Hypertension and associated factors among patients attending HIV clinic at Korle-Bu Teaching Hospital

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SUMMARY

Objectives: This study determined the prevalence of hypertension and its associated factors among patients attending the HIV clinic at the Korle-Bu Teaching Hospital (KBTH).

Design: A hospital-based cross-sectional study was conducted at KBTH. The prevalence of hypertension was estimated among study participants, and socio-demographic, lifestyle, anthropometric, metabolic and HIV/ART-related factors associated with hypertension were determined by logistic regression modelling.

Setting: Study participants were recruited from the HIV clinic at the KBTH.

Participants: A total of 311 Persons Living with HIV were recruited as study participants

Interventions: Simple random sampling technique was used to recruit study participants. A questionnaire adapted from the WHO STEPwise approach to chronic disease risk-factor surveillance was used to collect study participants' data.

Results: The prevalence of hypertension was 36.7%, and the factors associated with hypertension were increasing age, positive family history of hypertension, minimal exercising, current BMI ≥25.0 kg/m^2, total cholesterol level ≥5.17 mmol/L, exposure to anti-retroviral therapy (ART) and increasing duration of ART exposure.

Conclusions: This study shows a high prevalence of hypertension among patients attending the HIV clinic at KBTH, associated with exposure to ART and increasing duration of this exposure. Blood pressure monitoring should move from routine to a more purposeful screening of patients for hypertension. Patients with the identified risk factors should be encouraged to have regular blood pressure measurements at home and not only when they visit the HIV clinic.

Keywords: Hypertension, HIV, Persons Living with HIV, Anti-retroviral therapy, Korle-Bu Teaching Hospital
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INTRODUCTION

Management of HIV/AIDS has gone through a series of changes over the three decades of the HIV epidemic. The chronic nature of HIV infection requires lifelong ART to suppress HIV viral replication, reducing morbidity and mortality continuously. However, ART is restricted by treatment barriers such as complex dosing, drug-drug interactions, toxicities and metabolic complications. These metabolic complications are also risk factors for morbid conditions like hypertension, type II diabetes and dyslipidaemia.[1]

Therefore, a virtually limitless number of drug combinations may be taken by patients undergoing treatment for HIV infection with co-morbid conditions. This markedly increases the risk of drug interactions leading to possible adverse drug reactions, resulting in medication non-adherence, treatment failure and poor response rate of patients to ART.

Available data suggests that in sub-Saharan Africa (SSA), chronic cardiovascular diseases (CVDs) are increasing among PLWH[2] and are recognised as a major

public health problem. Consequently, medical care for PLWH focuses more on controlling and preventing age- and metabolic-related co-morbidities. There is evidence that both HIV infection and ART are risk factors for developing non-communicable diseases (NCDs) in resource-limited settings, including the likelihood of developing chronic pathologies.[3]

In SSA, there is ongoing demographic change, with several populations showing an increase in life expectancy and an ageing population. In addition, there is an epidemiologic transition in terms of disease burden from infectious to non-communicable diseases like CVDs. This has resulted in several patients Living with HIV as a chronic infectious disease with NCD co-morbidities like diabetes, kidney disease and hypertension.[4] The prevalence of NCDs is also increasing rapidly[5], bringing interaction between HIV, ARVs and hypertension in the PLWH population. Hypertension as a co-morbidity in PLWH has become an important public health challenge as it influences patient management and service delivery at HIV clinics and is associated with increased mortality in PLWH.[6] Although there are increasing worldwide concerns of co-morbidity among PLWH, less is known about its burden in resource-limited settings. In resource-limited settings, additional research is needed to understand their risk and impact better and identify optimal models of care to address this challenge in the areas where most older PLWHs will be receiving care. This study determined the prevalence of hypertension and its associated factors among patients attending the HIV clinic at KBTH in Accra, Ghana. This will help identify PLWH on ART who could benefit from interventions to prevent or delay the onset of complications of hypertension and thereby improve the overall quality of life.

METHODS

Study design and population

A hospital-based cross-sectional study was conducted from February 2016 to May 2016. The study population comprised 20,000 HIV-positive patients who attended the HIV clinic, and the sampling frame was the electronic register of patients. The patient population (as at the time the study was conducted) was made up of about 11,000 on ART (ART-exposed), with the rest not yet on ART (ART-naïve). ART-exposed was defined as administering either two nucleosides reverse transcriptase inhibitors -NRTI (or one NRTI and one nucleotide reverse transcriptase inhibitor) + one non-nucleoside reverse transcriptase inhibitors-NNRTI or 2 NRTIs (or one NRTI and one NtRTI) + one protease inhibitor. ART-naïve were patients yet to initiate ART at the time of the study. Each patient was scheduled to attend the clinic at least once every three months for clinical assessment and medication dispensing (for patients on ARVs). PLWH aged 18 years and above, non-pregnant (for females) and attending the HIV clinic for at least six months were considered for inclusion in the study. Patients excluded from the study were patients with a prior diagnosis of hypertension before HIV infection diagnosis, patients with suboptimal adherence to HIV clinic follow-up visits or ART medication <95% (Adherence was measured using the proportion of days covered-PDC)[7], patients in hospitalisation and patients diagnosed with AIDS.

Sample size

A minimum sample size of 308 was calculated based on estimating a population parameter for cross-sectional studies[8] using the prevalence of hypertension in PLWH previously reported as 25.6%.[9] A total of 311 PLWH were recruited as study participants.

Sampling procedure and data collection

A simple random sampling technique was used to select study participants as follows. The sampling unit was individuals attending the HIV clinic. The maximum cycle of a patient attending the HIV clinic is three months, i.e., a patient is likely to present to the clinic at least once every 36-clinic days. The sampling was done to give every patient an equal chance of being represented; hence, the number of patients sampled per clinic day was eight. Computer generated random sequence of eight unique code numbers was generated from the sampling frame (list of patients booked for a clinic day) for each clinic day for 40 clinic days, and these were the patients recruited into the study. A questionnaire adapted from the WHO STEPwise approach to chronic disease risk-factor surveillance[10] was used to collect study participants' data. In addition, other relevant clinical characteristics were obtained from the study participant's medical history record (clinical folder). The questionnaire was administered to study participants to collect data on socio-demographic characteristics, life-style characteristics and family history of cardiovascular disease. Blood pressure and anthropometric measurements were made, and fasting blood samples were taken for metabolic/biochemical parameters. Current blood pressure readings were measured and categorised per WHO and European Society of Hypertension/European Society of Cardiology recommendations.[11] Hypertension was defined as current systolic blood pressure (sBP) ≥140 mmHg or diastolic blood pressure (dBP) ≥90 mmHg on two different days and/or self-reported/medical record history of current antihypertensive therapy.[11] BMI was calculated using the Quetelet index.[12] Abdominal obesity (waist-to-hip ratio) was defined as a waist-to-hip ratio of ≥0.85 for women and a waist-to-hip ratio of ≥0.90 for men.[13] Abdominal obesity (waist circumferences) was defined as >88 cm for women and waist circumference >102 cm for men.[13]

Fasting plasma glucose was classified according to the American Diabetes Association guidelines.[14] The Estimated glomerular filtration rate (eGFR) was estimated and classified according to the CKD-EPI creatinine equation.[15] Total cholesterol, HDL-Cholesterol, LDL-Cholesterol and Triglycerides were estimated and classified using the National Cholesterol Education Program and Adult Treatment Panel III (NCEP/ATP III) guidelines.[16] HIV and ART-related data were extracted from the clinical folders of the study participants. ART exposure was categorised into ART-exposed and ART-naïve. ART-exposed was defined as the administration of either two NRTIs (or one NRTI and one NtRTI) + one NNRTI or 2 NRTIs (or one NRTI and one NtRTI) + one PI. The prevalence of hypertension was estimated among the study participants, and socio-demographic, lifestyle, anthropometric, metabolic and HIV/ART-related factors associated with hypertension were determined by logistic regression modelling.

Data management and statistical analysis

Stata® 14 software was used to analyse the data. Continuous variables were reported as mean ± SD or median with interquartile range if not normally distributed. The prevalence of hypertension was compared among subgroups using the two-proportion Z-test. A logistic regression analysis was carried out to determine hypertension-related factors. The preliminary bivariable analysis was designed to determine the associated factors grouped under socio-demographic and lifestyle factors, anthropometric and metabolic/biochemical factors and HIV /ART-related factors. After that, a multivariable logistic regression model was generated using the purposeful selection of the covariates method.[17] The performance of the final model was assessed on "calibration" using the Hosmer-Lemeshow goodness-of-fit test statistic and on discrimination using the Receiver Operating Characteristics (ROC) area under the curve (AUC). The discrimination of the variables was considered; poor if AUC < 0.6, moderate if AUC is 0.60-0.80, good if AUC is 0.81-0.99 and perfect if AUC=l.00.[18]

RESULTS

A total of 311 PLWH were recruited as study participants, comprised of 252 ART-exposed (with 13.9%, n=35 on PI-based ART) and 59 ART-naïve. This was made up of 76.2% females. Most study participants were 40 years old and above (73.0%, n=227). The overall prevalence of hypertension in 311 study participants was 36.7% (95% CI, 31.3-42.3) (Table 1). The prevalence of hypertension in study participants aged ≥40 years (40.5%, [95% CI, 34.1-46.9]) was significantly higher compared with the prevalence in study participants aged <40 years (26.2%, [95% CI, 16.8-35.6]) (p=0.020). The prevalence of hypertension in ART-exposed study participants (41.3% [95% CI, 35.2-47.3]) was significantly higher compared with the ART-naive study participants (16.9%, [95% CI, 7.4-26.5]) (p<0.001) (Table 1).

Table 1 Prevalence of hypertension in study participants

Group	Total number (N)	Number of hypertensives (n)	Prevalence [95% CI]	p-value
All	311	114	36.7 [31.3-42.3]	-
Age group				
<40 years	84	22	26.2 [16.8-35.6]	0.020
≥40 years	227	92	40.5 [34.1-46.9]	
Sex				
Male	74	30	40.5 [29.4-51.7]	0.427
Female	237	84	35.4 [29.4-41.5]	
ART exposure				
ART-naive	59	10	16.9 [7.4-26.5]	<0.001
ART-exposed	252	104	41.3 [35.2-47.3]	

CI=Confidence interval; ART= Anti-retroviral Therapy

Tables 2, 3 and 4 show the bivariable logistic regression analysis results of factors associated with hypertension. Increasing age, inadequate exercising, employment status and family history of cardiovascular disease were associated with hypertension in the bivariable analysis (Table 2). Table 3 shows that a current body mass index of ≥25.0 kg/m^2, elevated levels of total cholesterol and LDL-cholesterol and reduced levels of estimated glomerular filtration rate (eGFR) were associated with hypertension in the bivariable analysis (Table 3). HIV/ART-related factors associated with hypertension in the bivariable analysis were exposure to ART and duration of both HIV infection and ART exposure (Table 4).

Table 2 Bivariable analysis of socio-demographic and lifestyle factors associated with hypertension in participants

		Blood pressure status			
Characteristic		**Hypertensive (N=114)**	**Non-hypertensive (N=197)**	**Crude odds ratio**	
		n (%)[1]	n (%)[1]	**[95% CI]**	**p-value**
Age (years), median (Interquartile range)		49.0 [40.8-57.0]	42.0 [37.0-48.0]	1.07 [1.06-1.10]	<0.001
Sex	Male	30 (40.5)	44 (59.5)	1.24 [0.73-2.12]	0.427
	Female	84 (35.4)	153 (64.6)	1.00	
Educational level	Tertiary/Professional	4 (44.4)	5 (55.6)	0.96 [0.23-4.06]	0.956
	Secondary	31 (32.6)	64 (67.4)	0.58 [0.28-1.21]	0.146

		Blood pressure status			
Characteristic		**Hypertensive (N=114)**	**Non-hypertensive (N=197)**	**Crude odds ratio**	
	Basic/Primary	59 (36.2)	104 (63.8)	0.68 [0.35-1.34]	0.263
	None	20 (45.5)	24 (54.5)	1.00	
Religion	Moslem	16 (45.7)	19 (54.3)	1.53 [0.75-3.11]	0.240
	Christianity	98 (35.5)	178 (64.5)	1.00	
Marital status	Single	21 (36.8)	36 (63.2)	1.12 [0.59-2.13]	0.739
	Widowed/Divorced/Separated	47 (39.2)	73 (60.8)	1.23 [0.74-2.05]	0.424
	Married/Co-habiting	46 (34.3)	88 (65.7)	1.00	
Employment status	Unemployed	20 (52.6)	18 (47.4)	2.12 [1.07-4.19]	0.032
	Employed	94 (34.4)	179 (65.6)	1.00	
Smoking status	Ever smoker	5 (38.5)	8 (61.5)	1.08 [0.35-3.40]	0.890
	Never-smoker	109 (36.6)	189 (63.4)	1.00	
Alcohol consumption	Drinker	37 (37.8)	61 (62.2)	1.07 [0.65-1.76]	0.785
	Abstainer	77 (36.2)	136 (63.8)	1.00	
Family history of CVD	Present	21 (53.8)	18 (46.2)	2.25 [1.14-4.42]	0.019
	Absent	93 (34.2)	179 (65.8)	1.00	
Fruit intake	Rare/Never	79 (79.8)	20 (20.2)	0.89 [0.49-1.62]	0.705
	Most at times	173 (81.6)	39 (18.4)	1.00	
Exercising	Rare/Never	88 (40.7)	128 (59.3)	1.82 [1.08-3.09]	0.025
	Most at times	26 (27.4)	69 (72.6)	1.00	

[1]Row percentages; CI=Confidence interval; CVD=cardiovascular disease

Table 3 Bivariable analysis of anthropometric and metabolic/biochemical factors associated with hypertension in study participants

		Blood pressure status			
Characteristic		Hypertensive (N=114)	Non-hypertensive (N=197)	**Crude odds ratio**	
		n (%)[1]	n (%)[1]	**[95% CI]**	**p-value**
Current body mass index	≥25.0 kg/m^2	67 (43.2)	88 (56.8)	1.77 [1.12-2.82]	0.017
	<25.0 kg/m^2	47 (30.1)	109 (69.9)	1.00	
Abdominal obesity (WHR)	Present	44 (38.3)	71 (61.7)	1.12 [0.69-1.80]	0.653
	Absent	70 (35.7)	126 (64.3)	1.00	
Abdominal obesity (WC)	Present	26 (45.6)	31 (54.4)	1.58 [0.88-2.83]	0.122
	Absent	88 (34.6)	166 (65.4)	1.00	
Fasting plasma glucose	Elevated	13 (41.9)	18 (58.1)	1.28 [0.60-2.72]	0.521
	Normal	101 (36.1)	179 (63.9)	1.00	
Total Cholesterol	Hypercholesterolemia	72 (44.2)	91 (55.8)	2.00 [1.24-3.20]	0.004
	Normal total cholesterol	42 (28.4)	106 (71.6)	1.00	
HDL-cholesterol	Abnormal	10 (32.3)	21 (67.7)	0.81 [0.37-1.78]	0.593
	Normal	104 (37.1)	176 (62.9)	1.00	
LDL-cholesterol	Elevated	51 (44.0)	65 (56.0)	1.64 [1.02-2.64]	0.040
	Normal	63 (32.3)	132 (67.7)	1.00	
Triglycerides	Elevated	5 (45.5)	6 (54.5)	1.46 [0.44-4.90]	0.540
	Normal	109 (36.3)	191 (63.7)	1.00	
Estimated glomerular filtration rate	Reduced	26 (54.2)	22 (45.8)	2.35 [1.26-4.38]	0.007
	Normal	88 (33.5)	175 (66.5)	1.00	

[1]Row percentages; CI=Confidence interval; HDL=High-density lipoprotein; LDL=Low-density lipoprotein; WC=Waist circumference; WHR=Waist-to-hip ratio

Table 4 Bivariable analysis of HIV/ART-related factors associated with hypertension in study participants

		Blood pressure status			
Characteristic		Hypertensive (N=114)	Non-hypertensive (N=197)	**Crude odds ratio**	
		n (%)[1]	n (%)[1]	**[95% CI]**	**p-value**
HIV sub-type	HIV-II only	1 (14.3)	6 (85.7)	0.31 [0.04-2.61]	0.280
	Mixed (Type I and II)	33 (43.4)	43 (56.6)	1.42 [0.84-2.41]	0.294
	HIV-I only	80 (35.1)	148 (64.9)	1.00	
Nadir CD4+ T-cell count	<350 cells/μL	82 (37.3)	138 (62.7)	1.10 [0.66-1.82]	0.726
	≥350 cells/μL	32 (35.2)	59 (64.8)	1.00	
Current CD4+ T-cell count	<350 cells/μL	32 (39.0)	50 (61.0)	1.15 [0.68-1.93]	0.604
	≥350 cells/μL	82 (35.8)	147 (64.2)	1.00	
ART exposure	ART-exposed	104 (41.3)	148 (58.7)	3.44 [1.67-7.11]	0.001
	ART-naive	10 (16.9)	49 (83.1)	1.00	
Duration of HIV infection (years), median (IQR)		9.3 [5.7-11.4]	7.0 [4.1-10.2]	1.11 [1.04-1.18]	0.002
Duration of ART administration (years), median (IQR)		7.0 [3.4-10.0]	4.3 [0.0-8.1]	1.14 [1.08-1.21]	<0.001

Presence of co-morbidities	Present	27 (39.7)	41 (60.3)	1.18 [0.68-2.05]	0.555
	Absent	87 (35.8)	156 (64.2)	1.00	

[1]Row percentages; CI= Confidence interval; ART=Highly Active Anti-retroviral Therapy; IQR=Interquartile range

Table 5 shows the multivariable logistic regression results of factors associated with hypertension using a purposeful selection of variables method. Among the socio-demographic and lifestyle factors studied, age, positive family history of cardiovascular disease and exercising were significantly associated with hypertension (p<0.05) (Table 5). Current body mass index of ≥25.0 kg/m^2 and abdominal obesity due to high waist circumference were also significantly associated with hypertension (p<0.05). The presence of hypercholesterolemia was significantly associated with hypertension (aOR=2.86 [95% CI: 1.30-6.28]; p=0.009) but not elevated levels of LDL-cholesterol (p=0.365) in the multivariable logistic regression model (Table 5). Study participants who were ART-exposed had increased odds of hypertension compared with those who were ART-naive (aOR=5.84 [95% CI, 2.23-15.31]; p<0.001) and the odds of hypertension increases by 15% (95% CI, 1.09-1.22; p=001) for every one-year increase in ART administration (Table 5).

Table 5 Multivariable logistic regression analysis of factors associated with hypertension

Characteristic	Adjusted odds ratio [95% CI]	p-value
Age (years)	1.10 [1.06-1.14]	**<0.001**
Family history of hypertension/CVD		
Present	2.23 [1.02-4.86]	***0.045***
Absent	1.00	
Exercising		
Rare/Never	1.94 [1.06-3.55]	***0.032***
Most at times	1.00	
Current body mass index		
≥25.0 kg/m^2	2.18 [1.24-3.83]	***0.007***
<25.0 kg/m^2	1.00	
Abdominal obesity (waist circumference)		
Present	2.15 [1.08-4.27]	***0.029***
Absent	1.00	
Total cholesterol		
Hypercholesterolemia	2.86 [1.30-6.28]	***0.009***
Normal total cholesterol	1.00	
LDL-cholesterol		
Elevated	0.69 [0.32-1.53]	0.365
Normal	1.00	
ART exposure		
ART-exposed	5.84 [2.23-15.31]	***<0.001***
ART-naive	1.00	
Nadir CD4+ T-cell count		
≤350 cells/µL	0.51 [0.25-1.04]	0.064
>350 cells/µL	1.00	
Duration of ART administration (years)	1.15 [1.09-1.22]	***0.001***
Duration of HIV infection (years)	1.05 [0.97-1.13]	0.194

CI=Confidence interval; CVD=cardiovascular disease; ART= Anti-retroviral Therapy; LDL=Low-density lipoprotein

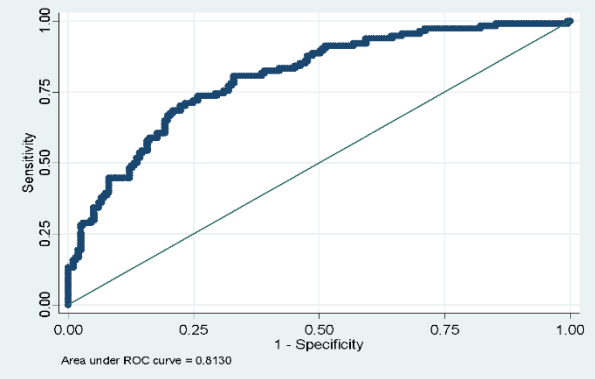

Figure 1 Receiver operating characteristics for "calibration" of the multivariable logistic regression model of factors associated with hypertension.

Post-estimation analysis indicated that the generated model was "good" on "discrimination" with an area under the receiver operating characteristics curve of 0.81 (95% CI, 0.75-0.85; p<0.001) (Figure 1). In terms of "calibration", the generated model gave a Hosmer-Lemeshow goodness-of-fit test χ^2 value of 4.49 (p=0.810), indicating no evidence of lack of goodness of fit between the predicted probabilities and the "true" probabilities.

DISCUSSION

The present study revealed that the prevalence of hypertension in patients attending the HIV clinic at KBTH in Accra was 36.7%. Hypertension is the leading risk factor for CVD and cerebrovascular mortality [19] and has been reported to be common among PLWH. [20,21] Several prevalence figures of hypertension in PLWH have been reported globally, ranging from 19.9% in Brazil [22] to 31.5% in Southern America Cohort.[23] Results of other studies in SSA among PLWH (ART-exposed and ART-naive combined) indicate the prevalence of hypertension ranging from a low of 14.0% in Botswana to a high of 32.0% in Kenya.[24] In Ghana, the reported prevalence of hypertension among PLWH on ART and ART-naïve were 36.9% and 23.4%, respectively.[20]

In the present study, the 41.3% prevalence of hypertension in ART-exposed study participants was significantly higher (p<0.001) compared with the ART-naive group and is comparable with other studies reported in SSA of 65% in Botswana [25], 38.0% in Cameroon [26], 34.9% in Zimbabwe [27] and 36.9% in Ghana.[20] Whilst some studies, both in Europe and SSA, have indicated no significant difference in hypertension prevalence between ART-ex-

posed and ART-naive patients [28], other studies have indicated otherwise.[20,26] A previous study conducted in Ghana determining the prevalence of hypertension in ART-exposed PLWH indicated a systolic hypertension prevalence of 15.2% and a diastolic hypertension prevalence of 23.8%.[9] Whilst the results of this study are higher than that reported by Ngala and Fianko[9], this could be attributed to the fact that the present study indicated a mean duration of ART exposure of 84 months and was conducted in the largest cohort of HIV-care in Ghana. Duration of ART exposure has been shown to be associated with hypertension in other studies.[21,27]

Results from the present study indicate that factors associated with hypertension were increasing age, family history of cardiovascular disease/hypertension, exercising, body mass index and abdominal obesity. Other factors were total cholesterol, exposure to ART and duration of exposure to ART. Increasing age is a well-known risk factor for hypertension in the general population, particularly those 40 years and above. In the present study, the odds of hypertension increase by 10% for every additional one-year increase in age. This result is comparable and consistent with other studies conducted in PLWH in both developed [29,30] and developing countries [26,28,31,] including Ghana.[20] Hejazi et al., [32] reported a 7% increase in odds of hypertension for every one-year increase in age, which is comparable with the results of the present study, whilst Sarfo et al. reported an adjusted odds ratio of 2.08 per 10 years to increase in age.[20] The contribution of ageing to the pathogenesis of hypertension has been attributed to arterial stiffness owing to reduced elasticity of the large arteries, which occurs with ageing.[33] This reduced elasticity is attributed to smooth-muscle hypertrophy and thinning, collagen deposition, fragmenting and fracture of the elastin fibres in the arteries.[34] Some studies have argued about an accelerated ageing process in PLWH, but this continues to be a subject of debate and research in light of the near-normal life expectancy of PLWH in the present ART era.

A positive family history of CVD/hypertension was associated with hypertension, consistent with other studies that have associated positive family history of hypertension with increased odds of hypertension in PLWH.[20,21] Although some studies have reported no such association[26], the fact that there are several reports on the interaction between genetics, renal dysfunction and the resultant salt and water retention imbalance which leads to hypertension in the general population [33] supports the results of this study.

Several epidemiological studies have demonstrated the relevance of regular physical exercise in reducing the incidence of hypertension in the general population.[35]

The results of the present study are consistent with the knowledge that physical inactivity is a risk factor for hypertension and is comparable with the results of other studies conducted in PLWH in SSA.[27] Regular physical exercise is proposed to reduce the incidence of hypertension through several mechanisms, including a decrease in oxidative stress (and reactive oxygen species), a decrease in inflammation, body weight and an increase in endothelial function. [35]

Concerning the anthropometric parameters investigated in this study, BMI ≥25.0 kg/m^2, and abnormal waist circumference (as a measure of abdominal obesity) was established to be associated with hypertension. Several epidemiological studies have established overweight/obesity as a risk factor for the incidence of hypertension in the general population and among PLWH.[29] Several studies among PLWH in SSA have also reported increased odds of hypertension in overweight/obese individuals.[20,21,26,27] Results of the present study, which indicated an increased odds of hypertension of 2.18 (95% CI, 1.24-3.83) in overweight/obese individuals is comparable to a report by Bloomfield et al., which studied a cohort of 12,194 PLWH in Kenya and indicated an increased odds of hypertension of 2.42 (95% CI, 1.88-3.09) in individuals with BMI ≥25.0 kg/m^2.[6] Many studies have drawn attention to increasing prevalence of overweight/obesity in PLWH, and this has been attributed to both a general age-related increase in body weight [36] and a tendency of PLWH to be overweight to remove or reduce suspicion and its accompanying stigmatisation of HIV infection.[37] Abnormal waist circumference, a measure of abdominal obesity or body fat distribution, was found to be associated with hypertension in this study. Absolute waist circumference >102 cm (in men) and >88 cm (in women) is classified as abdominal obesity.[38] A large body of scientific evidence abounds in the role played by abdominal obesity in the aetiology of cardio-metabolic abnormalities, including hypertension, dyslipidaemia, insulin resistance and type 2 diabetes. Mediation analysis for the lineal model conducted in a study by Nduka et al. emphasised the strong impact of central fat distribution in mediating the causal pathway between ART and increased blood pressure.[39] This observation is supported by previous studies indicating the mediation role played by waist circumference in the association between ART and hypertension.[40]

The present study is, therefore, consistent with the study by Nduka et al. [39] (as both ART and abdominal obesity were associated with hypertension) and other studies.[22] The results from the present study indicate an association between hypercholesterolemia and hypertension.

This is consistent with several reports associating hypercholesterolemia with an increased risk of hypertension in the general population[41] and among PLWH.[42]

An important finding of the present study is the association between ART exposure and hypertension. Although literature abounds in studies on the association between ART exposure and the risk of hypertension, the results have been inconclusive. However, a systematic review with a meta-analysis of 39 studies involving 44,903 participants concluded that systolic and diastolic blood pressure values were significantly higher among ART-exposed patients than ART-naive patients.[43] This study also reported a significantly increased risk of hypertension in ART-exposed patients compared with treatment-naive patients. Therefore, this study's findings are consistent with several other studies in SSA [26,44] and other sub-regions.[30] The amount of literature, including one systematic review and one propensity score-matching analysis, supporting the association between ART and hypertension is overwhelming, yet other studies have reported the lack of association between ART and hypertension in SSA. [38] The present study reported an adjusted odds ratio of 5.84 (95% CI, 2.23-15.31), comparable with a similar study conducted elsewhere in Ghana which reported an increased odds of hypertension of 5.00 in ART-exposed individuals compared with ART-naive individuals.[9] Various mechanisms have been postulated to account for the association between ART exposure and hypertension, including premature and/or accelerated development of atherosclerosis leading to the blockage of the blood vessel lumen, ART-induced immune activation, increased intestinal bacterial translocation and low-grade inflammation. These developments may promote atherosclerosis, increased arterial stiffness[45], involvement of ARVs in lipid and glucose metabolism resulting in lipodystrophy syndrome and the activation of the renin-angiotensin system. Another finding in this study is the association between the length of anti-retroviral usage and the increased risk of hypertension. This result is consistent with other reports of an increased risk of hypertension with increasing duration of ART among PLWH in SSA [27,44] and the systematic review and meta-analysis results.[43]

Inferences from the results of this study should be done in the context of the study design, as temporality cannot be established. There is no information on the timing of the outcome relative to the exposures hence this limits any causal inference, including reverse causation (outcome-changing exposure) for some of the factors found to be associated with hypertension in the regression modelling analysis. However, in an effort to reduce the effect of reverse causation for HIV/ART-related factors, potential study participants were excluded if they have been diagnosed with hypertension prior to HIV infection diagnosis/initiation of ART. Another limitation of this study is that data were based on measurements taken at one point according to clinical indications and will be assumed to reflect their chronic condition. Study participants did not receive a definitive diagnosis of hypertension based on the measurements, but the 2012 WHO Stepwise approach to chronic disease risk-factor surveillance instrument was used. In addition, factors like family history of CVD/hypertension, smoking, alcohol use, and physical inactivity were based on study participants' self-report. Thus, respondents can be tempted to present themselves more favourably by giving health-conscious answers in "social desirability" [26]. However relevant that is, and to the best of our knowledge, this is the first study conducted in KBTH HIV Clinic, Ghana's largest HIV cohort, to assess the general risk of hypertension among PLWH using a purposeful selection of covariates method in regression modelling. Regarding policy-relevant recommendations, further research into the feasibility of integrating NCD care into HIV-care requirements so that patients need not seek this care from clinics where they may feel uncomfortable disclosing their HIV status. In addition, blood pressure monitoring should move from being routine at the KBTH HIV clinic to a more purposeful screening of patients for hypertension, and patients should be encouraged to have regular blood pressure measurements at home and not only when they visit the clinic. In addition, waist circumference as a marker of abdominal obesity should be regularly measured in patients attending the HIV clinic at the KBTH in Accra.

CONCLUSION

The outcome of this study clearly shows a high prevalence of hypertension in patients attending the HIV clinic at the KBTH. This observed high prevalence of hypertension could be due to an "unmasking" of an already high predisposition to hypertension by the HIV infection itself, the initiation of ARVs and an ageing HIV cohort. Multivariable regression modelling to hypertension-associated factors indicated that in addition to the known traditional risk factors for hypertension, HIV-related factors, i.e., exposure to ART and duration of this ART exposure, were also associated with hypertension.

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REFERENCES

1. Busari OA, Busari, O. E. Cardiac diseases and metabolic syndrome in HIV infection. *Archives Medical Review Journal.* 2013;22:377-392.
2. Hyle EP, Mayosi BM, Middelkoop K, et al. The association between HIV and atherosclerotic cardiovascular disease in sub-Saharan Africa: a systematic review. *BMC Public Health.* 2017;17(1):954.
3. Fabian J, Naicker S, Goetsch S, Venter WD. The clinical and histological response of HIV-associated kidney disease to anti-retroviral therapy in South Africans. *Nephrol Dial Transplant.* 2013;28(6):1543-1554.
4. Remais JV, Zeng G, Li G, Tian L, Engelgau MM. Convergence of non-communicable and infectious diseases in low- and middle-income countries. *Int J Epidemiol.* 2013;42(1):221-227.
5. Bosu WK. Epidemic of hypertension in Ghana: a systematic review. *BMC Public Health.* 2010;10:418.
6. Bloomfield GS, Hogan JW, Keter A, et al. Blood pressure level impacts risk of death among HIV seropositive adults in Kenya: a retrospective analysis of electronic health records. *BMC infectious diseases.* 2014;14:284.
7. Ankrah DNA, Lartey M, Agyepong I, Leufkens HGM, Mantel-Teeuwisse AK. Adherence and Treatment Change among HIV/AIDS Patients in Ghana – A Nested Case Control Study. *J AIDS Clin Res* 2015; 6(10).
8. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? *Indian J Psychol Med.* 2013;35(2):121-126.
9. Ngala RA, Fianko K. Effects of HIV infection and Antiretroviral Therapy on Cardiovascular Diseases. *Trends Mol. Sci.* 2014;6:1-12.
10. (WHO) WHO. *The WHO STEPwise Approach to Chronic Disease Risk Factor Surveillance.* Geneva: World Health Organization;2008a.
11. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Journal of hypertension.* 2013;31(7):1281-1357.
12. WHO. *Physical status : The use of and interpretation of anthropometry , report of a WHO expert committee.* Geneva: World Health Organisation;1995.
13. WHO. *WHO STEPS Instrument.* Geneva, Switzerland2012.
14. American Diabetes A. Diagnosis and classification of diabetes mellitus. *Diabetes care.* 2012;35 Suppl 1:S64-71.
15. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Annals of internal medicine.* 2009;150(9):604-612.
16. National Cholesterol Education Program Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation.* 2002;106(25):3143-3421.
17. Bursac Z, Gauss, C. H., Williams, D. K. & Hosmer, D. W. Purposeful selection of variables in logistic regression. *Source Code Biol Med.* 2008;3:17.
18. Dodoo AN, Fogg C, Asiimwe A, et al. Pattern of drug utilisation for treatment of uncomplicated malaria in urban Ghana following national treatment policy change to artemisinin-combination therapy. *Malar J.* 2009;8:2.
19. (WHO) WHO. *Global Health Risks: Mortality and Burden of Dosease Attributable to Selected Major Risks.* Geneva: World Health Organisation.;2009b.
20. Sarfo FS, Nichols M, Singh A, et al. Characteristics of hypertension among people living with HIV in Ghana: Impact of new hypertension guideline. *Journal of clinical hypertension.* 2019;21(6):838-850.
21. Sarfo FS, Singh A, Tagge R, Mensah G, Ovbiagele B. Duration of anti-retroviral therapy among people living with HIV and incidence of hypertension in Ghana. *Journal of clinical hypertension.* 2020;22(12):2361-2371.
22. Arruda Junior ER, Lacerda HR, Moura LC, et al. Profile of patients with hypertension included in a cohort with HIV/AIDS in the state of Pernambuco, Brazil. *Arq Bras Cardiol.* 2010;95(5):640-647.
23. Cahn P, Leite O, Rosales A, et al. Metabolic profile and cardiovascular risk factors among Latin American HIV-infected patients receiving HAART. *Braz J Infect Dis.* 2010;14(2):158-166.
24. Nyabera RA, Yonga, G., Mwangemi, F. & Bukachi, F. Evaluation of a project integrating cardiovascular care into HIV programmes.S17. *Cardiovascular Journal of Africa.* 2011;22(S17).
25. Shapiro RL, Souda S, Parekh N, et al. High prevalence of hypertension and placental insufficiency, but no in utero HIV transmission, among women on HAART with stillbirths in Botswana. *PLoS One.* 2012;7(2):e31580.
26. Dimala CA, Atashili J, Mbuagbaw JC, Wilfred A, Monekosso GL. Prevalence of Hypertension in HIV/AIDS Patients on Highly Active Anti-retroviral Therapy (HAART) Compared with HAART-Naive

Patients at the Limbe Regional Hospital, Cameroon. *PLoS One.* 2016;11(2):e0148100.
27. Mutede BR, Magure, T., Gombe, N. T., Bangure, D., Tshimanga, M. & Mungati, M. . Prevalence and factors associated with hypertension among anti-retroviral therapy patients aged 15 years and above in Makonde Distrct, Zimbabwe, 2012: An analytic cross sectional study. . *World Journal of Cardiovascular Diseases.* 2015;5:266-277.
28. Sander LD, Newell K, Ssebbowa P, et al. hypertension, cardiovascular risk factors and antihypertensive medication utilisation among HIV-infected individuals in Rakai, Uganda. *Tropical medicine & international health : TM & IH.* 2015;20(3):391-396.
29. Medina-Torne S, Ganesan A, Barahona I, Crum-Cianflone NF. Hypertension is common among HIV-infected persons, but not associated with HAART. *Journal of the International Association of Physicians in AIDS Care.* 2012;11(1):20-25.
30. De Socio GV, Ricci E, Maggi P, et al. prevalence, awareness, treatment, and control rate of hypertension in HIV-infected patients: the HIV-HY study. *American journal of hypertension.* 2014;27(2):222-228.
31. Njelekela M, Muhihi A, Aveika A, et al. Prevalence of Hypertension and Its Associated Risk Factors among 34,111 HAART Naive HIV-Infected Adults in Dar es Salaam, Tanzania. *International journal of hypertension.* 2016;2016:5958382.
32. Hejazi N, Huang MS, Lin KG, Choong LC. Hypertension among HIV-infected adults receiving highly active anti-retroviral therapy (HAART) in Malaysia. *Global journal of health science.* 2013;6(2):58-71.
33. Oparil S, Zaman MA, Calhoun DA. Pathogenesis of hypertension. *Ann Intern Med.* 2003;139(9):761-776.
34. O'Rourke MF, Hayward, C. S. & Lehmann, E. D. Arterial stiffness. In: Hypertension. In: OPARAL SW, M. A. , ed. *A Companion to Brenner and Rector's The Kidney*. . Philadelphia: WB Saunders; 2000.
35. Diaz KM, Shimbo D. Physical activity and the prevention of hypertension. *Curr Hypertens Rep.* 2013;15(6):659-668.
36. Denue BA, Muazu, J., Gashau, W., Mbo, D. N. & Ajayi, N. A. Effects of highly active anti-retroviral therapy (HAART) on blood pressure changes and its associated factors in HAART naive HIV-infected patients in North eastern Nigeria. . *Archives of Applied Science Research.* 2012;4(3):1447-1452.
37. Edwards JK, Bygrave H, Van den Bergh R, et al. HIV with non-communicable diseases in primary care in Kibera, Nairobi, Kenya: characteristics and outcomes 2010-2013. *Transactions of the Royal Society of Tropical Medicine and Hygiene.* 2015;109(7):440-446.
38. Ogunmola OJ, Oladosu OY, Olamoyegun AM. Association of hypertension and obesity with HIV and anti-retroviral therapy in a rural tertiary health center in Nigeria: a cross-sectional cohort study. *Vasc Health Risk Manag.* 2014;10:129-137.
39. Nduka CU, Uthman OA, Kimani PK, Malu AO, Stranges S. Impact of body fat changes in mediating the effects of anti-retroviral therapy on blood pressure in HIV-infected persons in a sub-Saharan African setting. *Infect Dis Poverty.* 2016;5(1):55.
40. Antonello VS, Antonello IC, Grossmann TK, Tovo CV, Pupo BB, Winckler Lde Q. Hypertension--an emerging cardiovascular risk factor in HIV infection. *J Am Soc Hypertens.* 2015;9(5):403-407.
41. Halperin RO, Sesso HD, Ma J, Buring JE, Stampfer MJ, Gaziano JM. Dyslipidemia and the risk of incident hypertension in men. *Hypertension.* 2006;47(1):45-50.
42. Kagaruki GB, Mayige MT, Ngadaya ES, et al. Magnitude and risk factors of non-communicable diseases among people living with HIV in Tanzania: a cross sectional study from Mbeya and Dar es Salaam regions. *BMC public health.* 2014;14:904.
43. Nduka CU, Stranges S, Sarki AM, Kimani PK, Uthman OA. Evidence of increased blood pressure and hypertension risk among people living with HIV on anti-retroviral therapy: a systematic review with meta-analysis. *Journal of human hypertension.* 2016;30(6):355-362.
44. Ngala RAF, K. Effects of HIV infection and Antiretroviral Therapy on Cardiovascular Diseases. . *Trends Mol. Sci.,* . 2014;6:1-12.
45. Boccara F, Lang S, Meuleman C, et al. HIV and coronary heart disease: time for a better understanding. *J Am Coll Cardiol.* 2013;61(5):511-523.