Cardiovascular Comorbidities, Hypertension and Associated Factors in Adults Living with HIV in Jos, Nigeria.

Amusa G,[1] Awokola B,[2] Osaigbovo G,[1] Uhunmwangho C,[1] Abene E,[3] Gimba Z,[3] Imoh L.[4]
[1]Department of Medicine, University of Jos and Jos University Teaching Hospital, PMB 2084, Jos, Plateau State; Nigeria.
[2]Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom and Disease Control and Elimination, Medical Research Council, Fajara; Gambia.
[3]Department of Internal Medicine, Jos University Teaching Hospital, PMB 1976, Jos, Plateau State; Nigeria.
[4]Department of Chemical Pathology, University of Jos, PMB 2084, Jos, Plateau State; Nigeria.
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Corresponding author. email: drganiamusa@gmail.com and amusag@unijos.edu.ng.

Abstract

Background: HIV infection is reported to predispose to cardiovascular diseases (CVD) through multiple mechanisms. Recent reports indicate the emergence of a CVD epidemic within the HIV pandemic with attendant consequences. This study sought to assess the burden of cardiovascular comorbidities, hypertension and associated factors in PLHIV in Jos, Nigeria.

Methods: This was a cross-sectional study involving three hundred eligible adult clients (including 100 who had not started antiretrovirals) of the HIV clinic of Jos University Teaching Hospital selected using a simple random sampling technique. Relevant history, physical examination and investigations were obtained along with clinical data from hospital records. Data was analyzed using STATA version 13, p-value < 0.05 was considered significant.

Results: Among the participants, 122 (40.7%) had clinical evidence of cardiovascular comorbidities; 168 (56.0%) had an abnormal echocardiogram and 177 (59.0%) had an abnormal electrocardiogram. Clinically, hypertensive heart disease 72 (24.0%) was the commonest comorbidity. Effusive pericardial disease 88 (29.3%) was the most common echocardiography finding and atrial ectopics 78 (26.0%) was the commonest electrocardiography finding. Hypertension 78 (26.0%) was the commonest major risk factor identified. Furthermore, the participants on antiretrovirals had significantly higher degrees of comorbidities and risk scores compared to those not yet on antiretrovirals.

Conclusion: PLHIV have a significant burden of cardiovascular comorbidities, hypertension and associated risk factors in our environment. Integration of the management of cardiovascular diseases is recommended for inclusion as part of standard care in HIV care programs to mitigate attendant consequences in these patients.

Keywords: Antiretroviral therapy, Cardiovascular comorbidities, Hypertension, Electrocardiographic abnormalities, Echocardiographic abnormalities, Nigeria.

Introduction

The United Nations and its agencies describe HIV/AIDS as a pandemic.[1,2] The burden is disproportionately huge in sub-Saharan Africa (SSA) where it affects mostly productive age groups with attendant socio-economic consequences.[1,2] Globally, over 20 million deaths are attributed to HIV/AIDS and about 75% of these occured in SSA.[1,2] In Nigeria, the national prevalence as of 2018 was estimated to be 1.5% and 2.1% in north-central Nigeria.[2] A recent modelling survey however estimated 2022 national prevalence as 2.1%.[3] This represents over 10% of the global population of PLHIV and an unenviable position as a Country with the third largest burden.[1,2.]

Before the availability of effective Antiretroviral Therapy (ART), researchers had noted that untreated PLHIV had an increased burden of CVD compared to uninfected controls.[4-6] With the widespread use of ART, the contribution of drug-related cardio-metabolic alterations and increasing lifespan took on an even greater significance.[4-6] Decades later, this has led to reports of the emergence of a CVD epidemic within the HIV/AIDS epidemic with consequent alterations in previous patterns of morbidity and mortality.[4,5,7] The reasons are reported to be multi-factorial and involve the contributions of HIV, ART and predisposing lifestyles.[4,5,7] Specifically, hypertension a major CVD risk factor, and harbinger of CVD is reported to cause more than a 30% increase in cardiovascular mortality and a 50% increase in all-cause mortality among PLHIV.[8-11] Based on this evidence, concerned authorities are advocating that HIV infection be classified as a major CVD risk factor and integration of cardio-metabolic care in HIV care programs.[8-11]

This study aimed to assess the burden of cardiovascular comorbidities, hypertension, and associated factors in adult PLHIV in Jos, Nigeria. Furthermore, it aimed to assess the predictors of cardiovascular comorbidities, hypertension, and moderate-high risk scores in adults PLHIV in Jos, Nigeria.

Methodology

Study site and population:

The study was conducted at the HIV clinic of Jos University Teaching Hospital (JUTH) in Jos, Plateau State, Nigeria where over 21,000 persons from across Nigeria (mostly from north-central, northeast, and northwest) receive HIV care. The study population are adult clients diagnosed with HIV infection and receiving care at the site.

Inclusion and exclusion criteria

Adults confirmed to have HIV infection and enrolled for care at the HIV clinic of JUTH were included in the study while persons with pregnancies or within six months post-partum, acute illnesses and severe psychiatric illnesses that impair normal functioning were excluded from the study.

Study design

This was a hospital-based cross-sectional study carried out over 12 weeks from January to March 2018.

Sample size estimation

The sample size was calculated using Bennett Fischer's formula.[12.] $n = \frac{(Zi\,a)^2 (P)(1-P)}{d^2}$

n = minimum sample size

Zi – a = 1.96 from the Z table at 96% confidence interval

P = prevalence of hypertension in HIV/AIDS, 25% was used.[13,14.]

Precision set at 5% allowable margin of error

Therefore $N = \frac{(1.96)^2 (0.25)(1\text{-}0.25)}{(0.05)^2} = 288$

Three hundred eligible adults with HIV infection (200 on ART, 100 not yet on ART) were enrolled in the study.

Study procedure:

Pretest of data collection instruments

A structured interviewer-administered questionnaire was developed for the collection of relevant sociodemographic and clinical data. The questionnaire was pretested two weeks before the commencement of the main study. It was administered to 30 selected clients and repeated a week later to determine the degree of reproducibility and concordance and this was found to be nearly 100% in all cases.

Data collection

Each participant was interviewed to obtain relevant demographic and clinical history. They were also grouped into social classes using the method by Olusanya et al.[15] Physical activity was graded according to the WHO guidelines.[16] Anthropometric and cardiovascular examinations were performed according to standard recommendations and findings documented.[17] Blood pressure was measured using Omron M6 sphygmomanometers (accuracy ±2mmHg) with appropriate cuff size in both arms in a sitting position after a 5-10-minute rest. Two additional recordings were made using the limb with the higher value; the average was taken to give a representative value.

Serum lipid profile, fasting plasma glucose, serum creatinine, and uric acid assessments were done. Low-density lipoprotein (LDL) was calculated using the Friedewald formula (LDL = TC - HDL – TG/2.2; all in mmol/L),[18] and the estimated glomerular filtration rate was calculated using the MDRD calculator.[19] Estimated 10-year CHD risk was calculated using the Framingham risk score spreadsheet.[20] Further relevant clinical information (duration of HIV, duration of ART, clinical history of risk factors and CVD, baseline/recent CD4 count, and viral load) was obtained from the records of each participant and documented.

Electrocardiography

Each participant had twelve lead electrocardiography done using General Electric Medical Systems Information Technologies MAC 1200 ST v.1.2 electrocardiograph machine and interpretation done according to standard definitions.[21]

Echocardiography

Echocardiography was done using the General Electric Vivid q echocardiography machine according to the American Society of Echocardiography guidelines.[22-23] The ejection fraction (EF) and fractional shortening (FS) were taken as measures of systolic function. The E/A ratio and E-wave deceleration time (DT), were taken as measures of diastolic function. The average of measurements in three cardiac cycles was taken.[22-23.]

Definition of Terms

Cardiovascular comorbidity was defined as a clinical diagnosis of a specific cardiovascular disease supported by findings from physical examination, electrocardiography, and echocardiography.[22-25]

Hypertension was defined as a persistent elevation of blood pressure ⩾ 140/90 mmHg according to JNC V11 classification or current use of antihypertensive medication.[25,26] Other CVD risk factors reported were defined according to standard definitions.[17,27-29]

Framingham risk score (FRS) was used to triage participants into three risk categories: high risk (10-year risk > 20%), moderate risk (10-year risk 10% to 20%), or low risk (10-year risk < 10%).[28,29] Individuals with a clinical form of cardiovascular disease or with diabetes belong in the high-risk category.[30,31] Moderate risk also includes patients with 2 or more major risk factors and 10-year risk < 10%. Low-risk patients are those with 1 major risk factor or none and 10-year risk < 10%.[30,31.]

Statistical analysis:

Data was analysed using the STATA statistical software version 13. Quantitative variables were summarised using mean and standard deviation (SD). Categorical variables were expressed using frequencies and percentages. The student t–test or non-parametric Mann-Whitney/Kruskal-Wallis tests were used to compare the means of the 2 groups (age, FRS and relative risk). The Chi-Square (X^2) test was used to test the significance of association between categorical variables (CVD and risk factors). Fisher exact test was used where the frequency of a cell was <5, Multiple logistic regression analysis was performed to determine

which HIV parameters (CD4 ⩾ 200cells/ml (recent and baseline values), detectable viral load, ART use, duration of HIV) are predictors of cardiovascular comorbidities as a group, hypertension, and moderate-high FRS using variables that had a p-value of <0.05 on univariate analysis. In all cases, a p-value of <0.05 was considered statistically significant. The presence or absence of cardiovascular comorbidities, hypertension, and moderate-high FRS were the main outcomes.

Ethical consideration:

The ethical approval for the study was obtained from the Health Research Ethics Committee of JUTH (JUTH/DCS/ADM/127/XXX/195), and administrative approval for the access and use of data was also obtained from the AIDS Prevention Initiative in Nigeria. The nature of the study was explained in detail to each participant in the language they best understood. Consenting participants were required to sign the consent forms or append their thumbprints where appropriate. Participants were at liberty to withdraw from the study at any stage without any negative consequence and information obtained was treated as confidential.

Results

Three hundred persons confirmed to have HIV infection were enrolled in this study. Everyone completed most aspects of the study. There were 177 females (59.0%) and 123 males (41.0%). The mean age of the participants was 41.2±13.2 years, most were in the fourth decade of life and social class 5 was the most common social class. (Table 1).

Table 2 shows the prevalence of hypertension, other specific CVD risk factors, and the Framingham risk scores. Hypertension was the most common major CVD risk factor found in 78 (26.0%) of participants. Furthermore, the FRS, relative risk and FRS categories of those on antiretrovirals were significantly poorer compared to those yet to commence antiretrovirals.

Figure 1 shows the pattern of antiretroviral therapy, the majority 98 (49.0%) were on a combination of two nucleoside reverse transcriptase inhibitors (NRTI). Figure 2 shows the blood pressure pattern of the participants. Overall, 87 (29.0%) had pre-hypertension and among those with hypertension, the majority 45 (15.0%) had combined hypertension.

Table 3 shows cardiovascular comorbidities (clinical, electrocardiographic, and echocardiographic) found in the participants, 122 (40.7%) had cardiovascular comorbidity. Clinically, hypertensive heart disease was the commonest 72 (24.0%), 168 (56.0%) had echocardiographic abnormalities while 177 (59.0%) electrocardiographic abnormalities. The commonest echocardiographic abnormality was effusive pericardial disease 168 (56.0%) and the commonest electrocardiographic abnormality was atrial ectopics 78 (26.0%).

Table 4 shows the results of multiple logistic regression analysis to determine which parameters after univariate analysis emerged as predictors of hypertension, moderate-high FRS, and comorbid cardiovascular diseases. HIV duration ⩾ 2 years, duration of ART use ⩾ 2 years and CD4 ⩽ 200 cells/ml at baseline emerged as predictors of cardiovascular comorbidities amongst others for hypertension and moderate-high Framingham risk score.

Table 1: Socio-demographic characteristics of the study population

Variable	Population N=300(100%)	HIV+ART+ N=200(100%)	HIV+ART- N=100(%)	P-value
Gender				0.768
Female	177(59.0)	123(61.5)	59(59.0)	
Male	123(41.0)	77(38.5)	41(41.0)	
Age groups				0.294
20-29	78(26.0)	49(24.5)	29(29.0)	
30-39	95(31.7)	64(32.0)	31(31.0)	
40-49	54(18.0)	34(17.0)	20(20.0)	
50-59	36(12.0)	27(13.5)	9(9.0)	
= 60	37(12.3)	27(13.5)	10(10.0)	
Age (mean±SD)	41.2±13.2	41.5±12.9	40.9±13.1	0.913
Marital status				0.910
Single	73(24.3)	47(28.5)	26(13.0)	
Married	129(43.0)	87(44.5)	42(42.0)	
Separated	45(15.0)	29(14.5)	16(16.0)	
Widowed	53(17.7)	37(16.5)	16(16.0)	
Social class				0.782
	14(4.7)	8(4.0)	6(6.0)	
	20(6.7)	15(7.5)	5(5.0)	
	40(13.3)	27(13.5)	13(13.0)	
	88(29.3)	61(30.5)	27(27.0)	
	138(46.0)	89(44.5)	49(49.0)	
Residence:				0.081
Urban	183(61.0)	115(66.5)	68(68.0)	
Rural	117(39.0)	85(42.5)	32(32.0)	

HIV+ART+: HIV positive on antiretrovirals, HIV+ART-: HIV negative not yet on antiretrovirals

Table 2: Prevalence of risk factors, and risk scores in the study population

Variable	Population N=300(100%)	HIV+ART+ N=200(%)	HIV+ART- N=100(%)	P-value A vs B
CVD risk factors				
Significant Alcohol Intake	93(31.0)	52(26.0)	41(41.0)	0.008
Smoking	35(11.7)	17(8.5)	18(18.0)	0.016
Inadequate Physical Activity	99(33.0)	41(20.5)	58(58.0)	0010
Increased Waist Circumference	132(44.0)	105(52.5)	27(27.0)	0.001
Overweight/Obesity	60(20.0)	50(25.0)	20(10.0)	0.335
Hypertension	78(26.0)	64(32.0)	14(14.0)	0.001
Dyslipidaemia	66(22.0)	54(27.0)	12(12.0)	0.003
Diabetes Mellitus	24(8.0)	20(10.0)	4(4.0)	0.075
Hyperuricemia	32(10.7)	24(12.0)	8(16.0)	0.291
Metabolic syndrome	33(11.0)	26(13.0)	6(6.0)	0.065
Degree of clustering of risks				0.006
<2	144(48.0)	84(42.0)	60(60.0)	
3-4	94(31.3)	64(32.0)	30(30.0)	
>4	65(21.7)	52(26.0)	13(13.0)	
Risk score (Framingham)				
FRS score (mean±SD)	9.68±2.56	11.7±3.1	6.3±2.0	0.001
Relative risk (mean±SD)	3.68±1.06	5.8±1.1	2.2±0.6	0.001
Risk score category				0.029
Low/intermediate risk	132(44.0)	70(35.0)	48(48.0)	
Intermediate Risk	120(40.0)	90(45.0)	30(30.0)	
High Risk	48(16.0)	40(20.0)	16(16.0)	

HIV+ART+: HIV positive on antiretrovirals, HIV+ART-: HIV positive not yet on antiretrovirals , relative risk -ratio of index FRS divided by that ideal for age

Figure 1: Patterns of antiretroviral therapy in the study population

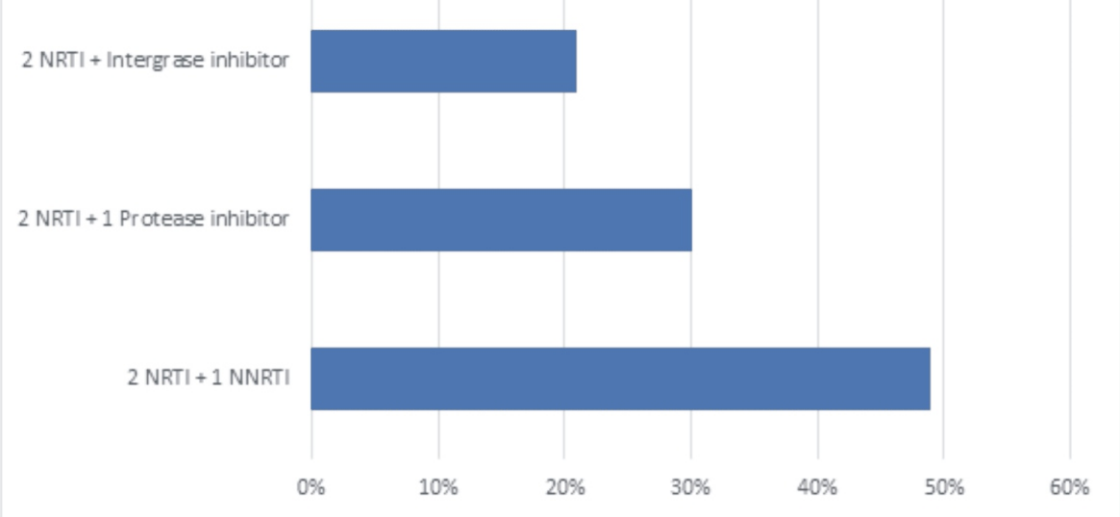

Figure 2: Blood pressure patterns in the study population

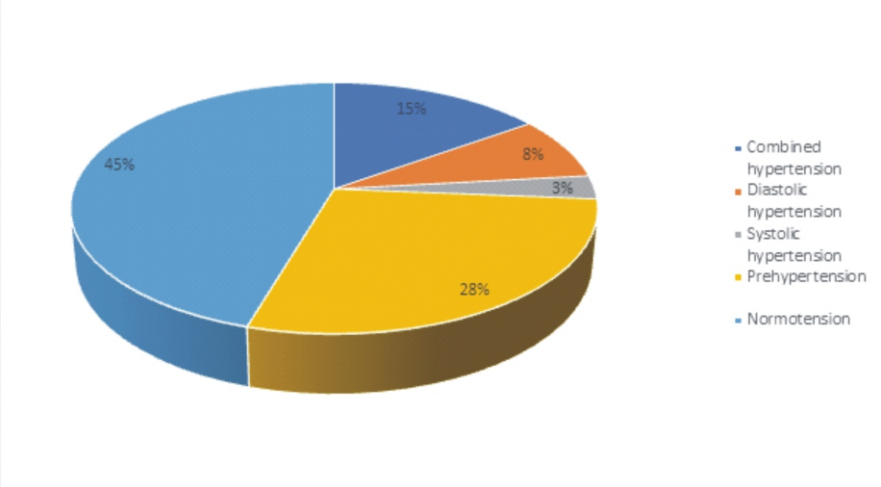

Table 3: Prevalence of cardiovascular comorbidities in the study population

Cardiovascular co-morbidities	N=300(100%)
Clinical diagnosis	122(40.7)
Hypertensive heart disease	72(24.0)
Heart failure	34(11.3)
Peripheral vascular disease	27(9.0)
Ischaemic heart disease	22(7.3)
Chronic kidney disease	18(6.0)
Stroke	7(2.3)
Others	11(3.7)
Echocardiographic abnormalities	168(56.0)
Pericardial disease	88(29.3)
Left ventricular diastolic dysfunction	69(23.0)
Left ventricular systolic dysfunction	60(20.0)
Left ventricular hypertrophy (concentric)	52(17.3)
Mitral valve regurgitation (moderate)	37(12.3)
Tricuspid valve regurgitation	34(11.3)
Septal wall dyskinesia	24(8.0)
Pulmonary hypertension	24(8.0)
Left ventricular hypertrophy (eccentric)	23(7.7)
Left ventricular posterior wall dyskinesia	17(5.7)
Dilated cardiomyopathy	18(6.0)
Vegetations (Endocarditis)	14(4.7)
Isolated right ventricular dilatation	5(1.7)
Rheumatic valvular disease	4(1.3)
Others	11(3.7)
Electrocardiographic Abnormalities	177(59.0)
Atrial ectopics	78(26.0)
Ventricular ectopics	71(23.7)
Sinus tachycardia	58(19.3)
Left ventricular hypertrophy	51(17.0)
Left atrial enlargement	47(15.7)
T wave inversion	43(14.3)
Non-Specific intraventricular conduction defect	36(12.0)
Poor R wave progression	33(11.0)
Left axis deviation	27(9.0)
Incomplete right bundle branch block	22(7.3)
Right atrial enlargement	16(5.3)
Generalized low voltages	19(6.3)
Atrial fibrillation	14(4.7)
Right ventricular hypertrophy	11(3.7)
Others	23(7.7)

Table 4: Multiple logistic regressions for independent predictors of cardiovascular comorbidities, hypertension, and moderate-high risk scores in the study population

Variable	Odds ratio	95% Confidence interval	P-value
Cardiovascular comorbidities[a]			
HIV duration ≥ 2 years	1.558	1.267 - 3.130	0.006
ART duration ≥ 2 years	2.115	1.492 - 2.881	0.031
CD4 count (recent)≤200c/ml	1.434	1.198 - 3.055	0.057
CD4 count (baseline) ≤200c/ml	2.145	1.275 - 2.802	0.008
Viral load (detectable ≥50c/ml)	1.524	1.161 - 6.274	0.054
BMI (≥25)	1.065	0.936 - 1.944	0.188
Age (≥40yrs)	1.103	0.845 - 1.515	0.095
Hypertension[a]			
HIV duration ≥ 2 years	1.869	1.397 - 2.085	0.027
ART duration ≥ 2 years	2.207	1.758 - 2.720	0.011
CD4 count (recent) ≤200c/ml	1.752	1.0715 - 7.078	0.067
CD4 count (baseline)≤200c/ml	2.719	1.712 - 3.523	0.017
Viral load (detectable≥50c/ml)	1.336	0.131 - 13.671	0.807
BMI (≥25)	2.187	1.910 - 4.159	0.045
Age (≥40yrs)	2.442	1.483 - 3.984	0.033
Moderate-high Framingham risk score[a]			
HIV duration ≥ 2 years	2.635	1.412 - 4.449	0.028
ART duration ≤ 2 years	2.831	1.550 - 4.181	0.031
CD4 count (recent) ≤200c/ml	1.387	1.101-3.180	0.081
CD4 count (baseline) ≤200c/ml	1.814	1.376 - 2.835	0.016
Viral load (detectable ≥50c/ml)	1.718	1.183 -11.687	0.602
BMI (≥25)	1.202	1.693 - 3.012	0.083
Age (≥40yrs)	1.163	1.012 - 1.713	0.125

[a] present versus absent

Discussion

Sociodemographic characteristics of the study participants

In sub-Saharan Africa, studies report a preponderance of young productive age groups, low socioeconomic status, and slight female preponderance amongst PLHIV particularly those enrolled in the HIV programs. This study's population sociodemographic characteristics are similar to the trend in SSA.[1,36-40] HIV/AIDS is known to be associated with low socioeconomic class and tends to impoverish individuals and communities by multiple pathways.[41] Some studies have reported low socioeconomic class as a significant predictor of increased cardiovascular risk and cardiovascular disease.[1,39,41] A multi-centre study in the US found that having a low socioeconomic class was identified as the strongest risk factor for moderate-high risk score and CVD in PLHIV.[41] Generally, in Africa, females also tend to seek care earlier than males, which explains the higher number of female participants coupled with the anatomic and socioeconomic characteristics of females which makes them more susceptible to contracting the virus. The sociodemographic characteristics of the study participants therefore

make the findings generalizable to natural real-world findings in Nigeria and SSA.[1-3.]

Cardiovascular comorbidities in the study population

Cardiovascular disease as it is known tends to exist as a spectrum of specific disease entities with similar risk factors and aetiopathogenesis. Clinically, two out of every five of the study participants had comorbid CVD; more common findings were hypertensive heart disease, heart failure, peripheral vascular diseases and ischaemic heart diseases amongst others. Hypertensive heart disease is a spectrum of symptomatic cardiovascular changes secondary to hypertension. It was the most common cardiovascular comorbidity diagnosed clinically among the study participants. Hypertension, in the general population, is the foremost CVD risk factor which singularly is responsible for the most amount of cardiovascular and all-cause morbidity and mortality across the world.[23,24,42,43] The pathogenesis is multifactorial in PLHIV and involves HIV, ART, some medications for opportunistic infections, and behavioral factors amongst others.[5,10,45,46]

Comorbidity of HIV and hypertension can range from 24-32% and up to 52% according to literature,[13,14] and is documented to cause about a 30% increase in cardiovascular morbidity/mortality and a 50% increase in all-cause morbidity/mortality amongst PLHIV.[14] The dangers of uncontrolled hypertension, as in the general population is protean amongst PLHIV.[5-9,14,37] Hypertension predisposes to other conditions such as diabetes mellitus, ischaemic heart disease and heart failure amongst others.[5-9,14,37] It is easily diagnosable in clinical settings and due to its level of influence on morbidity and mortality has been designated by the WHO amongst others as the fulcrum for cardio-metabolic disease prevention and management in the general population and by extension PLHIV.[9-11,34,35,43.]

End organ damage and failure such as stroke, chronic kidney failure and heart failure are the endpoints of the cardiovascular disease spectrum and the strongest risk factor for these is hypertension.[5-9,14,37] Comorbidity of HIV and hypertension is reported to worsen the risk for target end-organ damage and failure significantly. The condition of untreated HIV and hypertension is a time bomb that greatly increases cardiovascular risks to dangerous levels predisposing to rapid and often fatal target end-organ damage and failure.[4-6,9-11] HIV is known to be directly cardiotoxic and stimulate a chronic inflammatory state with the elaboration of deleterious compounds harmful to the vessels such that arteriosclerosis and atherosclerosis are promoted with a procoagulant milieu which is dangerously aggravated in the setting of uncontrolled hypertension.[4-6,9-11,45,46] In PLHIV, the presentation of these particularly that of heart failure can be variable with acute, chronic, or acute on chronic symptoms and signs. As in the general population, the burden of heart failure, and other end-organ damage/failure in PLHIV are increasing at greater rates than in the general population.[4-6,9-11,45,46.]

Electrocardiographic abnormalities:

The target end-organs bear the brunt of CVD risk factors, especially in comorbid states. The earliest signs of these may be found during electrocardiography even in the asymptomatic patients. Three in every five of the participants had an abnormal electrocardiogram. The common findings were atrial/ventricular ectopics and sinus tachycardia amongst others. Comparable findings have been reported by other authors about the burden and spectrum of electrocardiographic abnormalities found among PLHIV.[4,5,40,47,48] Electrocardiographic abnormalities are known to reveal the presence of underlying systemic or CVD with consequent deleterious impacts on prognosis. They are caused by a complex interaction between HIV, ART, dyselectrolytemia, and certain medications used to treat opportunistic infections.[4,5,40,45-47,48] Arrhythmias, a dangerous form of electrocardiographic abnormality may cause sudden cardiac death and are responsible for about 20% of cardiac-related deaths in PLHIV.[48] Atrial fibrillation is a common but dangerous arrhythmia in the general population and is a major risk factor for strokes, sudden cardiac death, and other cardioembolic diseases; it was found in one in every twenty participants. Other dangerous arrhythmias such as ventricular arrhythmias are associated with

drugs like Pentamidine used in the treatment of pneumocystis carinii infection, it is structurally similar to procainamide, and can cause torsade de pointes a form of ventricular tachycardia when used parenterally.[48] Furthermore, efavirenz a commonly used antiretroviral is associated with acquired long QT syndrome which may cause sudden cardiac death.[48] In addition, electrocardiographic diagnosis of left ventricular hypertrophy found in one in every five participants is reported to be associated with an increase in all-cause mortality in PLHIV. The causes include hypertension, diabetes mellitus, and the use of protease inhibitors amongst others. [4,5,45-47,48.]

Echocardiographic abnormalities:

Echocardiographic abnormalities are among the earliest changes that may suggest HIV infection. These changes may occur as early as the stage of acute seroconversion and are present throughout a lifetime after HIV infection. Echocardiography assesses the structure and function of the cardiovascular system and in certain cases such as left ventricular dysfunction is correlated with poor prognosis. More than half of the participants were found to have an abnormal echocardiogram. These findings were comparable to those obtained in studies from other parts of Nigeria and Africa where different echocardiographic findings in the CVD spectrum are prevalent based on locality.[4,5,49,50] The common echocardiographic abnormalities were effusive pericardial diseases, left ventricular dysfunction, and left ventricular hypertrophy. Echocardiographic surveys have established pericardial diseases are a common finding in HIV-infected persons. It has been associated with shortened survival independent of CD4 count with prevalence ranging from 10–59% although the majority of these are asymptomatic.[49] Cases of massive pericardial effusion with cardiac tamponade, and constrictive pericarditis have also been reported.[49,50] In Africa, tuberculosis is the major cause of large pericardial effusion, although it can also be caused by HIV, opportunistic infections, malignancies such as Kaposi Sarcoma, or part of a generalized effusive serous process as a consequence of enhanced cytokine expression.[49,50] Left ventricular hypertrophy and dysfunction were common echocardiographic findings in this study and have been reported by other studies.[4,5,49,50] Researchers suggest that hypertrophy associated with ventricular dysfunction represents an early phase of the cardiomyopathic process and is reported to be associated with HIV progression, increased morbidity and increased mortality.[50,51] A study estimated median survival as 101 days in HIV-infected persons with left ventricular dysfunction, as against 476 days of survival in patients with normal heart analyzed by echocardiography at similar infection stage.[49.]

Dilated cardiomyopathy was identified in about one in every twenty participants. Studies have reported an increased rate amongst PLHIV and associated with increased viral load and low CD4 counts.[51,52] A study in Lagos reported a prevalence of 5% in patients with a CD4 count of less than 100 copies/ml. In another study in Cameroon, it was reported that a relationship between low CD4 count and the likelihood of cardiomyopathy.[51] In a similar study involving 296 HIV-positive patients in Britain, a prevalence of about 4% and association with a CD4 count of less than 100 cells/ml was reported.[50] Another study in Zimbabwe reported a prevalence of 9%, most of whom were in the advanced stage of the disease.[49] Himmelman et al in their study reported a prevalence of 11% of the 70 HIV-positive participants studied.[49] Corallo et al on the other hand reported a rate of 17.6% of 102 participants with advanced disease. Barbaro et al in a prospective study of 952 asymptomatic HIV-positive patients reported dilated cardiomyopathy in 76 patients (8%), with a mean annual incidence rate of 15.9 cases per 1000 patients.[53] They concluded that dilated cardiomyopathy may be related either to a direct action of HIV on the myocardial tissue or to an autoimmune process induced by HIV, possibly in association with other cardio-tropic viruses in the setting of immunodeficiency.[53]

Some studies have indicated that the prognosis and survival of patients with HIV who develop dilated cardiomyopathy is poor.[49] Nutritional factors have been linked with dilated cardiomyopathy in HIV-positive patients. Deficiency of selenium and other trace elements has been associated with dilated cardiomyopathy in these patients.[50-52] Selenium deficiency as a cause of HIV-related heart muscle

disease may be of considerable interest in Africa where patients often present with multiple nutritional deficiencies, prolonged diarrhea, and wasting. Selenium supplementation has been shown to improve cardiac dysfunction in these patients.[49,50-52] Also cardiotoxic effect of antiretroviral drugs such as Zidovudine has also been implicated in HIV cardiomyopathy.[49,50-52.]

Hypertension and associated cardiovascular disease risk factors in the study population

Hypertension is a major CVD risk factor with pleiotropic manifestations and a significant impact on morbidity and mortality in the general population.[26,29,43,44,54] It is the single most important risk factor in terms of morbidity and mortality.[26,29,43,44,54] Hypertension is central to the prevention, detection, and management of CVD in the general population and consequent to its role in the CVD spectrum. It is a harbinger of increased cardiovascular risk and actual cardiovascular disease. [26,29,43,44,54,55] In PLHIV, the impact of hypertension increases exponentially in terms of morbidity and mortality.[6,14,37,55] A study reported a significant increase in cardiovascular mortality by 30% and all-cause mortality by 50% in PLHIV with hypertension comorbidity.[8-11,37,55]

Hypertension was found in about a third of participants in this study and the degree of clustering with other risk factors makes that more worrisome. Furthermore, another third of the participants had prehypertension and may develop hypertension sooner rather than later. Also, about two-thirds of participants had one form of CVD risk factor or the other while more than half had a clustering of risk factors. In addition, hypertension and several of the CVD risk factors were significantly commoner in those on antiretrovirals suggesting their role in the pathogenesis of CVD.[1,2,8,9,14,46,55] Furthermore, the participants on antiretrovirals in this study had a significantly higher risk score than those yet to commence antiretrovirals. PLHIV take antiretrovirals from the time of diagnosis of HIV infection and for life thereafter. Antiretroviral therapy is known to significantly increase CVD risks on an already increased risk in PLHIV with these risks becoming more pronounced with time. The findings in this study are in agreement with similar across the globe.[1,2,8,9,14,46,55]

In a preliminary analysis of data from this study published previously, hypertension was identified in about a third of those sampled.[40] In contrast, an earlier study in Jos reported a prevalence of 19.3% before the commencement of ART and 50.2% twelve months after the commencement of ART although the study was a mixed-method study.[41] The results from Jos and several other studies from Africa and other parts of the world are comparable to what was found in this study. A systematic review estimated the prevalence of hypertension amongst PLHIV to range from 25-35% and sometimes as much as 51% with regional variability.[14] In 2018, a global systematic review and meta-analysis estimated about 9 million cases of hypertension in PLHIV globally with 59.2% living in SSA.[55] The reviews concurred that PLHIV on ART have a statistically significant higher prevalence of hypertension than those not on ART; thus, inferring that ART though essential to survival amongst PLHIV predisposes the same to hypertension and other CVD.[14,55] As in the general population, there is a growing call for the integration of the management of cardiovascular diseases in HIV care programs with hypertension central to the identification and management of such.[8-11,34,35]

As hypertension is common, easily identifiable, and tends to cluster with other risk factors, its detection and subsequent investigation tend to unmask the presence of others.[8-11,34,35] Consequently the WHO and other health bodies build CVD prevention and reduction programs around the prevention, detection, and management of hypertension across the world. The same is advocated as part of standard care for HIV.[8-11,34,35,43] There is indeed a concerted effort by the WHO and concerned authorities to alert medical practitioners on the emergence of the CVD pandemic within the HIV/AIDS pandemic and the need to identify and manage them appropriately within the HIV care programs.[8-11,34,35,43] Despite the preponderance of evidence, this has not been implemented in the majority of centres offering HIV care particularly in resource-limited settings across the world.[8-11,34,35,43.]

Independent predictors of cardiovascular comorbidities, hypertension, and moderate-high FRS scores in the study population

Cardiovascular disease as previously stated is a spectrum of specific entities intertwined along a common pathway beginning with shared risk factors and aetiopathogenesis to specific individual CVD and ending up in target end-organ damage and failure. Hypertension is central to this as a harbinger of other risk factors and a catalyst that accelerates pathologic cardiovascular processes. The predictors of hypertension found in the study participants were duration of HIV infection ⩾ 2 years, duration of ART ⩾ 2 years, baseline CD4 count ⩽ 200 copies/ml, BMI ⩾25, and age ⩾ 40 years. Aging and obesity are established risk factors for hypertension in the general population hence not unexpectedly emerge as predictors of hypertension in this study.[3-5] A similar trend was observed for cardiovascular comorbidities as a group whereby the duration of HIV infection ⩾ 2 years, duration of ART ⩾2 years, and baseline CD4 count ⩽200 copies/ml were statistically significant as predictors of cardiovascular comorbidity in general. For moderate-high risk score; only, the duration of HIV infection ⩾ 2 years, duration of ART ⩾ 2 years, and baseline CD4 count ⩽ 200 copies/ml emerged as predictors. The findings in this study are in agreement with findings from previous similar studies.

HIV infection and ART are lifelong and are known to accelerate the aging process due to chronic generalized inflammatory processes with consequent cardiomyopathic processes, neuropathy, nephropathy, arteriosclerosis, atherosclerosis, and resetting of the mitochondria in the cardio-metabolic pathway. These coupled with the influence on traditional CVD risk factors predispose to hypertension and different cardiovascular comorbidities along the spectrum.[46,47,56,57.]

In addition, baseline CD4 count ⩽ 200 cells/ml signifies a chronic inflammatory state and severity of HIV infection with consequent re-setting of immunologic memory. The improvement in CD4 levels after commencement of ART appears to create an immunologic flux which leads to a persistence of chronic inflammatory state with contributions from ART (particularly protease inhibitors) itself. Some studies have reported the same findings whereby baseline (nadir or trough) CD4 count have been related to the development of comorbid cardiovascular diseases, hypertension, and increased cardiovascular risk.[56,57.]

Conclusion

Persons living with HIV/AIDS have a significant burden of cardiovascular comorbidities, hypertension, and other cardiovascular risk factors. Integration of routine screening and management for cardiovascular risk factors and comorbidities is recommended in HIV care programs. This will significantly reduce morbidity, improve quality of life, and prolong life in these patients.

Acknowledgments

The first author received a research seed grant, research methodology, and manuscript writing training from STAMINA funded by the Fogarty International Centre/ National Institutes of Health; Award Number D43 TW010130. Research methodology and manuscript writing training was also received from PATSMECOR/Global MECOR programs of the American Thoracic Society.

The authors also acknowledge Professor BN Okeahialam, Professor SS Danbauchi, Professor OO Agbaji and Professor AS Sagay for their invaluable contributions to this work.

Conflict of interests

The authors declare that they do not have any conflict of interest.

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