Echocardiographic Findings and Associated Factors in HIV Infected Patients at a Tertiary Hospital in Ethiopia

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Abstract

Background: Non-communicable diseases including cardiovascular diseases are becoming an important part of Human Immunodeficiency Virus (HIV) care. Echocardiography is a useful non-invasive tool to assess for cardiac disease and different echocardiographic abnormalities have been seen previously. Available evidence on the echocardiographic abnormalities in Ethiopia is scarce. The aim of this study was to investigate the echocardiographic abnormalities in HIV infected patients and factors associated with the findings.

Methods: A cross-sectional study was conducted on 285 patients with HIV infection including collection of clinical and echocardiographic data. Logistic regression was used to examine the association between echocardiographic abnormalities and associated factors with variables with a p-value of < 0.05 in the multivariate model considered statistically significant.

Results: Diastolic dysfunction was the most common abnormality seen in 30.1% of the participants followed by regional wall motion abnormality (22.2%), left ventricular hypertrophy (10.3%), enlarged left atrium (8.1%), pulmonary hypertension (3.5%) and pericardial effusion (2.1%). Almost all patients had normal left ventricle systolic function. Diastolic dysfunction was independently associated with increasing age, elevated blood pressure and left ventricular hypertrophy while regional wall motion abnormality was associated with male gender, increasing age and abnormal fasting blood glucose. Left ventricular hypertrophy was associated with increasing age and blood pressure and the later was associated with left atrial enlargement. The level of immunosuppression did not affect echocardiography findings.

Conclusions: A high prevalence of echocardiographic abnormalities was found and included diastolic dysfunction, regional wall motion abnormality, left ventricular hypertrophy and left atrial enlargement. Male gender, age above 50 years, elevated blood pressure and elevated fasting blood glucose were associated with echocardiographic abnormalities. Appropriate screening and treatment of echocardiographic abnormalities is needed.

Background

Human Immunodeficiency Virus (HIV) infection, with the widespread use of Antiretroviral Treatment (ART), is showing an evolving trend from a predominantly infectious ailment to a systemic disease that leads to increased manifestations of non-communicable diseases (1). With increased longevity, patients are faced with increasing morbidity and mortality from cardiovascular diseases (2, 3). HIV infected patients have increased risk of developing cardiac dysfunction and a large share of the suffering is considered to be related to HIV infection itself (4).

During earlier periods of the infection, the most common cardiovascular manifestations of HIV were pericardial effusion and cardiomyopathy (5). This pattern has persisted to be seen in developing countries but in affluent societies, with widespread use of ART, it is shifting gradually to diastolic dysfunction,

coronary artery disease and pulmonary hypertension (5). Echocardiography is a useful non-invasive diagnostic imaging modality that is valuable in the diagnosis of these cardiac manifestations (6).

Different mechanisms have been proposed for development of cardiac disease in HIV. Direct infection of myocardium by the virus, opportunistic infections, chronic inflammation, lipodystrophy and cardiac autoimmunity are included among others (4, 7, 8). Certain ART medications, use of substances such as alcohol and nutritional deficiency also contribute (7, 8).

Knowing the adverse effects of the infection on the heart early by readily available and non-invasive diagnostic test can help patients prevent morbidity and can be accomplished by the use of echocardiography for screening and monitoring in this group of population (9).

Much of the evidence regarding this subject is mostly derived from studies outside of Africa. In addition, data regarding the echocardiographic abnormalities in HIV infected patients in Ethiopia is very scanty and has mostly focused on specific diagnosis and not on comprehensive echocardiographic assessment. In this study we investigate the echocardiographic findings in HIV infected patients and factors associated with the findings.

Methods

Study design and participants

A cross sectional study was conducted on patients with HIV infection on ART at St. Paul's hospital millennium medical college (SPHMMC) HIV treatment clinic in Addis Ababa, Ethiopia. Adult HIV clinic at SPHMMC has a total of 4,685 patients on active follow-up, with average monthly patient of 1,700 and serves up to 70 patients per day. All patients are on ART unless deferred for clinical reasons. There are 2,552 patients that are expected to visit the clinic over the data collection period of 6 weeks from January 6, 2019 to February 15, 2019. Assuming a 26% prevalence of echocardiographic abnormalities in HIV infected patients (10), 5% margin of error, 95% confidence interval and adjusting for the finite size of the population using population correction formula, the calculated sample size was 265 patients and 285 patients were finally included in the study. Selection of participants was done using systematic random sampling from routine ART clinic visit, with every ninth patient coming in the morning for follow up invited to participate in the study and the subsequent patient included if the ninth patient did not give consent to participate. All patients above 18 years of age that gave written consent to participate were included and pregnant patients were excluded from the study.

Data collection

A questionnaire was conducted regarding participants' socio-demographic characteristics and cardiovascular risk factors. Data regarding HIV infection was retrieved from patient follow-up charts. Subsequently, physical examination including blood pressure measurement, weight and height measurement was done. The diagnosis of Hypertension was made in accordance with 2018 ESC/ESH (European society of cardiology and European society of hypertension) guideline for management of

arterial hypertension and hypertension was diagnosed if systolic blood pressure was 140 mm/Hg and/or diastolic blood pressure was 90 mm/Hg and above (11). Body mass index (BMI) was classified according to World Health Organization classification (12). Biochemical analysis was done to determine participants' fasting blood glucose (FBG) and serum cholesterol levels.

Finally, two-dimensional transthoracic echocardiography, including M mode, color Doppler, pulse wave, and continuous wave Doppler was done by experienced cardiologists using an GE VIVID E9 with 1–5 MHz transducers. Participants were placed in the left lateral supine position and examined in standard parasternal and apical views. Echo and Doppler study measurements and interpretation was made in accordance with recommendations of the American Society of Echocardiography guidelines.

Normal chamber measurement values were defined according to current guidelines, along with measurement of ejection fraction (EF) by quantitative biplane Simpson method. Global left ventricle (LV) systolic function was estimated using ejection fraction which was considered normal if it was 52–72% and 54–74%, and reduced if it was less than or equal to 52% and 53% in males and females respectively (13). Diastolic function was categorized according to the progression of diastolic dysfunction as follows: normal; Grade I, defined as impaired relaxation without evidence of increased filling pressures; Grade II, defined as impaired relaxation associated with moderate elevation of filling pressures or pseudo normal filling, and Grade III, defined as advanced reduction in compliance or reversible or fixed restrictive filling (14). LV size was estimated based on the internal diastolic diameter in M mode and normal values were considered as 42–58.4 mm and 37.8–52.2 mm for males and females respectively and right ventricle (RV) basal diameter was considered normal if 25–41 mm. Left atrium anteroposterior dimension was considered normal if 30–40 mm and 27–38 mm in males and females respectively (13). Right atrium minor axis dimension was considered normal if 29 to 45 mm (15).

Pulmonary hypertension was defined by a tricuspid regurgitant velocity of ≥ 2.9 m/sec on transthoracic echocardiography which translated to a right ventricular pressure above 35 mmHg. A tricuspid regurgitant velocity 3.5 m/sec, which translates into a pulmonary arterial pressure/right ventricular systolic pressure of ≥ 50 mmHg, was considered moderate-to-severe pulmonary hypertension (16). LV septal wall thickness was considered normal if it was ≤ 10 mm in males and 9 mm in females. Furthermore, mild left ventricular hypertrophy (LVH) (10 – 12 mm, for women and 11–13 mm for men), moderate LVH (L 13–15 mm for women and 14–16 mm for men) and severe LVH (> 15 mm for women and > 16 mm for men) classifications were used (13). Pericardial effusion was considered small when less than 10 mm, moderate when 10–20 mm, large when > 20 mm, and very large if > 25 mm (17).

If any abnormality was detected, patients were linked to a cardiologist for follow up.

Data analysis

Data was summarized using percentages, mean, standard deviation (SD) and presented in tables and text. The independent Student t-test was used to compare continuous variables and the Chi square and Fisher's exact test, when assumptions of chi-square test were not met were used to compare categorical variables.

Logistic regression was used to examine the association between echocardiographic abnormalities and associated factors. Variables with P-value < 0.2 in the univariate analysis were included in the multivariate logistic regression model. All variables with a p-value of < 0.05 in the multivariate model were considered statistically significant. Associations between variables were presented in odds ratios (OR) with 95% confidence interval (CI).

Ethical approval

This study was approved by the Institutional Review Board of SPHMMC. Written informed consent was obtained from all participants. Each participant's information was collected using anonymous questionnaire.

Results

Sociodemographic characteristics

A total of 285 HIV infected patients on ART participated in the study, out which 90 (31.6%) were male and 195 (68.4%) were female. The mean age (SD) of study participants was 44.7 years (10.3), with the youngest participant being 19 and the oldest 83 years old. Female participants were younger with 38.9% being less than 40 years compared to 14.6% of males ($P < 0.001$).

The mean of the most recent Cluster of differentiation 4 (CD4) count (SD) was 566.9 cells/mm³ (269) and ranged from 55-1477 cells/mm³. Viral load was done in 74% of the participants and the mean of the most recent result was 5,634 copies/mL (undetectable – 272,719 copies/mL) with 73.5% having undetectable viral load. The mean number of years since HIV diagnosis was 10.6 (3.9) years. The mean duration on ART was 10.07 (3.9) years with males being on ART for longer mean years than females ($P = 0.016$). Around 70.7% were taking Tenofovir Disoproxil Fumarate (TDF) and Lamivudine with Efavirenz or Nevirapine.

Only 5 (1.8%) were active smokers and 7 (2.5%) consumed alcohol in the past one month.

Measurement of fasting blood glucose was done and 66.1% had normal measurements. Out of the total participants, 21.6% had hypertension based on the mean blood pressure measurement. Dyslipidemia was seen in 67.6% and 10.9% were obese (Table 1).

Table 1
Sociodemographic and clinical characteristics of participants, SPHMMC, Addis Ababa, 2020

	Total	Male N (%)	Female N (%)	P-value
Age group				< 0.001
≤ 39 years	85 (31%)	13 (14.6%)	72 (38.9%)	
40–59 years	163 (59.5%)	67 (75.3%)	96 (51.9%)	
≥ 60	26 (9.5%)	9 (10.1%)	17 (9.2%)	
CD4 count				0.614
< 200	17 (7.2%)	6 (8.1%)	11 (6.7%)	
200–349	35 (14.8%)	8 (10.8%)	27 (16.6%)	
350–499	50 (21.1%)	18 (24.3%)	32 (19.6%)	
≥ 500	135 (57%)	42 (56.8%)	93 (57.1%)	
Viral load				0.337
< 50	166 (79%)	54 (83.1%)	112 (77.2%)	
≥ 50	44 (21%)	11 (16.9%)	33 (22.8%)	
Current regimen				0.31
TDF/3TC/EFV OR NVP	199 (70.8%)	61 (69.3%)	138 (71.5%)	
AZT/3TC/EFV OR NVP	56 (19.9%)	17 (19.3%)	39 (20.2%)	
TDF/3TC/LPV/R	4 (1.4%)	3 (3.4%)	1 (0.5%)	
Other	22 (7.8%)	7 (8%)	15 (7.8%)	
Blood pressure				0.008
SBP < 130 and DBP < 85	183 (65.4%)	46 (52.3%)	137 (71.4%)	
SBP 130–139 and/or DBP 85–89	36 (12.9%)	13 (14.8%)	23 (12%)	
SBP 140–159 and/or DBP 90–99	41 (14.6%)	21 (23.9%)	20 (10.4%)	
SBP ≥ 160 and/or DBP ≥ 100	20 (7.1%)	8 (9.1%)	12 (6.3%)	
Current tobacco smoker	5 (1.8%)	3 (3.4%)	2 (1%)	0.181
Alcohol drink in the last 1 month	7 (2.5%)	3 (3.4%)	4 (2.1%)	0.682
Fasting blood glucose				0.905

3TC – Lamivudine, ART – Anti-Retroviral Treatment, AZT – Zidovudine, EFV – Efavirenz, LPV – Lopinavir/ritonavir, NVP – Nevirapine, TDF - Tenofovir Disoproxil Fumarate

	Total	Male N (%)	Female N (%)	P-value
Less than 100	180 (66.2%)	54 (64.3%)	126 (67%)	
100–125	67 (24.6%)	22 (25.2%)	45 (23.9%)	
126 or more	25 (9.2%)	8 (9.5%)	17 (9%)	
Dyslipidemia	188 (67.6%)	63 (71.6%)	125 (65.8%)	0.336
Obesity	30 (10.9%)	10 (11.5%)	20 (10.6%)	0.821
Mean years since diagnosis	10.6 ± 3.9	11.2 ± 4.1	10.3 ± 3.9	0.071
Mean years on ART	10.07 ± 3.9	10.9 ± 3.9	9.7 ± 3.9	0.016
3TC – Lamivudine, ART – Anti-Retroviral Treatment, AZT – Zidovudine, EFV – Efavirenz, LPV – Lopinavir/ritonavir, NVP – Nevirapine, TDF - Tenofovir Disoproxil Fumarate				

Echocardiography parameters

All but one patient had normal ejection fraction with median ejection fraction of 66% (Interquartile range 62–70%). Most participants (69.9%) had normal diastolic function. More males (59.4%) had diastolic dysfunction compared to females (23%) ($P < 0.01$). Diastolic dysfunction was seen more often in participants above 60 years of age (40.3%) compared to individuals below 40 years of age (9.2%) ($P < 0.001$). It was also more frequently seen in hypertensive individuals ($P < 0.001$), obese participants ($P = 0.0012$) and in individuals who have been on ART for more than 10 years ($P = 0.032$).

Most of the participants had normal chamber dimensions. The left atrium was enlarged in 23 (8.3%) of the participants while right ventricle, left ventricle and right atrium was enlarged in 1.1%, 0.4% and 1.1% of participants respectively. Left atrial enlargement was more likely to be seen in hypertensive individuals (21.3% Vs 4.5%) ($P < 0.001$). It was also seen more frequently in obese participants (23.3% Vs 6.1%) ($P = 0.001$) and with increasing duration of HIV diagnosis ($P = 0.007$).

Ten patients (3.5%) had elevated systolic pulmonary artery pressure.

Among the participants 8.5% had mild left ventricular hypertrophy and 1.8% had moderate to severe hypertrophy. LVH was seen more commonly in males (16.5% Vs 7.7%) ($P = 0.013$) and in participants 40 years of age and above (14.6% Vs 1.1%) ($P = 0.002$). As expected, LVH was seen more often in individuals with mean blood pressure in the hypertensive range (26.2%) compared to normotensive ones (6%) ($P < 0.001$) (Table 2).

One patient had thrombus in the left ventricle and 8 patients had congenital heart disease. Among the valve lesions, two participants had moderate or severe mitral regurgitation and one had moderate or severe aortic regurgitation. Three participants had moderate or severe aortic stenosis and one patient had

moderate or severe mitral stenosis. Six patients had pericardial effusion. Two participants had vegetation one on the mitral and the other on the aortic valve. No patient had atrial thrombus.

Table 2
Echocardiography parameters of patients, SPHMMC, Addis Ababa, 2020

Echocardiography parameter	Total	Male N (%)	Female N (%)	P – value
Ejection fraction	66 ± 5.6			
Reduced ejection fraction	1 (0.4%)	0	1 (0.5%)	0.453
Mean left ventricle end-diastolic diameter	42.1 ± 5.1			
Enlarged left ventricle end-diastolic diameter	1 (0.4%)	0	1 (0.5%)	0.494
Mean left atrium end-diastolic diameter	33.1 ± 4.6			
Enlarged left atrium end-diastolic diameter	23 (8.1%)	11 (12.4 %)	12 (6.2%)	0.078
Mean right ventricle end-diastolic diameter	31.7 ± 4.5			
Enlarged right ventricle end-diastolic diameter	3 (1.1%)	2 (2.2%)	1 (0.5%)	0.192
Mean right atrium end-diastolic minor axis dimension	33.6 ± 4.4			
Enlarged right atrium end-diastolic minor axis dimension	1 (0.4%)	1 (1.1%)	0	0.319
Left ventricle diastolic dysfunction				
None	197 (69.9%)	48 (69.6 %)	147 (77 %)	< 0.001
Grade 1	75 (26.6%)	38 (55.1 %)	37 (19.3 %)	
Grade 2	10 (3.5%)	3 (4.3 %)	7 (3.7 %)	
Systolic pulmonary artery pressure				0.838
Normal	273 (96.5%)	86 (97.7 %)	185 (%)	
Mild elevation	5 (1.8%)	1 (1.1 %)	4 (%)	
Moderate elevation	1 (0.4%)	0	1 (%)	
Severe elevation	4 (1.4%)	1 (1.1 %)	3 (%)	
Pericardial effusion	6 (2.1%)	1 (1.1 %)	5 (2.6 %)	0.669
Left ventricular hypertrophy				0.013
None	252 (89.7%)	71 (83.5 %)	179 (92.3 %)	
Mild	24 (8.5%)	12 (14.1 %)	12 (6.2 %)	

Echocardiography parameter	Total	Male N (%)	Female N (%)	P – value
Moderate	2 (0.7%)	2(2.4 %)	0	
Severe	3 (1.1%)	0	3 (1.5 %)	

Most of the participants (71.4%) had a final conclusion of a normal echocardiography study. The most common abnormal finding was regional wall motion abnormality seen in 22.2% of the participants followed by congenital heart disease in 3.2% and rheumatic valvular heart disease in 1.2%. Females were more likely to have a normal echocardiography study (79.4 %) compared to males (53.8 %) and males were more likely to have regional wall motion abnormality (35.9 %) compared to females (15.9 %) ($P = 0.001$). Regional wall motion abnormality was diagnosed more frequently in individuals above 60 years of age with as high as 34.8% having such finding compared to 6.2% of individuals below 40 years of age ($P < 0.001$). It was also more commonly seen in hypertensive participants ($P\text{-Value} = 0.027$), participants with dyslipidemia ($P = 0.021$) and with those with longer years on ART for more than 10 years ($P = 0.007$) (Table 3).

Table 3
Echocardiography conclusion of patients, SPHMMC, Addis Ababa, 2020

Conclusion of echocardiography	Total	Male N (%)	Female N (%)	P = 0.001
Normal	177 (71.4%)	42 (53.8 %)	135 (79.4 %)	
Regional wall motion abnormality	55 (22.2%)	28 (35.9 %)	27 (15.9 %)	
Rheumatic Valvular	3 (1.2%)	2 (2.6 %)	1 (0.6 %)	
Non-Rheumatic Valvular	2 (.8%)	2 (2.6 %)	2 (1.2 %)	
Cardiomyopathy	2 (0.8%)	1 (1.3 %)	1 (0.6 %)	
Hypertensive heart disease	1 (0.4%)	2 (2.6 %)	1 (0.6 %)	
Congenital	8 (3.2%)	5 (6.4 %)	3 (1.8 %)	

Predictors of echocardiography parameters

In multivariable analysis, participants with elevated blood pressure were 4 times as likely to have LVH on echocardiography (95% CI 1.657–9.585; $P = 0.002$) and participants above 50 years of age had 3 times increased risk of having LVH (95% CI 1.213–7.095; $P = 0.017$). Hypertension also increased the odds of having an enlarged left atrium by 4.1 times (95% CI 1.3–13.15; $P = 0.0016$) and the odds of having diastolic dysfunction by 2.3 times (95% CI 1.05–4.93). LVH (AOR 12.914, 95% CI 3.36–49.61; $P < 0.001$) and age above 50 (AOR 3.4, 95% CI 1.717–6.725; $P < 0.001$) were other factors independently associated

with diastolic dysfunction. Ischemic heart disease was more likely to be seen in males (AOR 2.54, 95% CI 1.197–5.37; $P = 0.015$), in participants above 50 years of age (AOR 3.552, 95% CI 1.631–7.733; $P = 0.001$) and participants with FBG above 100 mg/dL (AOR 2.297, 95% CI 1.1–4.8; $P = 0.027$). There were no factors independently associated with elevated systolic pulmonary artery pressure. The severity of HIV infection did not contribute significantly to echocardiography findings (Table 4).

Table 4
Multivariate logistic regression of factors associated with echocardiography parameters, SPHMMC, Addis Ababa, 2020

LVH		Enlarged left atrium		Diastolic dysfunction		Ischemic heart disease		Elevated PASP	
	AOR 95% CI	P- value	AOR 95% CI	P- value	AOR 95% CI	P- value	AOR 95% CI	P- value	AOR 95% CI
Gender									
Female							1		
Male							2.54 (1.2– 5.37)	0.015	
Age									
≤ 50	1				1		1		
Above 50	2.93 (1.21– 7.1)	0.017			3.4 (1.72– 6.73)	0.00	3.55 (1.63– 7.73)	0.001	
Blood pressure									
Normal	1		1		1				
Elevated	4.4 (1.82– 10.63)	0.001	4.14 (1.3– 13.15)	0.0016	2.27 (1.05– 4.93)	0.038			
Fasting blood glucose									
< 100 mg/dL							1		
≥ 100 mg/dL							2.297 (1.1– 4.8)	0.027	
LVH									
No					1				
Yes					12.91 (3.36– 49.61)	0.00			
AOR – Adjusted odds ratio, CI – Confidence interval, LVH – Left ventricular hypertrophy, PASP – Pulmonary artery systolic pressure									

Discussion

There was a high prevalence of echocardiographic abnormalities found in this study of HIV infected individuals. The prevailing abnormalities identified were diastolic dysfunction, regional wall motion abnormality, LVH and left atrial dilation.

Diastolic dysfunction (DD), predominantly grade I (impaired relaxation) was reported in 30.1% of the participants with normal systolic function. Similar to our finding, diastolic dysfunction has been reported to be the most common finding previously (7, 9, 18, 19). High prevalence ranging from 42.8% in India to as high as in 85.7% in Congo have been reported in the past (3, 7, 9, 18, 19). The lowest report of diastolic dysfunction was from a study on patients with early HIV infection of only 2% (20). Other studies report prevalence from 9.25% to 19.9% (2, 21) with a recent systematic review reporting pooled prevalence of 29.3%, a number similar to our study (4). Similar to this study, increasing age has been shown to be an independent risk factor for DD in HIV patients (9) and is also a known risk factor in the general population (22). Hypertension and LVH are other risks for DD seen in previous studies also supported by our findings (3, 5, 9, 22, 23). HIV infection is also a risk factor for DD by itself (3). The level of immunosuppression and viral load did not affect finding of DD in this or some other studies (3, 7). The mechanisms behind DD in HIV infection is multifactorial with hypertension, LVH, direct myocardial viral infection (HIV itself, *Mycobacterium avium*, *Cryptococcus neoformans*, *Toxoplasma gondii*), neoplastic involvement (Lymphoma, Kaposi Sacroma), infiltrative diseases (amyloidosis, tuberculosis), increased inflammation, immunosuppression, increased HIV related atherosclerosis, Nucleoside/Nucleotide reverse transcriptase inhibitor (NRTI) induced mitochondrial damage and cardiomyopathy all potentially contributing (3, 18). DD precedes systolic dysfunction and is considered an early finding of myocardial disease that needs follow up (19).

LVH was seen in 10.3% of our study participants. Previous studies have reported prevalence of LVH from 4% to 46.9% (2, 3, 18, 23-25). This variation could be explained by the use of different methods for assessment of LVH including indexing for body surface area and height which was not done in our study. A study done on patients receiving ART showed hypertension to be a risk for LVH, supporting a similar finding in our study (23). Age and hypertension are known risk factors for LVH in the general population (26). The severity of HIV infection was not shown to be a risk for LVH which was also the case from previous findings (3, 23-25). A study that compared HIV infected patients to controls have shown that the infection itself increases risk of LVH (3). Several factors contribute to LVH in HIV. Infection of myocardium and subsequent local release of cytokines, opportunistic infections, use of ART particularly protease inhibitors, subclinical atherosclerosis and state of increased inflammation may all play a role (3, 24). LVH is an important precursor to the development of hypertensive heart disease and is associated with cardiovascular mortality and therefore needs close follow-up and treatment (9, 26).

Diagnosis of ischemic heart disease was made after the echocardiographic finding of pathologic contraction (regional wall motion abnormality) was seen in 22.2%. This is higher than most previous studies which reported regional wall motion abnormality from 1 % to 23.2% (7, 9, 10, 21, 27). This large difference could be explained by the exclusion of patients with known ischemic heart disease except in

two of the studies which had the higher prevalence of 13.5% and 23.2% which is close to our finding (9, 10). In addition to HIV infection itself, traditional cardiovascular risk factors such as increasing age, male gender and diabetes are supplementary risk factors (28, 29). HIV infected patients have increased risk for coronary artery disease with increasing reports (7, 8). The major proposed mechanism is increased endothelial dysfunction but also includes lipodystrophy and impaired glucose metabolism (7, 8). Certain ART medications increase level of dyslipidemia, insulin resistance and C-reactive protein that increase the risk of coronary artery disease (5, 8). They also have increased prevalence of traditional cardiovascular risk factors (5). With increasing longevity and decreasing opportunistic infections, coronary artery disease is expected to become an increasing burden (8). Regional wall motion abnormality is an earlier stage of global LV dysfunction that mandates appropriate management (7).

Left atrial enlargement (LAE) was seen in 8.1% of our participants. Previous studies reported atrial enlargement from 2.4%, 7.7% and 40% (2, 9, 23). The difference could be explained by the use of different cutoff points; usage of linear measurement of LA anteroposterior size and not LA volume measurement in our study; and lack of adjustment made for body surface area. Measurement of linear dimension as opposed to volume does not reflect accurate LA size as the LA enlarges in different dimensions during LA remodeling (13). A study comparing HIV infected and non-infected controls showed larger LA size in infected individuals (3). Hypertension was the only factor independently associated with LAE in our study. Previous studies also found associations with hypertension and LVH (2, 23). Similar to our finding, CD4 and viral load have not found to be significant previously (23). LAE in the general population, has been shown to be a risk factor for cardiovascular disease including heart failure, atrial fibrillation and stroke (23, 30).

Pericardial effusion was seen in only 6 (2.1%) of the participants which was mostly small or moderate and none of the patients had cardiac tamponade that needed drainage. There is a trend toward decreasing pericardial effusion in HIV patients particularly in developed countries (5). Studies from Congo and Cameroon showed prevalence of effusion of 20.4% and 46.5% respectively, showing very high prevalence in Africa (31, 32). Others reported prevalence of as low as 4% to 16.6% (7, 8, 10, 21, 27, 30, 33, 34) and in one study only two patients had pericardial effusion (35). There is a difference of the participants of the studies with some including patients with profound immunosuppression. Pericardial effusion is seen mainly in patients with lower CD4 counts (10, 21, 27, 33). The pathophysiology includes pericarditis caused by the virus and opportunistic infections such as Mycobacterium Tuberculosis, Cryptococcus Neoformans and Herpes Simplex (30). Malignancies such as Lymphoma and Kaposi Sarcoma which have become less common with the widespread use of ART are other potential causes (5, 30). Patients with pericardial effusion potentially have higher mortality and therefore needs management as many of the causes are potentially treatable (31).

Reduced ejection fraction was seen in only one patient. A systematic review and meta-analysis published in 2018 showed the pooled prevalence of reduced ejection fraction below 50% was 12.3% which was more reduced in patients with AIDS showing the possible relation with immunodeficiency and opportunistic infections and showed lower prevalence in patients on ART potentially explaining the preserved ejection

fraction in our patients (4). There are some studies where four percent or less of the studied population had low ejection fraction (2, 3, 20).

Similarly, the systematic review and meta-analysis reported prevalence of pulmonary hypertension in 11.5% of patients while this study revealed prevalence of 3.6% (4). A study done in similar Ethiopian setting showed prevalence of 14% (16). However, other studies also revealed low prevalence of 2.6% and 3.3% (2, 7). The sensitivity of echocardiography for pulmonary hypertension is not satisfactory and invasive tests may be required in patients with strong clinical suspicion as it is associated with increased mortality (16, 36).

There are certain limitations to this study. The cross-sectional nature of the study hinders from making final conclusions about echocardiographic findings and associated factors. There was also no control group for comparison. Despite these limitations our study provides a detailed assessment of echocardiographic findings in a large sample of HIV infected patients and provides new information for the population in the country that was limited to only few echocardiographic parameters. We recommend for future studies to be done taking our limitations into consideration and using a longitudinal study nature that takes the effect of time and long ART use into account.

Conclusions

In conclusion, a high prevalence of echocardiographic abnormalities was found in this study of HIV infected individuals including diastolic dysfunction, regional wall motion abnormality, LVH and left atrial enlargement. Male gender, age above 50 years, elevated blood pressure and elevated fasting blood glucose were associated with echocardiographic abnormalities. With increasing cardiovascular disease in HIV infected population, appropriate screening, therapeutic interventions and follow-up is needed.

Abbreviations

3TC – Lamivudine

AOR – Adjusted odds ratio

ART - Antiretroviral Treatment

AZT – Zidovudine

BMI - Body mass index

CD4 – Cluster of differentiation 4

CI – Confidence interval

DD - Diastolic dysfunction

EF - Ejection fraction

EFV – Efavirenz

FBG - Fasting blood glucose

HIV - Human Immunodeficiency Virus

LAE - Left atrial enlargement

LPV – Lopinavir/ritonavir

LV - Left ventricle

LVH - Left ventricular hypertrophy

NVP – Nevirapine

PASP – Pulmonary artery systolic pressure

RV - Right ventricle

OR - Odds ratio

SD - Standard deviation

SPHMMC - St. Paul's hospital millennium medical college

TDF - Tenofovir Disoproxil Fumarate

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of SPHMMC. Written informed consent was obtained from all participants.

Consent for publication

Written informed consent including for data publication was obtained from all participants.

Availability of data and materials

The datasets used in this study are available from the corresponding author on reasonable request.

Competing interests

All authors declare that we have no conflict of interest regarding this manuscript.

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Authors' contributions

EW conceived and designed the study; EW, HM, AE, HB, MA, AA were involved in data collection; EW, HF, MA, AA assured the data completeness and data entry; EW, HF performed the statistical analysis; EW, HF prepared the original draft; EW, HF revised the manuscript and performed editing. All authors read and approved the final manuscript.

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