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Characteristics of hypertension among people living with HIV in Ghana: Impact of new hypertension guideline

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Abstract

Data on the burden of hypertension among people living with HIV (PLWH) in Africa are limited, especially after new expert consensus hypertension guidelines were published in 2017. The authors sought to assess the prevalence and factors associated with hypertension among PLWH. This is a cross-sectional study involving PLWH on combination antiretroviral therapy (cART) ($n = 250$) compared with sex-matched cART-naïve PLWH ($n = 201$) in Ghana. Hypertension was defined as blood pressure $\geq 140/90$ mm Hg or use of antihypertensive drugs. The authors also assessed the prevalence and predictors associated with hypertension using the recent guideline recommended cutoff BP $\geq 130/80$ mm Hg. Multivariate logistic regression models were fitted to identify factors associated with hypertension among PLWH. The mean age of PLWH on cART was 45.7 ± 8.6 years, and 42.9 ± 8.8 years among PLWH cART-naïve with 81% of study participants being women. The prevalence of hypertension among PLWH on cART and PLWH cART-naïve was 36.9% and 23.4%, $P = 0.002$ at BP $\geq 140/90$ mm Hg and 57.2% and 42.3%, respectively, $P = 0.0009$, at BP $\geq 130/80$ mm Hg. Factors associated with hypertension at BP $\geq 140/90$ mm Hg in the PLWH group with adjusted odds ratio (95% CI) were increasing age, 2.08 (1.60-2.71) per 10 years, and body mass index, 1.53 (1.24-1.88) per 5 kg/m² rise. At BP $\geq 130/80$ mm Hg, cART exposure, aOR of 1.77 (95% CI: 1.20-2.63), family history of hypertension, aOR of 1.43 (1.12-1.83), and hypertriglyceridemia, aOR of 0.54 (0.31-0.93), were associated with hypertension. Among PLWH, cART exposure was associated with higher prevalence of hypertension per the new guideline definition, a finding which warrants further investigation and possible mitigation.

1 | INTRODUCTION

People living with HIV (PLWH) infection are at a heightened risk of major adverse cardiovascular events (MACE) than uninfected persons.^{1,2} The accentuated cardiovascular disease (CVD) risk in HIV has been attributed to the persistent immune activation and inflammation from HIV infection,^{3,4} pro-atherogenic lipid abnormalities

induced by HIV infection, and combination antiretroviral therapy (cART).^{5,6} Additional contributions from prevailing traditional risk factors such as hypertension, diabetes mellitus, and dyslipidemia, and lifestyle factors such as cigarette smoking, alcohol use, and eating patterns may amplify the effect of HIV-associated elevation of cardiovascular risk.⁷ Addressing the increased CVD risk among the HIV population is an urgent priority in low and middle income

(LMICs) in sub-Saharan Africa (SSA) which bears a twin burden of having the highest prevalence of HIV on the globe and an astronomical rise in mortality, morbidity, and disability-adjusted years from cardiovascular diseases in recent decades.

Hypertension is an important CVD risk factor affecting 1 billion adults globally and is a leading modifiable risk factor for MACE.^{8,9} Hypertension has been recognized as a growing problem in HIV-infected adults.¹⁰⁻¹³ The prevalence of hypertension in PLWH was 13% in a large US cohort¹⁴ and 25% among a Swiss cohort.¹⁵ In comparison, 27.9% of patients initiating cART in Uganda,¹⁶ 38% of Cameroonian PLWH on cART versus 19% of cART-naïve,¹⁷ and 12.7% of Ethiopian PLWH on cART had hypertension.¹⁸ Overall, a recent meta-analysis of worldwide data found 35% of PLWH on cART had hypertension compared with 30% among PLWH who were not on cART.¹⁹ Of note, PLWH with hypertension have a higher risk of MACE and increased all-cause mortality relative to HIV-infected adults with normal blood pressure or HIV-uninfected population with hypertension.^{1,20} There is a dearth of studies with a focus on assessing the risk factors for hypertension among PLWH on cART compared with PLWH who are cART-naïve in SSA. Moreover, most of the studies evaluating the burden of hypertension among PLWH were performed before the recent American College of Cardiology/American Heart Association revised definitions for hypertension with lower blood pressure thresholds.²¹

The Evaluation of Vascular Event Risk while on Long-term Anti-retroviral Suppressive Therapy (EVERLAST) Study seeks to characterize the burden of cardiovascular risk among patients with HIV on cART in Ghana. We have shown in a recent report among Ghanaian PLWH that hypertension was associated with subclinical atherosclerosis at a carotid intimal media thickness (CIMT) cutoff value of 1.00 mm.²² Carotid atherosclerosis is a harbinger of MACE in the HIV population.² Hence, characterizing the epidemiology of hypertension among PLWH in SSA is essential to guide the development of evidence-based interventions to mitigate this cardinal risk factor for CVDs. Our main focus for this present analysis is to assess the factors associated with hypertension among a cross-section of PLWH on cART compared with those who are cART-naïve at a tertiary medical facility in Ghana. We sought to further assess the knowledge, attitudes, and practices on hypertension among Ghanaian PLWH. Our attention on the PLWH cohort is driven by the fact that they represent a population with more frequent contact with health care facilities and personnel. Thus, targeted control of CVD risk factors such as hypertension is an attainable goal for prevention of adverse cardiovascular outcomes.

2 | METHODS

2.1 | Study design and population

The Evaluation of Vascular Event Risk while on Long-term Anti-retroviral Suppressive Therapy (EVERLAST) Study is designed as a case-control study to compare CVD risk by assessing for the presence of the major traditional vascular risk factors among Ghanaian PLWH on cART compared with age- and sex-matched PLWH who are cART-naïve.

Ethical approval for the study was obtained from the Kwame Nkrumah University of Science and Technology Committee of Human Research Publications and Ethics. Cases were PLWH aged ≥ 30 years receiving cART for at least 1 year at the HIV clinic of the Komfo Anokye Teaching Hospital, a tertiary medical facility in Kumasi, Ghana. We consecutively enrolled 201 PLWH aged ≥ 30 years who were cART-naïve at the HIV clinic matched by sex and age band of ± 5 years.

2.2 | Study evaluations

A standardized data collection form was developed to collect information on socio-demographic characteristics, including age, sex, educational status, monthly income, and marital status. Among the PLWH, we collected data through interview and review of medical record chart extraction on HIV disease characteristics, such as current CD4 cell count, HIV-1 viral load, past and current history of cART, and duration on cART. We assessed the traditional vascular risk factors using history-taking, physical examination, and by collecting blood samples for measurement of HBA_{1c} and fasting lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides). The following definitions were used for traditional vascular risk factors.

- Blood pressure (BP) (mean of three measurements) was taken on each study participant following a standard protocol. A cutoff of at least 140/90 mm Hg according to WHO definitions²³ or use of antihypertensive drugs was regarded as indicators of hypertension as a primary outcome measure. Hypertension was also defined using the recent American College of Cardiology/American Heart Association guideline of systolic BP ≥ 130 mm Hg and diastolic BP ≥ 80 mm Hg.²¹ Hypertension subtypes including isolated systolic hypertension (ISH) defined as a systolic BP ≥ 140 and diastolic BP < 90 mm Hg; isolated diastolic hypertension (IDH) defined as systolic BP < 140 mm Hg and diastolic BP ≥ 90 mm Hg; and systolic-diastolic hypertension (SDH) defined as systolic BP ≥ 140 and diastolic BP ≥ 90 mm Hg according to Franklin criteria.²⁴
- Dyslipidemia was defined as a fasting total cholesterol concentration ≥ 5.2 mmol/L, HDL cholesterol ≤ 1.03 mmol/L, LDL cholesterol ≥ 3.4 mmol/L, or serum triglyceride ≥ 1.7 mmol/L, according to National Cholesterol Education Program guidelines.²⁵
- Obesity was defined using the WHO guidelines with a waist-to-hip ratio (WHR) cutoff of 0.90 (men) and 0.85 (women) or body mass index (BMI) of 30 kg/m² for obesity.²⁶ WHR was used to assess burden of central adiposity, and BMI was used to further categorize participants into underweight, ideal weight, overweight, and obese.
- Physical activity was defined as regular involvement in moderate exercise (walking, cycling, or gardening) or strenuous exercise for 4 hours or more per week and was assessed via self-report.
- Dietary history included frequency of intake of green leafy vegetables, fruits, and addition of salt at the table.

- Alcohol users were categorized into two groups (current users versus former user or never used). Similarly, smoking status was also categorized into three groups (those who have never smoked, former smokers, and individuals who smoked any tobacco in the past 12 months).

Educational status was assessed by asking participants the highest level of educational attainment with categorization into none, primary, secondary, and tertiary level. Household monthly income was categorized into five categories: >1000 Ghana cedis, 500-1000 GHs, 100-499 GHs, <100 GHs, and don't know.

Furthermore, we assessed the knowledge, attitudes, and practices of study participants on hypertension using a questionnaire with seven questions covering topics such as the WHO definitions for hypertension, the health risks of uncontrolled hypertension, and treatments available for controlling hypertension.

2.3 | Statistical analysis

Comparisons of demographic, lifestyle, vascular risk factors, and hypertension among the two groups (PLWH on cART and PLWH not on cART) were performed using Student's *t*-test for continuous parametric variables and chi-square tests for discrete variables. Descriptive analyses were performed for subtypes of hypertension. Systemic arterial hypertension defined as a BP \geq 140/90 mm Hg as a primary outcome measure and predictors of this outcome in the entire PLWH cohort, PLWH on cART, and PLWH not on cART were assessed using bivariate and multivariate logistic regression. Point prevalence for hypertension was defined as proportion with BP \geq 140/90 mm Hg or use of antihypertensive medications divided by sample size of group analyzed. Putative factors in models included demographic variables such as age, sex, location of residence, anthropometric measures, such as BMI, traditional vascular risk factors such as lipid subfractions (ie, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), dietary factors; HIV-related factors such as WHO clinical status, and CD4 counts. Factors with a *P*-value of <0.05 at the bivariate level of analysis were included in a multivariable model. In secondary analysis, factors associated with a BP \geq 130/80 mm Hg²¹ were also assessed using the same set of putative variables. Correlations between serum triglyceride concentrations and age, blood pressure, and body mass index were assessed in an exploratory, post hoc fashion using Pearson's correlation tests to gain insights into the protective associations observed between hypertriglyceridemia and hypertension. In all analyses, a *P*-value of <0.05 was considered statistically significant. Statistical analysis was performed using GraphPad Prism version 7 and SPSS version 21.

3 | RESULTS

3.1 | Characteristics of study participants

There were 250 PLWH on cART, and 201 PLWH who were cART-naïve recruited between April 2017 and August 2018. There was a preponderance of females who constituted 81.4% of the entire

sample size with no differences between the two groups according to sex but the PLWH on cART were significantly older than those not on cART, mean age of 45.7 ± 8.6 years versus 42.9 ± 8.8 years, $P = 0.0006$. Other socio-demographic characteristics are shown in Table 1. Current or previous cigarette smoking was low overall at 7.1% and alcohol use was 8.2% with no significant differences were observed between the two groups. The PLWH on cART were however more physically active compared with PLWH not on cART, 38.0% vs 22.4%, $P = 0.0004$. The nadir CD4 T-cell counts at diagnosis were significantly lower among the PLWH on cART compared with cART-naïve group with a corresponding higher frequency of individuals with advanced clinical stages of HIV disease as shown in Table 1.

3.2 | Burden and characteristics of participants with hypertension

There were 139 (30.8%) participants with hypertension in the entire PLWH cohort with a significantly higher prevalence in the PLWH on cART group (36.9%) compared with PLWH cART-naïve group (23.4%), $P = 0.002$. Among those with hypertension, 44.7% of PLWH cART-naïve, and 40.2% of PLWH on cART, were on antihypertensive therapy.

The prevalence of hypertension increased with age of PLWH being 20% for age 30-39 years, 27% for 40-49 years, 48% for 50-59 years, 57% for 60-69 years group, and 50% for 70+ years (Figure S1A). Using the updated ACC/AHA definition²¹ for hypertension, rates were 39%, 49%, 69%, 73%, and 50% for age groups 30-39, 40-49, 50-59, 60-69, and 70+ years, respectively (Figure S1B). By subtypes of hypertension, 59.2% had combined systolic-diastolic hypertension, 20.8% had isolated diastolic hypertension, and 20.0% had isolated systolic hypertension, with age distribution depicted in Figure S1C. PLWH on cART were more likely to have BP \geq 160/100 mm Hg than PLWH cART-naïve, 11.6% vs 4.0%, $P = 0.003$.

A comparison of characteristics between those with hypertension and those without is shown in Table 2. In brief, those with hypertension were significantly older, had a longer duration of HIV diagnosis, and had higher indicators of obesity determined using either BMI-defined or central obesity indicators such as waist-to-hip ratio. On the contrary, those with hypertension were less likely to have raised serum total cholesterol and triglyceride (Table 2).

3.3 | Risk factors for hypertension

Among the entire PLWH cohort, hypertension was associated with increasing age, cART exposure, family history of hypertension, elevated body mass index, and raised total serum cholesterol and triglyceride on bivariate analysis. In adjusted analyses, the factors that remained significantly associated with hypertension and adjusted odds ratio (95% CI) were increasing age, 2.08 (1.60-2.71) for each 10 years increase in age, and increasing body mass index, 1.53 (1.24-1.88) for each 5 kg/m² rise in BMI, as shown in Table 3. Increasing age and BMI remained independently associated with

TABLE 1 Characteristics of PLWH on cART versus those who are cART-naïve

Characteristics	PLWH on cART N = 250	PLWH cART-naïve N = 201	P-value
Age, mean ± SD	45.7 ± 8.6	42.9 ± 8.8	0.0006
Female, n (%)	203 (81.2)	164 (81.6)	0.92
Location of residence			
Urban	169 (67.6)	153 (76.5)	0.01
Semi-urban	17 (6.8)	3 (1.5)	
Rural	64 (25.6)	44 (22.0)	
Educational level			
None	69 (27.6)	54 (27.1)	0.06
Primary	100 (40.0)	58 (29.1)	
Secondary	67 (26.8)	72 (36.2)	
Tertiary	14 (5.6)	15 (7.6)	
Marital status			
Never married	19 (7.6)	26 (13.0)	0.054
Married	122 (48.8)	105 (52.8)	
Divorced/separated	52 (20.8)	39 (19.6)	
Widow	57 (22.8)	29 (14.6)	
Monthly income			
>1000 GHs	42 (16.8)	30 (14.9)	<0.0001
500-1000 GHs	88 (35.2)	51 (25.4)	
100-499 GHs	77 (30.8)	74 (36.8)	
<100 GHs	7 (2.8)	27 (13.4)	
Don't know	36 (14.4)	19 (9.5)	
Duration of HIV diagnosis (years), mean ± SD	8.6 ± 4.4	1.3 ± 2.5	<0.0001
Smoking			
No smoking	3 (1.2)	1 (0.5)	0.70
Previous smoking	14 (5.6)	10 (5.0)	
Current smoking	233 (93.2)	190 (94.5)	
Current alcohol use	20 (8.0)	17 (8.5)	0.86
Fruit intake			
0 serving/d	15 (6.0)	8 (4.0)	0.001
1-3 servings/d	89 (35.9)	106 (53.3)	
4-7 servings/d	144 (58.1)	85 (42.7)	
Vegetable intake			
0-1 servings	67 (27.0)	60 (30.2)	<0.0001
2 servings	134 (54.0)	63 (31.7)	
≥3 servings	47 (19.0)	76 (38.1)	
Salt at table			
Never	170 (68.5)	139 (69.9)	0.90
Occasional	17 (6.9)	11 (5.5)	
Sometimes	39 (15.7)	29 (14.5)	
Always	22 (8.9)	20 (10.1)	
Physical activity, n (%)	95 (38.0)	45 (22.4)	0.0004
CD4 count, nadir	237.3 ± 210.8	320.7 ± 278.6	0.0004

(Continues)

TABLE 1 (Continued)

Characteristics	PLWH on cART N = 250	PLWH cART-naïve N = 201	P-value
CD4 count, current	641.9 ± 331.5	320.7 ± 278.6	<0.0001
Clinical stage at diagnosis			
1	73 (30.3)	54 (27.3)	0.006
2	52 (21.6)	54 (27.3)	
3	91 (37.8)	85 (42.9)	
4	25 (10.3)	5 (2.5)	
Systolic BP, mean ± SD	127.4 ± 23.6	115.2 ± 22.8	<0.0001
Diastolic BP, mean ± SD	79.1 ± 13.5	76.2 ± 14.3	0.02
Blood pressure categories			
SBP < 120 mm Hg and/or DBP < 80 mm Hg	103 (41.4)	118 (58.7)	0.0003
SBP 120-139 and/or DBP 80-89 mm Hg	78 (31.3)	56 (27.9)	
SBP 140-159 and/or DBP 90-99 mm Hg	39 (15.7)	19 (9.4)	
SBP ≥ 160 and/or DBP ≥ 100 mm Hg	29 (11.6)	8 (4.0)	
Proportion with hypertension, n (%)	92 (36.9)	47 (23.4)	0.002
Proportion of HPT on Rx, n (%)	37 (40.2)	21 (44.7)	0.61
Proportion controlled on HPT Rx, n (%)	11 (29.7)	9 (42.9)	0.31
Total cholesterol, mean ± SD	4.96 ± 1.32	5.39 ± 1.42	0.0009
LDL cholesterol, mean ± SD	3.04 ± 1.05	3.30 ± 1.03	0.01
HDL cholesterol, mean ± SD	1.28 ± 0.49	1.40 ± 0.49	0.01
Triglyceride, mean ± SD	1.43 ± 0.95	1.49 ± 1.17	0.53
Dyslipidemia, n (%)	198 (79.2)	167 (83.1)	0.30
Raised total cholesterol, n (%)	108 (43.2)	112 (55.7)	0.008
Raised LDL cholesterol, n (%)	94 (37.6)	91 (45.3)	0.10
Low HDL cholesterol, n (%)	82 (32.8)	45 (22.4)	0.01
Raised triglyceride, n (%)	62 (24.8)	57 (28.4)	0.39
Body mass index, mean ± SD	27.1 ± 5.5	24.5 ± 5.1	<0.0001
BMI cutoff			
<18.5 kg/m ²	6 (2.4)	17 (8.5)	0.0009
18.5-24.9 kg/m ²	99 (40.1)	99 (49.3)	
25.0-29.9 kg/m ²	75 (30.4)	52 (25.9)	
>30.0 kg/m ²	67 (27.1)	33 (16.4)	
Waist-to-hip ratio, mean ± SD	0.88 ± 0.09	0.88 ± 0.07	0.55
Raised WHR	154 (61.6)	134 (66.7)	0.27
eGFR, mean ± SD	84.7 ± 10.6	84.7 ± 11.5	0.99

hypertension among PLWH on cART (Table 4). In addition to age and BMI, family history of hypertension was significantly associated with hypertension among PLWH cART-naïve with an adjusted OR of 1.72 (95% CI: 1.12-2.65).

3.4 | Sensitivity analysis

The prevalence of hypertension in the PLWH cohort overall was 51.1% using this updated ACC/AHA definition²¹ with a significant difference between the PLWH on cART (57.2%) and the PLWH cART-naïve group (42.3%), $P = 0.0009$. In bivariate analyses, six

factors were associated with hypertension according to the updated definition with the following unadjusted OR (95% CI): increasing age, 1.77 (1.41-2.22); exposure to cART relative to cART-naïve, 1.90 (1.31-2.77); increasing BMI, 1.45 (1.21-1.74); raised total serum cholesterol, 0.46 (0.32-0.67); raised serum triglyceride, 0.39 (0.25-0.60); and family history of hypertension, 1.47 (1.16-1.87). Upon adjustment, the three factors associated with hypertension were cART exposure, aOR of 1.77 (95% CI: 1.20-2.63), family history of hypertension, aOR of 1.43 (1.12-1.83), while hypertriglyceridemia was protective against hypertension, aOR of 0.54 (0.31-0.93). In exploratory analysis to find plausible explanations for the protective

TABLE 2 Characteristics of PLWH with hypertension compared with those without hypertension

Characteristics	PLWH with hypertension N = 139	PLWH without hypertension N = 312	Total N = 451	P-value
Age, mean ± SD	48.1 ± 8.5	42.8 ± 8.4	44.5 ± 8.8	<0.0001
Female, n (%)	109 (78.4)	258 (82.7)	367 (81.4)	0.28
Location of residence				
Urban	101 (72.7)	221 (71.1)	322 (71.6)	0.52
Semi-urban	8 (5.8)	12 (3.9)	20 (4.4)	
Rural	30 (21.5)	78 (25.0)	108 (24.0)	
Educational level				
None	41 (29.5)	82 (26.5)	123 (27.4)	0.13
Primary	56 (40.3)	102 (32.9)	158 (35.2)	
Secondary	37 (26.6)	102 (32.9)	139 (31.0)	
Tertiary	5 (3.6)	24 (7.7)	29 (6.5)	
Marital status				
Never married	11 (7.9)	34 (11.0)	45 (10.0)	0.04
Married	60 (43.2)	167 (53.9)	227 (50.6)	
Divorced/separated	37 (26.6)	54 (17.4)	91 (20.3)	
Widow	31 (22.3)	55 (17.7)	86 (19.2)	
Monthly income				
>1000 GHs	22 (16.3)	50 (16.2)	75 (16.8)	0.62
500-1000 GHs	42 (31.1)	97 (31.4)	139 (31.1)	
100-499	51 (37.8)	100 (32.4)	151 (33.8)	
<100	7 (5.2)	27 (8.7)	34 (7.6)	
Don't know	13 (9.6)	35 (11.3)	48 (10.7)	
Smoking				
No smoking	131 (94.2)	288 (92.3)	419 (92.9)	0.39
Previous smoking	8 (5.8)	20 (6.4)	28 (6.2)	
Current smoking	0 (0.0)	4 (1.3)	4 (0.9)	
Current alcohol use	11 (7.9)	26 (8.3)	37 (8.2)	0.88
Fruit intake				
0 serving/d	8 (5.8)	15 (4.8)	23 (5.1)	0.71
1-3 servings/d	56 (40.9)	139 (44.8)	195 (43.6)	
4-7 servings/d	73 (53.3)	156 (50.3)	229 (51.2)	
Vegetable intake				
0-1 servings	41 (29.9)	86 (27.7)	127 (28.4)	0.89
2 servings	59 (43.1)	138 (44.5)	197 (44.1)	
≥3 servings	37 (27.0)	86 (27.7)	123 (27.5)	
Salt at table				
Never	91 (66.4)	218 (70.3)	309 (69.1)	0.41
Occasional	12 (8.8)	16 (5.2)	28 (6.3)	
Sometimes	23 (16.8)	45 (14.5)	68 (15.2)	
Always	11 (8.0)	31 (10.0)	42 (9.4)	
Physical activity, n (%)	44 (31.7)	96 (30.8)	140 (31.0)	0.85
cART use				
Yes	92 (66.2)	158 (50.6)	250 (55.4)	0.002
No	47 (33.8)	154 (49.4)	201 (44.6)	

(Continues)

TABLE 2 (Continued)

Characteristics	PLWH with hypertension N = 139	PLWH without hypertension N = 312	Total N = 451	P-value
Duration of HIV diagnosis, mean ± SD	6.4 ± 5.6	4.7 ± 4.9	5.2 ± 5.2	0.002
CD4 count, nadir	302.7 ± 261.0	261.9 ± 239.1	274.4 ± 246.5	0.11
CD4 count, current	534.8 ± 336.6	484.5 ± 350.2	499.8 ± 346.5	0.16
Clinical stage at diagnosis				
1	40 (29.6)	87 (28.6)	127 (28.9)	0.57
2	34 (25.2)	72 (23.7)	106 (24.1)	
3	49 (36.3)	127 (41.8)	176 (40.1)	
4	12 (8.9)	18 (5.9)	30 (6.8)	
Total cholesterol, mean ± SD	4.8 ± 1.3	5.3 ± 1.4	5.1 ± 1.4	0.0003
LDL cholesterol, mean ± SD	3.05 ± 1.07	3.20 ± 1.04	3.16 ± 1.05	0.16
HDL cholesterol, mean ± SD	1.32 ± 0.48	1.34 ± 0.50	1.34 ± 0.49	0.59
Triglyceride, mean ± SD	1.34 ± 1.07	1.51 ± 1.04	1.46 ± 1.05	0.10
Dyslipidemia, n (%)	113 (81.3)	252 (80.8)	365 (80.9)	0.90
Raised total cholesterol, n (%)	55 (39.6)	165 (52.9)	220 (48.8)	0.009
Raised LDL cholesterol, n (%)	52 (37.4)	133 (42.6)	185 (41.0)	0.30
Low HDL cholesterol, n (%)	45 (32.4)	82 (26.3)	127 (28.2)	0.18
Raised triglyceride, n (%)	24 (17.3)	95 (30.5)	119 (26.4)	0.003
Body mass index, mean ± SD	27.6 ± 5.3	25.2 ± 5.4	25.9 ± 5.5	<0.0001
BMI cutoff				
<18.5 kg/m ²	2 (1.4)	21 (6.8)	23 (5.1)	0.0002
18.5-24.9 kg/m ²	48 (34.8)	150 (48.4)	198 (44.2)	
25.0-29.9 kg/m ²	43 (31.2)	84 (27.1)	127 (28.3)	
>30.0 kg/m ²	45 (32.6)	55 (17.7)	100 (22.3)	
Waist-to-hip ratio, mean ± SD	0.90 ± 0.07	0.87 ± 0.08	0.88 ± 0.08	0.0009
Raised WHR	98 (70.5)	190 (60.9)	288 (63.9)	0.05
eGFR, mean ± SD	85.7 ± 9.0	84.2 ± 11.7	84.7 ± 11.0	0.18

associations between hypertriglyceridemia and hypertension, we found inverse correlations between serum triglyceride and systolic BP (Pearson's $r = -0.16$, $P = 0.0006$), diastolic BP ($r = -0.12$, $P = 0.006$), and age ($r = -0.10$, $P = 0.03$) but no correlations with body mass index ($r = -0.05$, $P = 0.26$).

3.5 | Knowledge, attitudes, and practices on hypertension

Overall, 55.4% of PLWH had knowledge on what hypertension meant, but 73.8% and 75.8%, respectively, did not know the cut-offs for systolic and diastolic blood pressure readings for diagnosing hypertension, respectively. A majority (92.5%) expressed that hypertension was a serious health concern and expressed that taking medicines were very important in controlling blood pressure (92.5%). However, awareness of the role of lifestyle factors such as exercising (20.2%), less stress (26.2%), quitting smoking (5.8%), and weight loss (0.9%) in controlling hypertension was low (Table 5). Among

the possible complications of hypertension, in decreasing order of frequency, participants were aware of stroke (39.7%), heart attack (4.2%), and renal impairment (1.1%), but 54.1% were not aware of possible effects of hypertension. There were no significant differences between PLWH on cART and those not on cART regarding their knowledge and practices on hypertension.

4 | DISCUSSION

The prevalence of hypertension was higher among Ghanaian PLWH on cART at 37% compared with 23% among PLWH who were cART-naïve. This is in accord with a Norwegian study of similar sample size where rates of hypertension declined from 23% in PLWH on cART to 13% among PLWH cART-naïve.²⁷ Again, a recent case-control study from Denmark²⁸ found PLWH had a lower risk of hypertension compared with age- and sex-matched controls. Hypertension was significantly more common among PLWH on cART than cART-naïve participants

TABLE 3 Factors associated with hypertension among Ghanaians living with HIV

Predictors	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age, each 10 y older	2.02 (1.58-2.57)	<0.0001	2.08 (1.60-2.71)	<0.0001
Male sex	1.33 (0.81-2.19)	0.27	-	-
CD4 T-cell count, each 100 cells/mm ³ higher	1.07 (0.99-1.16)	0.11	-	-
WHO clinical stages, each stage higher	0.86 (0.68-1.07)	0.18	-	-
cART-exposed vs naive	1.95 (1.28-2.96)	0.002	1.34 (0.85-2.12)	0.21
Family history of hypertension	1.47 (1.15-1.87)	0.002	1.24 (0.95-1.62)	0.11
Body mass index, each 5kg/m ² rise	1.49 (1.24-1.80)	<0.0001	1.53 (1.24-1.88)	0.0001
Total serum cholesterol > 5.2 mmol/L	0.58 (0.39-0.87)	0.009	0.87 (0.51-1.48)	0.61
Total serum triglyceride > 1.70 mmol/L	0.48 (0.29-0.78)	0.004	0.61 (0.32-1.15)	0.13
Estimated glomerular filtration rate, each 15 mL/min higher	1.24 (0.90-1.71)	0.19	-	-
Cigarette use	0.90 (0.39-2.10)	0.81	-	-
Physical activity	1.05 (0.68-1.62)	0.81	-	-
Table added salt	1.20 (0.78-1.84)	0.41	-	-
Vegetable servings	0.95 (0.77-1.17)	0.60	-	-
Fruit servings	1.01 (0.90-1.13)	0.90	-	-
Alcohol use	0.94 (0.45-1.97)	0.88	-	-

in the present study. This finding should however be interpreted cautiously in the light of imperfect age-matching between cART-exposed and cART-naïve PLWH. Hence, in our multivariate logistic regression models, cART exposure was not significantly associated with hypertension with adjusted odds ratio of 1.34 (95% CI: 0.85-2.12). A worldwide meta-analysis reported a 35% prevalence rate of hypertension among PLWH on cART¹⁹ comparing favorably with the 37% found in our study. However, the investigators found a slightly higher rate of 30% among PLWH not on cART¹⁹ compared with a lower rate of 23% from our results. It is worth highlighting that among the 63 000+ study participants in the worldwide meta-analysis from a total of 49 studies,¹⁹ 38 studies were from HIC (US and Europe) with only 10 from SSA.

Increasing age was a key socio-demographic factor associated with occurrence of hypertension. It is also notable that 22% of PLWH in our cohort had obesity using BMI as an indicator and nearly 64% had evidence of central obesity based on having an elevated waist-to-hip ratio. This marks a significant departure from reports in the early phases of the ART era²⁹⁻³² where PLWH in Ghana were

profoundly emaciated from relentless wasting from HIV infection due to late presentation, diagnosis, and delayed initiation of cART. Indeed, elevated BMI was the only modifiable risk factor associated with hypertension among Ghanaian PLWH with each 5 kg/m² rise in BMI associated with 53% increased risk of hypertension in the entire HIV cohort. The association between an elevated BMI and hypertension persisted in models specifically looking at PLWH on cART, adjusted odds ratio of 1.46 (95% CI: 1.13-1.87), and also among PLWH not on cART with aOR of 1.47 (95% CI: 1.00-2.16) in agreement with other studies.^{27,33} Pathophysiologically, it has been posited that both HIV itself and ART can cause lipodystrophy leading to accumulation of central adiposity with deep and intricate causal links with hypertension via adipocytokines called adiponectin and leptin.³⁴ Plasma concentrations of adiponectin, a potent vasodilator through elaboration of endothelial nitric oxide, has been shown to be significantly lower among PLWH with metabolic syndrome.^{34,35} Furthermore, it has been shown that PLWH on cART have higher circulating levels of leptin, which acting via leptin receptors simultaneously trigger

Predictors	PLWH on cART		PLWH not on cART	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age, each 10 y older	1.99 (1.44-2.74)	2.17 (1.55-3.03)	1.92 (1.31-2.82)	1.92 (1.26-2.92)
Male sex	1.35 (0.71-2.57)	-	1.27 (0.56-2.87)	-
CD4 T-cell count, each 100 cells/mm ³ higher	1.05 (0.93-1.19)	-	1.15 (1.01-1.27)	1.09 (0.96-1.23)
WHO clinical stages, each stage higher	1.03 (0.80-1.34)	-	1.78 (0.90-3.53)	-
Duration of cART exposure in years	1.00 (0.93-1.08)	-	N/A	N/A
Viral load < 40 copies/mL	1.47 (0.84-2.59)	-	0.83 (0.59-1.16) ^a	-
Efavirenz-based cART vs nevirapine-based cART (referent)	1.42 (0.83-2.43)	-	N/A	N/A
Family history of hypertension	1.24 (0.90-1.70)	-	1.89 (1.28-2.78)	1.72 (1.12-2.65)
Body mass index, each 5 kg/m ² rise	1.31 (1.03-1.66)	1.46(1.13-1.87)	1.67 (1.20-2.32)	1.47 (1.00-2.16)
Total serum cholesterol > 5.2 mmol/L	0.61 (0.36-1.04)	-	0.63 (0.32-1.21)	-
Total serum triglyceride > 1.70 mmol/L	0.56 (0.30-1.06)	-	0.36 (0.15 - 0.87)	0.46 (0.18-1.16)
Estimated glomerular filtration rate, each 15 mL/min higher	1.10 (0.75-1.62)	-	1.18 (0.94-1.48)	-
Cigarette use	0.72 (0.24-2.11)	-	1.20 (0.31-4.73)	-
Physical activity	1.04 (0.61-1.77)	-	1.11 (0.50-2.45)	-
Table added salt	1.24 (0.71-2.16)	-	0.99 (0.72-1.35)	-
Vegetable servings	1.02 (0.75-1.39)	-	0.95 (0.72-1.35)	-
Fruit servings	0.93 (0.80-1.08)	-	1.10 (0.90-1.35)	-
Alcohol use	0.56 (0.20-1.60)	-	1.84 (0.64-5.27)	-

^aViral load, each log higher. Odds ratio that were significant with $P < 0.05$ in bold

activation of both the renin-angiotensin-aldosterone pathway and the sympathetic nervous system.^{36,37}

In a sensitivity analysis using a lower BP threshold $\geq 130/80$ mm Hg according to recent guidelines,²³ 58% of PLWH on cART had hypertension compared with 42% of PLWH cART-naïve. Given that HIV is considered a cardiometabolic risk factor, the proportion of PLWH that may require therapeutic lifestyle interventions and possibly medications to control elevated BP per the updated hypertension definition is expected to be substantial. We identified exposure to cART and family history

TABLE 4 Factors associated with hypertension among Ghanaians living with HIV on cART and those cART-naïve

of hypertension as factors associated with hypertension among PLWH while hypertriglyceridemia was protective at the lower BP cutoff $\geq 130/80$ mm Hg. Exposure to cART may mediate hypertension by immune reconstitution inflammatory syndrome, in addition to increasing other cardiometabolic risk factors such as adiposity. Previous studies have demonstrated a higher incidence of hypertension after initiating cART in PLWH with low nadir CD4 counts.^{38,39} We however did not observe significant differences in nadir CD4 counts between PLWH with hypertension and those without in our study. While a positive family history

TABLE 5 Knowledge and practices related to hypertension among Ghanaians living with HIV

Question	PLWH on cART N = 250	PLWH cART-naive N = 201	Total N = 451	P-values
1. What does the term hypertension mean?				
Raised blood pressure	135 (54.0)	115 (57.1)	250 (55.4)	0.49
2. What should be the upper/systolic blood pressure reading be to a hypertensive?				
≥140 mm Hg	4 (1.6)	4 (2.0)	8 (1.8)	0.93
<140 mm Hg	62 (24.8)	48 (23.9)	110 (24.4)	
I don't know	184 (73.6)	149 (74.1)	333 (73.8)	
3. What should be the lower/diastolic blood pressure reading be to a hypertensive?				
≥90 mm Hg	4 (1.6)	2 (1.0)	6 (1.3)	0.69
<90 mm Hg	54 (21.6)	49 (24.4)	103 (22.8)	
I don't know	192 (76.8)	150 (74.6)	342 (75.8)	
4. How serious of a health concern has high blood pressure been to you?				
Not at all serious	7 (2.8)	2 (1.0)	9 (2.0)	0.30
Somewhat serious concern	11 (4.4)	5 (2.5)	16 (3.5)	
Very serious concern	226 (90.4)	191 (95.0)	417 (92.5)	
No response	6 (2.4)	3 (1.5)	9 (2.0)	
5. How important do you think taking medicine is to keeping blood pressure under control?				
Not at all important	1 (0.4)	2 (1.0)	3 (0.7)	0.64
Somewhat important	14 (5.6)	8 (4.0)	22 (4.9)	
Very important	229 (91.6)	188 (93.5)	417 (92.5)	
No response	6 (2.4)	3 (1.5)	9 (2.0)	
6. What are the most important factors in controlling your blood pressure?				
Taking medications	146 (58.4)	126 (62.7)	272 (60.3)	0.36
Exercising	55 (22.0)	36 (17.9)	91 (20.2)	0.28
Less stress	71 (28.4)	47 (23.4)	118 (26.2)	0.23
Quitting smoking if you are smoking	14 (5.6)	12 (6.0)	26 (5.8)	0.87
Reducing salt intake in your diet	77 (30.8)	60 (29.9)	136 (30.2)	0.83
Reducing alcohol intake	16 (6.4)	18 (9.0)	34 (7.5)	0.31
Losing weight	3 (1.2)	1 (0.5)	4 (0.9)	0.43
All of the above	0 (0.0)	0 (0.0)	0 (0.0)	n/a
I don't know	59 (23.6)	42 (20.9)	101 (22.4)	0.49
7. High blood pressure can worsen or increase				
The risk of a heart attack	12 (4.8)	7 (3.5)	19 (4.2)	0.49
The risk of stroke	115 (46.0)	64 (31.8)	179 (39.7)	0.002
The risk of kidney problems	1 (0.4)	4 (2.0)	5 (1.1)	0.11
All the above	3 (1.2)	0 (0.0)	3 (0.7)	0.12
I don't know	116 (46.4)	128 (63.7)	244 (54.1)	0.0003

of hypertension would be expected to increase predisposition to hypertension via genetic pathways, the reasons for the paradoxical protective association between hypertriglyceridemia and hypertension are not immediately apparent to us. We consider this finding unexpected given that hypertriglyceridemia was significantly associated with hypertension in a Polish HIV cohort⁴⁰ and in the general population.⁴¹ In the Polish HIV cohort,⁴⁰ the authors noted though that hypertriglyceridemia was highly associated with protease inhibitor (PI)-based cART, but in this study,

>98% of cART-exposed PLWH were on non-nucleoside reverse transcriptase inhibitor (NNRTI)-based cART.

Among study participants, only 40% on cART and about 45% who were cART-naive with hypertension were receiving antihypertensive medications with BP control rates slightly but non-significantly better in the cART-naive cohort. This observation highlights an unmet need for comprehensive cardiovascular risk management programs among PLWH attending HIV clinics in Ghana and perhaps in other countries of Africa. Indeed, a particularly worrying finding among

our study was that participants with PLWH on cART had low level of knowledge, attitudes, and practices on hypertension compared with those PLWH not on cART. On average, PLWH on cART had had their HIV diagnosis for about 8 years and have had frequent contacts with the health care delivery system. The frequent visits by PLWH to hospital for care represent an important opportunity for education on CVD risk prevention and management. Low levels of awareness of hypertension fester poor control, leading to its devastating outcomes in LMICs. Given the high frequency of adiposity and lipid abnormalities observed in the cohort, evidence-based treatment guidelines together with strengthening health care systems are urgent priorities. An essential ingredient to achieving this goal is identifying the individual, health care-level and systemic-level barriers to CVD risk management within the specific context of the HIV population. A key barrier to surmount would be sustained financing for the purchase of medications for CVD prevention among patients with HIV given that cART is highly subsidized but CVD preventive medicines are not. Furthermore, enhancing adherence to CVD medicines through mobile health technology as has been shown in the context of stroke in Ghana^{42,43} would all require systematic testing through clinical trials to assess their efficacy and potential implementation in our setting. On a much broader scale, our previous report shows a highly prevalent but poorly controlled hypertension rate in the general population based on evidence gleaned from our HIV-negative sample.²² This may explain why we found that HIV per se was not to be independently associated with stroke occurrence in a low endemic country such as Ghana,⁴⁴ although the burden of stroke and poor outcomes continue to rise in the subregion⁴⁵⁻⁴⁸ due to a myriad of factors hampering the control of key CVD risk factors.⁴⁹

4.1 | Strengths and limitations

No causal inferences can be drawn from our study given its cross-sectional design. Our inclusion criterion was an age cutoff of 30 years and above to improve our yield of adults at higher risk of CVD, and we believe this might have contributed to the higher rates of hypertension overall in our study population due to exclusion of lower age groups. However, our primary focus for the present analysis was to compare the relative risk of hypertension in PLWH on cART compared with PLWH cART-naïve. Matching for sex was achieved, but the age among PLWH on cART was significantly higher than those of PLWH who are cART-naïve. We addressed this limitation by performing unconditional logistic regression analysis, but there may still be unmeasured confounders. Further prospective studies are needed to evaluate the determinants and outcomes of hypertension in the HIV population in Ghana. Importantly, the development and implementation of CVD guidelines for screening, detection, prevention, and treatment of the key cardiovascular risk factors among HIV population in SSA is urgent, given the potential pharmacokinetic and pharmacogenetic interactions between cART and classes of CVD medications such as lipid-modifying agents and antihypertensive agents.

In conclusion, 30% Ghanaians living with HIV have hypertension which is associated with increasing age and obesity. A comprehensive strategy based on implementation of high quality, culturally tailored, evidence-based interventions to address the rising cardiovascular risk among PWH in Ghana and indeed across SSA is an urgent priority.

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CONFLICT OF INTEREST

All authors have no conflicts to declare.

AUTHOR CONTRIBUTIONS

FSS, CJ, and BO were involved in developing the study concept and design. All authors were involved in data acquisition, data management, and interpretation of results. Data analysis was performed by FSS. This submission was drafted by FSS; all other authors were involved in editing and review. All authors have approved the final version of this submission.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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