Research Article
Volume 12:9, 2021

Journal of AIDS & Clinical Research

ISSN: 2155-6113 **Open Access**

Hypertension and Associated Factors among Patients on HIV Antiretroviral Therapy at Korle-Bu Teaching Hospital

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Abstract

Background: The chronic nature of HIV infection requires lifelong Antiretroviral Therapy (ART) to continuously suppress HIV viral replication, reducing morbidity and mortality. Management of co-morbidities is one of the major challenges associated with the multi-drug regimens used for HIV therapy. Hypertension as a co-morbidity in Persons Living with HIV (PLHIV) has become an important public health challenge and importantly influence patient management and service delivery at HIV clinics. This study determined the prevalence of hypertension among patients attending HIV clinic at the Korle-bu Teaching Hospital (KBTH) and also explored the nature of the relationship between HIV/ART and hypertension in order to help identify individuals who could benefit from interventions to prevent or delay the onset of complications of hypertension and thereby improve the overall quality of life of PLHIV

Methods: A simple random sampling technique was used to recruit study participants based on the routine clinic attendance sample frame. A questionnaire adapted from WHO STEPwise approach to chronic disease risk-factor surveillance was modified and used for the collection of study participants' data. The prevalence of hypertension was estimated among study participants. Socio-demographic, lifestyle, anthropometric, metabolic and HIV/ART-related factors associated with hypertension were determined by logistic regression modelling using the purposeful selection of covariates method.

Results: A total of 311 PLHIV were recruited as study participants. The present study revealed that the prevalence of hypertension in patients attending HIV clinic at KBTH 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 ART and increasing duration of ART exposure.

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

Keywords: Hypertension • HIV • Antiretroviral Therapy • Korle-Bu Teaching Hospital

Abbreviations: ART: Antiretroviral Therapy • ARV: Antiretroviral • CVD: Cardiovascular Disease • eGFR: Estimated Glomerular Filtration Rate • FPG: Fasting Plasma Glucose • HDL-C: High-density Lipoprotein Cholesterol • IQR: Interquartile Range • HIV: Human Immunodeficiency Virus • LDL-C: Low-density Lipoprotein Cholesterol • NACP: National AIDS Control Program/STD • PLHIV: Persons Living with HIV • SSA: sub-Saharan Africa • SD: Standard Deviation • TC: Total Cholesterol • TG: Triglycerides • WC: Waist Circumference • WHO: World Health Organization • WHR: Waist-to-hip ratio

Introduction

Management of HIV/AIDS has gone through a series of changes over three decades of HIV epidemic. A number of critical advances have been made in care and treatment of HIV positive patients and Antiretroviral therapy (ART) now reaches most of those eligible, resulting in dramatic reductions of illness and death. The chronic nature of HIV infection requires lifelong ART [1] to continuously suppress HIV viral replication, reducing morbidity and mortality. However, ART is restricted by treatment barriers such as complex dosing, drug-drug interactions and toxicities. In addition, some HIV-positive patients still require concomitant treatment with drugs for opportunistic infections and medication to treat unrelated medical conditions and/or the metabolic complications of ART [2]. These metabolic complications are also risk factors of other morbid conditions like hypertension, type II diabetes and dyslipidaemia [3]. Therefore, virtually limitless number of drug combinations may be taken by patients undergoing treatment of HIV infection with co-morbidity markedly increases the risk of drug interactions, treatment failure, medication non-adherence, poor response rate of patients to ART and adverse drug reactions. Management of co-morbidities is one of the major challenges associated with the multi-drug regimens used for HIV therapy and Cardiovascular Diseases (CVDs) are of particular concern due to Anti-retroviral (ARV) induced metabolic changes. Available data suggests that in Sub-Saharan Africa (SSA), chronic CVDs are increasing among HIV-positive patients [4] and is being recognized as a major public health problem in PLHIV [5]. Consequently, medical care for PLHIV is focusing more on control and prevention of age- and metabolic-related co-morbidities [6]. As more people in SSA begun taking antiretroviral

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Received 18 August 2021; **Accepted** 09 September 2021; **Published** 16 September 2021

treatment, mortality rates have dropped [7] and life expectancy of PLHIV has increased with studies indicating PLHIV on ART in SSA can achieve a normal life expectancy [8]. There is evidence that both HIV infection and ART as risk factors for development of Non Communicable Diseases (NCDs) in resource-limited settings including the likelihood of developing chronic pathologies like hypertension [9]. In SSA, there is ongoing demographic change with several populations showing an increase in life expectancy and an ageing population. In addition, there is epidemiologic transition in terms of disease burden from infectious diseases to non-communicable diseases like CVDs. This has resulted in several SSA populations increasingly demonstrating HIV as an infectious chronic disease like diabetes, kidney disease and hypertension [10]. Prevalence of NCDs, including hypertension are also increasing rapidly [11] bringing with it an interaction between HIV, ARVs and hypertension in the HIV-infected population. Hypertension as a co-morbidity in PLHIV has become an important public health challenge and importantly influence patient management and service delivery at HIV clinics as hypertension has been associated with mortality in PLHIV [12]. Although there are increasing worldwide concerns of co-morbidity among PLHIV and there is considerable research into the commonly occurring CVDs among PLHIV in resource-rich settings, less is known about the burden in resource-limited settings. In resource-limited settings, additional research is needed to better understand their risk and impact and identify optimal models of care to address this challenge in the areas where the majority of older PLHIV will be receiving care. This study primarily determined the prevalence of hypertension among patients attending HIV clinic at KBTH and also explored the nature of the relationship between HIV/ART and hypertension in order to help identify individuals who could benefit from interventions to prevent or delay the onset of complications hypertension and thereby improve the overall quality of life for PLHIV.

Research Methodology

Study design and population

A hospital-based cross-sectional study was conducted from February 2016 to May 2016 to determine the prevalence of hypertension among a cohort of patients attending the HIV Clinic of the KBTH in Accra, Ghana. All consenting HIV-positive patients aged 18 years and above, non-pregnant (for females) and have attended the HIV clinic for at least 6 months were eligible for recruitment into the study. Patients excluded from the study were patients with prior diagnosis of hypertension before HIV infection diagnosis or patients with sub-optimal adherence to HIV clinic follow-up visits/ART medication or patients in hospitalization/diagnosed with AIDS. Among those recruited for the cross-sectional study an unmatched case control study (hypertensive patients as cases and non-hypertensive patients as controls) was conducted to determine whether HIV/ART related factors were associated with hypertension.

Sample size

A minimum sample size was calculated based on the estimation of a population parameter for cross sectional studies [13].

$$Minimum\ sample\ size\ for\ Cross-sectional\ Study, N = \frac{(Z_{1-\frac{\alpha}{2}})^2 P(1-P)}{d^2}$$

N= Minimum sample size

P= Prevalence of hypertension in PLHIV from previous study = 25.6% [14]

$Z_{1-\frac{\alpha}{2}}$= unit normal deviate corresponding to Type I error of 5% = 1.96

d= margin of error anticipated=5.0%

Sampling procedure and data collection

A simple random sampling technique was used to recruit study participants based on routine clinic attendance. A questionnaire adapted from WHO STEPwise approach to chronic disease risk-factor surveillance [15] was modified and used for the collection of study participants' data. In addition, other relevant clinical characteristics were obtained from the medical history record (clinical folder) of the study participants. 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 taken for metabolic/biochemical parameters. Retrospective chart review for relevant clinical characteristics was obtained from medical history record (clinical folder) for each study participant. HIV and ART-related data were extracted from the clinical folders of the study participants. The prevalence of hypertension was estimated among the study participants and socio-demographic, lifestyle, anthropometric, metabolic and HIV/ART-related factors associated with hypertension was 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. Continuous variables were modelled in class or after log transformation. A logistic regression analysis was carried out to determine the factors associated with hypertension. The preliminary univariable analysis was designed to determine the associated factors as grouped under socio-demographic and life-style factors, anthropometric and metabolic/biochemical factors and HIV /ART -related factors. Thereafter, a multiple logistic regression model was generated using the purposeful selection of covariates method [16]. The performance of the final model was assessed on "calibration" using the Hosmer-Lemeshow goodness-of-fit test statistic. This was used to test the level of agreement between predicted probabilities and the 'true probabilities' using the mean of the observed outcomes within predefined groups of study participants [16]. This is done after the observations has been sorted (according to their expected probability) and partitioned into 10 groups of equal sizes. The C goodness-of-fit statistic gives a large "H" value with a corresponding small (Hosmer-Lemeshow χ^2) p-value if there is a significant difference between the observed outcome and the predicted outcome and this indicates evidence of lack of fit of the variables involved in the final model. The performance of the final model was also assessed on discrimination using the Receiver Operating Characteristics (ROC) area under the curve (AUC). This was used to verify whether a set of predictor variables in the final model were able to distinguish hypertension from non-hypertension and the AUC refers to the probability that a hypertensive person has a higher predicted probability than those who were non-hypertensive using the variables involved in the final model. 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 [17].

Results

A total of 311 PLHIV were recruited as study participants. This was made up of 76.2% females. Most of the study participants were 40 years and above (73.0%, n=227). The overall prevalence of hypertension in 311 study participants was 36.7% (95% CI, 31.3-2.3) (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).

Tables 2, 3 and 4 shows the results of univariable logistic regression analysis of factors associated with hypertension. Increasing age, inadequate exercising, employment status and presence of family history of cardiovascular disease were associated with hypertension in the univariable analysis (Table 2). Table 3 shows that 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 were associated with hypertension in the univariable analysis (Table 3). HIV/ART-related factors associated with hypertension in the univariable analysis were exposure to ART and duration of both HIV infection and ART exposure (Table 4).

Table 5 show results of the multivariable logistic regression of factors associated with hypertension using a purposeful selection of variables method. Among the socio-demographic and life-style factors studied, age, positive family

Table 1. Prevalence of hypertension in study participants.

Group	Total number (N)	Number of hypertensives (n)	Prevalence [95% CI]	p-value
All study participants	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

Table 2. Univariable analysis of socio-demographic and life-style factors associated with hypertension in study participants.

		Blood pressure status			
Characteristics		**Hypertensive (N=114)**	**Non-hypertensive (N=197)**	**Crude odds ratio**	
		n (%)	**n (%)**	**[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 (26.3)	44 (22.3)	1.24 [0.73-2.12]	0.427
	Female	84 (73.7)	153 (77.7)	1.00	
Educational level	Tertiary/Professional	4 (3.5)	5 (2.5)	0.96 [0.23-4.06]	0.956
	Secondary	31 (27.2)	64 (32.5)	0.58 [0.28-1.21]	0.146
	Basic/Primary	59 (51.8)	104 (52.8)	0.68 [0.35-1.34]	0.263
	None	20 (17.5)	24 (12.2)	1.00	
Religion	Moslem	16 (14.0)	19 (9.6)	1.53 [0.75-3.11]	0.240
	Christianity	98 (86.0)	178 (90.4)	1.00	
Marital status	Single	21 (18.4)	36 (18.3)	1.12 [0.59-2.13]	0.739
	Widowed/Divorced/Separated	47 (41.2)	73 (37.1)	1.23 [0.74-2.05]	0.424
	Married/Co-habiting	46 (40.4)	88 (44.7)	1.00	
Employment status	Unemployed	20 (17.5)	18 (9.4)	2.12 [1.07-4.19]	0.032
	Employed	94 (82.5)	179 (90.9)	1.00	
Smoking status	Ever smoker	5 (4.4)	8 (4.1)	1.08 [0.35-3.40]	0.890
	Never-smoker	109 (95.6)	189 (95.9)	1.00	
Alcohol consumption	Drinker	37 (32.5)	61 (31.0)	1.07 [0.65-1.76]	0.785
	Abstainer	77 (67.5)	136 (69.0)	1.00	
Family history of CVD	Present	21 (18.4)	18 (9.1)	2.25 [1.14-4.42]	0.019
	Absent	93 (81.6)	179 (90.9)	1.00	
Fruit intake	Rare/Never	79 (31.4)	20 (33.9)	0.89 [0.49-1.62]	0.705
	Most at times	173 (68.7)	39 (66.1)	1.00	
Exercising	Rare/Never	88 (77.2)	128 (65.0)	1.82 [1.08-3.09]	0.025
	Most at times	26 (22.8)	69 (35.0)	1.00	

CI=Confidence interval; CVD=cardiovascular disease

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). 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).

Post-estimation analysis indicated that the generated multivariable logistic 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 HIV clinic at KBTH in Accra was 36.7%. Hypertension is the leading risk factor for CVD and cerebrovascular mortality [18] and has been reported to be common among PLHIV [19]. Several prevalence figures of hypertension in PLHIV have been reported globally ranging from 19.9% in Brazil Arruda [20] to 31.5% in Southern America Cohort [21]. Results of other studies in SSA among PLHIV (ART-exposed and ART-naive combined) indicate prevalence of hypertension ranging from a low of 14.0% in Botswana to a high of 32.0% in Kenya [22].

In present study, 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 [23], 38.0% in Cameroon [24] and 34.9% in Zimbabwe [25]. Whilst some studies, both in Europe and SSA have indicated no significant difference in hypertension prevalence between ART-exposed and ART-naive patients

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

		Blood pressure status			
Characteristics		Hypertensive (N=114)	Non-hypertensive (N=197)	**Crude odds ratio**	
		n (%)	n (%)	**[95% CI]**	**p-value**
Current body mass index	≥25.0 kg/m^2	67 (58.8)	88 (44.7)	1.77 [1.12-2.82]	0.017
	<25.0 kg/m^2	47 (41.2)	109 (55.3)	1.00	
Abdominal obesity (WHR)	Present	44 (38.6)	71 (36.0)	1.12 [0.69-1.80]	0.653
	Absent	70 (61.4)	126 (64.0)	1.00	
Abdominal obesity (WC)	Present	26 (22.8)	31 (15.7)	1.58 [0.88-2.83]	0.122
	Absent	88 (77.2)	166 (84.3)	1.00	
Fasting plasma glucose	Elevated	13 (11.4)	18 (9.1)	1.28 [0.60-2.72]	0.521
	Normal	101 (88.6)	179 (90.9)	1.00	
Total Cholesterol	Hypercholesterolemia	72 (63.2)	91 (46.2)	2.00 [1.24-3.20]	0.004
	Normal total cholesterol	42 (36.8)	106 (53.8)	1.00	
HDL-cholesterol	Abnormal	10 (8.8)	21 (10.7)	0.81 [0.37-1.78]	0.593
	Normal	104 (91.2)	176 (89.3)	1.00	
LDL-cholesterol	Elevated	51 (44.7)	65 (33.0)	1.64 [1.02-2.64]	0.040
	Normal	63 (55.3)	132 (67.0)	1.00	
Triglycerides	Elevated	5 (4.4)	6 (3.1)	1.46 [0.44-4.90]	0.540
	Normal	109 (95.6)	191 (96.9)	1.00	
Estimated glomerular filtration rate	Reduced	26 (22.8)	22 (11.2)	2.35 [1.26-4.38]	0.007
	Normal	88 (77.2)	175 (88.8)	1.00	

CI=Confidence Interval; HDL=High-Density Lipoprotein; LDL=Low-Density Lipoprotein; WC=Waist Circumference; WHR=Waist-To-Hip Ratio

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

		Blood pressure status			
Characteristics		Hypertensive (N=114)	Non-hypertensive (N=197)	**Crude odds ratio**	
		n (%)	n (%)	**[95% CI]**	**p-value**
HIV sub-type	HIV-II only	1 (0.9)	6 (3.1)	0.31 [0.04-2.61]	0.280
Mixed (Type I and II)		33 (28.9)	43 (21.8)	1.42 [0.84-2.41]	0.294
	HIV-I only	80 (70.2)	148 (75.1)	1.00	
Nadir CD4+ T-cell count	<350 cells/μL	82 (71.9)	138 (70.1)	1.10 [0.66-1.82]	0.726
	≥350 cells/μL	32 (28.1)	59 (29.9)	1.00	
Current CD4+ T-cell count	<350 cells/μL	32 (28.1)	50 (25.4)	1.15 [0.68-1.93]	0.604
	≥350 cells/μL	82 (71.9)	147 (74.6)	1.00	
ART exposure	ART-exposed	104 (91.2)	148 (75.1)	3.44 [1.67-7.11]	0.001
	ART-naive	10 (8.8)	49 (24.9)	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 (23.7)	41 (20.8)	1.18 [0.68-2.05]	0.555
	Absent	87 (76.3)	156 (79.2)	1.00	

CI= Confidence Interval; ART=Highly Active Anti-Retroviral Therapy; IQR=Interquartile Range

Table 5. Multivariable logistic regression analysis of factors associated with hypertension.

Characteristics	**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

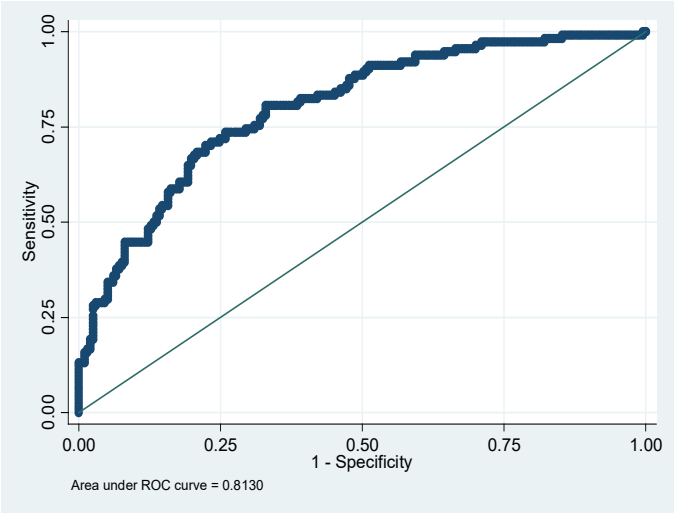

Figure 1. Receiver operating characteristics for "calibration" of multivariable logistic regression model of factors associated with hypertension.

[26], other studies have indicated otherwise [24]. It is important to note that a previous study conducted in Ghana determining the prevalence of hypertension in ART-exposed PLHIV indicated a systolic hypertension prevalence of 15.2% and a diastolic hypertension prevalence of 23.8% [14]. Whilst the results of this study is higher than the study reported by Ngala and Fianko, this could be attributed to the fact that present study indicated a mean duration of ART exposure of 84 months and was conducted in the largest cohort of HIV-care in Ghana [14]. Duration of ART exposure has been shown to be associated with hypertension in several studies [14,25].

Using purposeful selection of covariates method in the multivariable regression modelling, results from 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 general population and this is particularly evidenced in people of 40 years and above. In present study, the odds of hypertension increases by 10% for every additional one-year increase in age. This result is comparable and consistent with other studies conducted in PLHIV in both developed [27,28] and developing countries [14,26,29,30]. Hejazi et al. [31] had reported of a 7% increase in odds of hypertension for every one-year increase in age, which is comparable with the results of the present study. 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 [32]. This reduced elasticity is attributed to smooth-muscle hypertrophy and thinning, collagen deposition, fragmenting and fracture of the elastin fibres in the arteries [33]. Some studies have argued about an accelerated ageing process in PLHIV, but this continues to be a subject of debate and research in the light of the near-normal life expectancy of PLHIV in the present ART era.

In present study, a positive family history of CVD/hypertension was associated with hypertension. This finding is consistent with other studies that have associated positive family history of hypertension with increased odds of hypertension in PLHIV [20]. Although some studies have reported no such association [24], 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 [32] supports the results of this study.

Exercising, a life-style factor was established to be associated with hypertension in this study. Several epidemiological studies have demonstrated the relevance of regular physical exercise in reducing the incidence of hypertension in the general population [34]. The results of the present study are therefore consistent with the knowledge that physical inactivity is a risk factor for hypertension and is comparable with the results of other studies conducted in PLHIV in SSA [25]. Regular physical exercise is proposed to reduce the incidence of hypertension through several mechanisms including decrease in oxidative stress (and reactive oxygen species), decrease in inflammation, body weight and increase in endothelial function [34].

Of the anthropometric parameters investigated in this study, BMI ≥25.0 kg/m^2, and abnormal waist circumference (as a measure of abdominal obesity) were 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 PLHIV [27]. Several studies among PLHIV in SSA have also reported of increased odds of hypertension in overweight/obese individuals [24,25]. 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 HIV-positive study participants 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 [12]. Many studies have drawn attention to increasing prevalence of overweight/obesity in HIV-positive individuals and this has been attributed to both a general age-related increase in body weight [35] and a tendency of PLHIV to be overweight to remove or reduce suspicion and its accompanying stigmatisation of HIV infection [36].

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 [37]. A large body of scientific evidence abounds of the role played by abdominal obesity in the aetiology of cardio-metabolic abnormalities including hypertension, dyslipidaemia, insulin resistance and type 2 diabetes [38]. A mediation analysis for 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 that have indicated the mediation role played by waist circumference in the association between ART and hypertension [40]. The present study is thus consistent with the study by Nduka et al. [39] (as both ART and abdominal obesity were associated with hypertension) and other studies [20].

Reports from the present study indicate an association between hypercholesterolemia and hypertension. Results from the present study are thus consistent with several reports which associate hypercholesterolemia with an increased risk of hypertension in the general population [41] and among PLHIV [42]. The pattern of distorted lipid profile among PLHIV is seen mostly in patients on protease inhibitors and PI-based regimens have been shown to be atherogenic more than non PI-based regimens [43].

Other findings of the present study are the association between exposure to ART and hypertension and the association between duration of ART and hypertension. Although literature abounds in studies on the association between ART exposure and the risk of hypertension, the results have been inconclusive. A systematic review with meta-analysis of 39 studies involving 44,903 participants however concluded that both systolic and diastolic blood pressure values were significantly higher among ART-exposed patients compared with treatment-naive patients [44]. This study also reported of a significant increased risk of hypertension in ART-exposed patients compared with treatment-naive patients. The findings of this study is therefore consistent with several other studies in SSA [14,24] and other sub-regions [28]. While it may be overwhelming to notice the amount of literature, including one systematic review and one propensity score-matching analysis, supporting the association between ART and hypertension, other studies have reported the lack of association between ART and hypertension in SSA [37] and in other sub-regions [20]. The present study reported an adjusted odds ratio of 5.84 (95% CI, 2.23-15.31) which is highly comparable with a similar study conducted in Ghana which reported of an increased odds of hypertension of 5.00 in ART-exposed individuals compared with ART-naive individuals [14]. Various mechanisms have been postulated to account for the association between ART and hypertension including premature and/or accelerated development of atherosclerosis leading to blockage of the blood vessels lumen, ART induced immune activation, increased intestinal bacterial translocation and low-grade inflammation which, may promote atherosclerosis and increased arterial stiffness [45] and the involvement of ARVs in both lipid and glucose metabolism resulting in lipodystrophy syndrome and the activation of the renin angiotensin system [46].

Another finding in this study is the association between length of antiretroviral 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 PLHIV in SSA [14,25]and the results of the systematic review and meta-analysis [39].

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 as figures from the NACP show that the 45-49 years' age group has the highest prevalence of HIV in Ghana. Regression modeling analysis to determine factors associated with hypertension indicated that the risk factors for hypertension i.e., increasing age, positive family history of CVD/hypertension, inadequate exercising, general overweight/obesity and abdominal obesity were associated with hypertension. In addition, hypercholesterolemia, exposure to ART and duration of this ART exposure were also found to be associated with hypertension.

Limitations

Current study used a cross sectional study design to determine prevalence of hypertension and associated factors in patients attending HIV clinic at the KBTH in Accra. Inferences from 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 modeling 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 in time according to clinical indications and will be assumed to reflect their chronic condition. Study participant did not receive a definitive diagnosis of hypertension based on the measurements done, but nonetheless, 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, physical inactivity were based on study participants' self-report. Thus, it is possible for respondents to be tempted to present themselves in a more favorable way by giving health-conscious answers in what is termed "social desirability" (Dimala et al. 2016).

Strengths

Also relevant is that this is the first study conducted in Ghana's largest HIV cohort, to assess the general risk of hypertension among PLHIV using purposeful selection of covariates method in regression modeling.

Policy-relevant recommendations

Research into the feasibility of integration of NCD care into HIV-care so that patients need not seek this care from clinics where they may feel uncomfortable in disclosing their HIV status to attending healthcare givers.

Practice-related recommendations

Blood pressure monitoring should move from being routine at the KBTH HIV clinic to more of 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 HIV clinic at the KBTH in Accra.

Declarations

Ethics approval and consent to participate

The study was given ethical clearance [Protocol Identification Number: MS-Et/M.3-P 4.4/2015-2016] by the Ethical and Protocol Review Committee of the College of Health Sciences, University of Ghana. Permission was obtained from the clinician-in-charge of the HIV clinic at the KBTH and informed consent was sought and obtained from each study participant. Patients' data were de-identified during data capture, entry, analysis and storage by ensuring only the study codes were used consistently throughout the project cycle.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

Funding for this study was obtained from the office of Research, Innovation and Development (ORID) of the University of Ghana. The funding agency was not involved in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Authors' Contributions

ETN and RAT conceived and designed the study. RMA, RAT, FA and BS gave conceptual advice. RMA and WK assisted in funding acquisition. ETN, RAT, WK and BS did the statistical analysis and drafted the manuscript. RMA, RAT, WK and FA reviewed and edited the manuscript. All authors read and approved the final version of the manuscript.

Acknowledgement

We acknowledge the Office of Research, Innovation and Development (ORID) of the University of Ghana for the financial support they offered to undertake this work and also grateful to the entire staff and patients of HIV clinic, Korle-Bu Teaching Hospital for the assistance they gave us during the data collection period. We also thank the staff of Centre for Tropical Clinical Pharmacology and Therapeutics (UGMS) especially Mr. Caleb Buenortey and Mr. John Tsakpo for their support throughout this study.

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How to cite this article: Nartey, Edmund T., Raymond A. Tetteh, Francis Anto, and Bismarck Sarfo et al. "Hypertension and Associated Factors among Patients on HIV Antiretroviral Therapy at Korle-bu Teaching Hospital." J AIDS Clin Res 12 (2021): 862.