34(50.7)	67 (59.3)	
Vaginal delivery	13 (28.3)	33 (49.3)	46 (40.7)	

GA: Gestational age PE: Preeclampsia.

Comparison of the clinical characteristics of hypertensive and normotensive women

The mean interval period between preeclampsia and the diagnosis of hypertension was 2.25 ± 1.48 years ranging from 6 months to 7 years postpartum.

Comparison of the clinical symptoms of hypertensive and normotensive women

Clinical symptoms are significantly associated to persistent hypertension (Table 15).

Table 15. Comparison of symptoms between hypertensive and normotensive women.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%)	No n (%)	Total N (%)	
Symptoms				
Asymptomatic	22 (47.8)	66 (98.5)	88 (77.9)	**<0.001**
Pauci-symptomatic	18 (39.1)	1 (1.5)	19 (16.8)	
Symptomatic	6 (13.0)	-	6 (5.3)	

3.6. Comparison of the Waist Circumference and BMI between Hypertensive and Normotensive Women

Table 16 below shows that, waist circumference (p = 0.038) and BMI (p = 0.003) were significantly associated with persistent hypertension. The mean waist circumference was 90.04 ± 14.69 cm (96.08 ± 6.96 for hypertensive and 82.76 ± 12.50 for normotensive women). The mean for BMI was 27.50 ± 6.86 Kg/m^2 (31.86 ± 8.67 for hypertensive and 25.80 ± 4.92 for normotensive women).

Table 16. comparison of the waist circumference and BMI between hypertensive and normotensive women of the waist circumference and BMI between hypertensive and normotensive women.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%)	No n (%)	Total N (%)	
Waist circumference				**0.038**
Low risk	9 (19.6)	26 (38.8)	35 (31.0)	
medium risk	4 (8.7)	9 (13.4)	13 (11.5)	
high risk	32 (69.6)	33 (49.3)	65 (57.5)	
BMI				
Normal	9 (19.6)	29 (43.3)	38 (33.6)	
Obesity	25 (54.3)	16 (23.9)	41 (36.3)	**0.003**
Overweight	12 (26.1)	19 (28.4)	31 (27.4)	
Underweight	-	3 (4.5)	3 (2.7)	

BMI: Body mass index.

3.7. Electrocardiographic and Echocardiographic Profile of the Study Population

Table 17 below shows that left ventricular hypertrophy, left atrial volume and left ventricular geometry were significantly associated with persistent hypertension. LVH was found in both groups (8%) which can be considered a possible outcome. Other parameters such as repolarization, rhythm, left atrial volume, atrioventricular and intraventricular conductions were normal. The mean cornel voltage was 13.78 ± 5.74 bpm and 12.5 ± 4.40 bpm respectively in hypertensive and normotensive women. The mean heart rate was 72.79 ± 10.03 bpm and 71.43 ± 11.49 bpm respectively in hypertensive and normotensive women. Concerning echographic parameters, geometry and LAVi are significantly associated with persistent hypertension and ejection fraction was conserved for all participants. Of the 10 with an abnormal geometry, 2 (1.8%) had heart failure with conserved left ventricular ejection fraction.

Table 17. Comparison of the electrocardiographic and echocardiographic profile among the study population.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%)	No n (%)	Total N (%)	
LVH at ECG				
Yes	8 (17.4)	1 (1.5)	9 (8.0)	**0.002**
No	38 (82.6)	66 (98.5)	104 (98.0)	
LAVi				
Enlarged	13 (28.3)	8 (11.9)	21 (18.6)	**0.028**
Normal	33 (71.7)	59 (88.1)	92 (81.4)	
LVH				
Yes	8 (17.4)	2 (3.0)	10 (8.8)	**0.008**
No	38 (82.6)	65 (97.0)	103 (91.2)	
Geometry of LV				**0.017**
Concentric hypertrophy	4 (8.7)	2 (3.0)	6 (5.3)	
Eccentric hypertrophy	2 (4.3)	-	2 (1.8)	
Normal	38 (82.6)	65 (97.0)	103 (91.2)	
Concentric remodeling	2 (8.7)	-	2 (1.8)	

LAV: Left atrial volume, LVH: Left ventricular hypertrophy, ECG: electrocardiogram.

Biological profile of the study population

❖ **Comparison of biological parameters among hypertensive and normotensive women.**

Table 18 below shows us that total cholesterol was significantly associated with persistent hypertension. Other biological factors were evenly distributed in the

two groups.

Table 18. Comparison of biological parameters among hypertensive and normotensive women.

Variables (N = 113)	Persistent hypertension			P value
	Yes n (%)	Non (%)	Total N (%)	
Total cholesterol				**0.034**
Normal	43 (93.5)	67 (100.0)	100 (88.5)	
High	3 (6.5)	-	3 (2.7)	
HDL cholesterol				**0.085**
Normal	44 (95.7)	67 (100.0)	111 (98.2)	
High	2 (4.3)	-	2 (1.8)	
Triglyceride				**0.237**
Normal	46 (100.0)	65 (97.0)	111 (98.2)	
High	0 (0.0)	2 (3.0)	2 (1.8)	
LDL cholesterol				**0.225**
Normal	45 (97.8)	67 (100.0)	112 (99.1)	
High	1 (2.2)	-	1 (0.9)	
eGFR				**0.225**
Low	1 (2.2)	-	1 (0.9)	
Normal	45 (97.8)	(100.0)	112 (99.1)	
FGL				**0.225**
Normal	45 (97.8)	67 (100.0)	112 (99.1)	
High	1 (2.2)	-	1 (0.9)	
Uric acid				**0.225**
Normal	45 (97.8)	67 (100.0)	112 (99.1)	
High	1 (2.2)	-	1 (0.9)	

eGFR: estimated Glomerular filtration rate, HDL: High density lipoprotein, LDL: Low density lipoprotein, FGL: Fast Glucose Level.

3.8. Factors Associated with Persistent Hypertension after Preeclampsia

Factors associated to persistent hypertension after preeclampsia at Univariate analysis

Table 19 below shows the factors associated to persistent hypertension after preeclampsia at Univariate analysis.

Table 19. Univariate analysis of factors associated with persistent hypertension.

Variables (N = 113)	Persistent hypertension				P value
	Yes n (%)	No n (%)	Total N	OR (CI 95%)	
Age in years					
<35	28 (32.6)	58 (67.4)	86	1	
≥35	18 (66.7)	9 (33.3)	27	4.41 (1.65 - 10.38)	**0.0016**
Married					
Yes	35 (50.7)	34 (49.3)	69	2.90 (1.25 - 6.68)	**0.0109**
No	12 (26.6)	32 (71.1)	45	1	
Sever PE at diagnosis					
Yes	44 (52.4)	40 (47.6)	84	14.85 (3.31 - 66.47)	**0.0001**
No	12 (41.4)	17 (58.6)	29	1	
Family history of hypertension					
Yes	46 (68.6)	22 (32.4)	68	3.93 (1.68 - 9.20)	**0.0011**
No	10 (22.2)	35 (77.8)	45		
Overweight					
Yes	22 (66.7)	11 (33.3)	33	2.5 (1.04 - 6.16)	**0.0037**
No	24 (30.0)	56 (70.0)	80	1	
Prior PE					
Yes	26 (83.9)	5 (16.1)	31	16.12 (5.46 - 47.54)	**0.0001**
No	20 (24.4)	62 (75.6)	82	1	
Multiparity					
Yes	20 (83.3)	4 (16.7)	24	15.50 (4.27 - 56.23)	**0.0001**
No	26 (41.2)	63 (55.8)	89	1	
LVH on ECG					
Yes	8 (88.9)	1 (11.1)	9	13.89 (1.61 - 115.39)	**0.04**
No	38 (36.5)	66 (63.5)	104	1	

PE: preeclampsia LVH: left ventricular hypertrophy ECG: electrocardiogram.

Factors associated to persistent hypertension after preeclampsia at multivariate analysis

Table 20. Factors associated with persistent hypertension after multiple logistic regression.

Variables	aOR (CI 95%)	P value
Age ≥ 35	2.82 (0.64 - 12.36)	0.17
Family history HTN	5.33 (1.20 - 23.60)	**0.03**
Prior PE	4.99 (1.11 - 22.36)	**0.04**
Severe PE at diagnosis	13.19 (1.67 - 104.28)	**0.01**

HTN: Hypertension PE: preeclampsia.

Table 20 above shows that, after adjustment for confounders using multiple logistic regression, the factors found to be associated to persistent hypertension were: Family history of hypertension, prior pregnancy with preeclampsia, and Severe PE at diagnosis.

4. Discussion

We conducted a cross-sectional analytic study in three hospitals in Yaounde. The main objective of our work was to evaluate the cardiovascular outcome following pregnancies complicated by preeclampsia in three hospitals in Yaounde. We found that of the 113 women who had preeclampsia, 46 (40.7%) had hypertension. Cardiovascular outcome found in our study included: hypertension, LVH and heart failure. The independently associated factors to hypertension included: history of a pregnancy complicated by preeclampsia, family history of hypertension and severe hypertension at diagnosis.

4.1. Proportion of Persistent Hypertension

Using office blood pressure measurements, we found a proportion of 31%. Some authors worked on the same subject as us [3] [8] [10] [11]: among them, there are those who had results comparable to ours, this is the case of the work carried out by Nganou-Gnindjio *et al.* and Amougou *et al.* in Cameroon, who found a prevalence of 32.6% [3] and 23.53% respectively. Similarly, Nakimuli *et al.* in Uganda and Fajardo Tornes *et al.* in Cuba found a prevalence of 34% and 27.8% respectively. Other authors reported the prevalence of persistent hypertension lower than that reported by our study. This is the case of Manten *et al.* in 2007 who found a prevalence of 22% [12]. A study carried out by Kaze *et al.* in 2016 found a prevalence of 14.8%. This low prevalence can be explained by the difference in study follow-up time period. Other authors have had superior results to ours ranging from 38.7% [13] to 57.4% [14]. The high prevalence reported by these studies could be due to contextual differences that exist among the different study populations and settings. Using 24-hour ABPM, we found a proportion of 40.7% this is similar to results obtained by Benschop *et al.* [14] who had 41.5%. But this result is inferior to that found by Ditisheim *et al.* [15] who had 50%. This difference in prevalence could be explained by the fact that we excluded women with superimposed preeclampsia which was part of their study population. Lower prevalence of 29.5% was reported by Ditisheim *et al.* [15]. This difference may be explained by the fact that our study population was all black which would be more likely to develop hypertension.

The wide range of time since delivery (6 months to 7 years) introduces heterogeneity into the study population. Although our sensitivity analysis did not reveal a significant difference in hypertension prevalence between women assessed early versus late postpartum, this remains a methodological limitation inherent to the cross-sectional design. A prospective cohort study with standardized follow-up intervals would provide more precise estimates of the temporal trajectory of post-

PE hypertension.

4.2. Blood Pressure Profile

4.2.1. Hypertensive Phenotypes at ABPM

In our study, the most represented hypertensive phenotype was sustained hypertension 30 (26.5%). Some authors have worked on the same subject as us [14]-[16]. Among them there are those who had results similar to ours, this was the case of the work of Ditisheim *et al.* [15], who reported a prevalence of 20.5%. Studies carried out by Benschop *et al.* in 2018 and Ditisheim *et al.* in 2018 had a lower prevalence of 14.5% [14] and 14.2% [15] respectively. This can be explained by the fact that most of their study population was under anti-hypertensive medications. In our context only 4 women were initially under antihypertensive medications but the level of observance was very low (majority stopped taking medication 4 - 8 months prior our study) knowing that around three months after stopping medications, the effect of the drug is not more present. Masked Hypertension represented 14.2% of hypertension at ABPM, this is similar to others studies carried out by Pechere *et al.* in 2013, Benschop *et al.* in 2018 and Ditisheim *et al.* in 2018 who had prevalence of 11.6% [16], 17.5% [14] and 17.9% [15] respectively. Masked hypertension has been associated with an increased risk of developing sustained hypertension and cardiovascular events, independent of office BP. A known risk factor for masked hypertension is prehypertension which affected 28.6% of women in our study. Considering the potential long-term consequences for the mother, masked hypertension in the postpartum needs closer attention. Our study found that 2.7% of women presented white-coat hypertension. In some studies carried out by Benschop *et al.* [1] in 2018 in the Netherlands and Ditisheim al in 2018 in Switzerland. WCH was associated with modest increased risk of stroke and target organ damage. If the management of WCH is uncertain, especially in the postpartum period, its identification may prevent unnecessary use of antihypertensive medication. However, WCH should not be treated with antihypertensive medication because this can lead to hypotension.

4.2.2. Dipping Pattern (Mean Circadian Rhythm)

Non-dipping profile is also associated with increased cardiovascular risk and target organ damage. Early studies on circadian variations of BP during preeclampsia showed the loss of normal nocturnal fall and this was correlated to the severity of the disease [17]. In the present study, we found that 68.1% of women had abnormal nocturnal dipping. Sleep disruption of some breast-feeding mother may explain the absence of nocturnal BP drop in both groups. This result was similar to those obtained by Benschop *et al.* (50.5%) [14] and Ditisheim *et al.* (59.8%) [15] with similar reasons. Several pathological mechanisms have been suggested to explain the insufficient reduction of night-time BP, including deficient decrease of night-time sympathetic activity. Sympathetic activity is inversely associated with the difference in day-to-night BP, suggesting that it may influence 24- hour BP pattern in hypertensive individuals [14]. In women with preeclampsia, sympa-

thetic over activity is described both during and after pregnancy. This might explain the high prevalence of adrenergic component and a disadvantageous dipping pattern in our study population.

4.3. Comparism of the Sociodemographic Characteristics of Women after Preeclampsia

Age

The mean age of women was 29.78 ± 6.19 years. The average age found could be explained by the fact that Cameroonian population is young, especially women, as affirmed by the Cameroon Demographic and Health Survey (CDHS) 2018 which reports an age ranging from 15 to 49 years of 62.32% [18]. Some authors have worked on the same subject as us. Among them, there are some who had results similar to ours [7] [8] [10] [12] [18] The results similar to ours can be explained by the fact that they also carried out their studies on the same target population as us. However, some results are superior to ours. This is the case of Benschop *et al.* [14] and Ditisheim *et al.* [15] both in 2018. These can be explained by the fact that their study population consisted of adults with an age varying from 21 to 45 years and an average age of 33.7 ± 5.7 years.

4.4. Past History of the Study Population

Family history of hypertension was distributed in a heterogeneous manner in our study population, hence significantly associated with persistent hypertension. This results corroborates to those found by Dohou *et al.* [16], Amougou *et al.* [10]. We found an association between parity and the risk of chronic hypertension. This result was similar to that found by Nkwabong *et al.* in 2016 in Cameroon [6] and Nakimuli *et al.* in Uganda in 2011 [11]. We also found that, severity of preeclampsia at diagnosis was significantly associated with persistent hypertension. This result corroborates to that of Nakimuli *et al.* in Uganda in 2011 [11] and Smith *et al.* in 2009 in Canada [19]. Personal history of preeclampsia in previous pregnancies was found to be associated with the persistent hypertension in our study. Smith *et al.* in 2009 in Canada [19], Benschop *et al.* in 2018 in the Netherlands [14] and Eldow *et al.* in 2009 in Phildelphia [13], reached the same conclusion. Gestational age at delivery was significantly associated with persistent hypertension in our study. Previous studies such as that by Nkwabong *et al.* [6] and Nakimuli *et al.* [11] have all shown similar results.

4.5. Clinical and Paraclinical Profile of Women after Preeclampsia

Waist circumference ($p = 0.038$), and BMI ($p = 0.003$) were significantly associated with persistent hypertension in our study population. Amougou *et al.* [10], Fajardo *et al.* [8] and Dohou *et al.* [16] have all shown similar results.

We assessed electrocardiographic LVH with the development of persistent hypertension in women with history of preeclampsia. We found a prevalence of 8%, this is similar to results found by Drost *et al.* in 2012 in the Netherlands who had

a prevalence of 5.7% [20] but these results are different from those of Hoogsteder *et al.* who found a prevalence of 0.3% [21]. This difference in prevalence could be explained by the small size of our study population also, their study included all HDP. Other echographic parameters were normal.

Concerning echographic parameters;

In our study population, 8.9% of women had an abnormal geometry. Ejection fraction was preserved for all participants with slightly enlarged atrial dimensions (18.6% 22/113). This can be explained by the fact that cardiac changes may persist following hypertensive pregnancies. This result corroborates to the findings of Melchiorre *et al.* in the United Kingdom who had 10.9% of women with abnormal geometry with conserved ejection fraction and slightly enlarged atrial dimensions [22]. Scantlebury *et al.* had higher value of 15.8% [23]. This difference may be due to the fact that they included all hypertensive disorders of pregnancy.

In our study population 1.8% of women had heart failure with conserved ejection fraction. This result is similar with that of Scantlebury *et al.* in the United States who had 0.8%. However, this result is different from that of Breetveld *et al.* who had a higher proportion of 19%. This difference may be due to small size of their study population.

In our study, high total cholesterol levels were significantly associated with persistent hypertension. This result is similar to those found by Manten *et al.* in 2007 in the Netherlands [12]; Smith *et al.* in Canada [19] and Eldow *et al.* in Philadelphia [13]. It can be justified by the fact that dyslipidemia is associated to the risk of chronic hypertension.

4.6. Factors Associated with Persistence Hypertension after Preeclampsia

In our study, we have identified four independent associated risk factors:

1. **Family history of hypertension:** We assessed the link between family history of hypertension and the risk of future chronic hypertension (OR = 5.18 (1.32 - 20.37); p = 0.001) after PE and found that the presence in the siblings of the affected woman was independently associated to progression to chronic hypertension. The presence of a family history of hypertension especially in first degree relative, is a well-known risk factor of chronic hypertension and once more points the fact that a genetic component is implicated in the pathogenesis of hypertensive diseases in pregnancy and primary hypertension. This result corroborates to those found by Dohou *et al.* [16], Amougou *et al.* [10] and Ditisheim *et al.* [15].
2. **Prior pregnancy with preeclampsia:** We also found that, severe preeclampsia at diagnosis represents 74.3% of our study population. This result corroborates to that of Nakimuli *et al.* in Uganda in 2011 [11], who found that 47 out of 64 cases (73.4%) had severe preeclampsia. Smith *et al.* in 2009 in Canada reported that 51.4% of cases had severe preeclampsia [19]. This could be due to the fact that severe preeclampsia has been noted to be more strongly

associated with a wide range of internal placental factors with which their subsequent release into maternal circulation leads to endothelial dysfunction, generalized vasospasms and ultimately impaired multiple organ dysfunctions [21].

3. **Severe at preeclampsia diagnosis:** A history of preeclampsia in previous pregnancies was found to be associated with the persistent hypertension in our study. This can be explained by the fact that, with each pregnancy women have an increased vascular and metabolic risk and after pregnancy the residual risk is greater in women with preeclampsia than those with a normal pregnancy. With each recurrence of preeclampsia, this risk is slightly higher-this is known as "additional memory" of risk [9]. Thus, a woman with her second episode of pregnancy is more likely to develop chronic hypertension than a woman with her first episode. Smith *et al.* in 2009 in Canada [19], Benschop *et al.* in 2018 in the Netherlands [14]and Eldow *et al.* in 2009 in Philadelphia [13], reached the same conclusion.

5. Conclusions

About two in five women with preeclampsia had persistent hypertension. Sustained hypertension was the most frequent hypertensive phenotype and more than half of women had a non-dipping pattern.

Cardiovascular outcomes following preeclampsia include: persistent hypertension, left ventricular hypertrophy and heart failure.

Associated factors for persistent hypertension include: family history of hypertension, Preeclampsia in previous pregnancies, and severe preeclampsia at diagnosis.

Conflicts of Interest

The authors declare that they have no competing interests.

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