



WESTERN NIGERIA JOURNAL OF MEDICAL SCIENCES (WNJMS)

**ECHOCARDIOGRAPHIC PATTERNS IN PATIENTS WITH HUMAN
IMMUNODEFICIENCY VIRUS INFECTION**

ECHOCARDIOGRAPHIC PATTERNS IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

Eretan T¹, Eretan O¹, Akinola R², Balogun B², Adeola A³

1. Department of Radiology, University of Medical Sciences Teaching Hospital, Laje, Ondo, Nigeria.
2. Department of Radiology, Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria.
3. Department of Internal Medicine, Lagos State University Teaching Hospital, Ikeja Lagos, Nigeria.

Correspondences to: Eretan T, Department of Radiology, University of Medical Sciences Teaching Hospital, Laje, Ondo, Nigeria. Telephone: 08033559098. E-mail: thelmaeretan@gmail.com

ABSTRACT

Introduction: Human immunodeficiency virus (HIV) may cause progressive dysfunction of multiple organ systems including cardiac abnormalities some of which may be subclinical in nature. This study evaluated the echocardiographic patterns in patients with HIV infection.

Methods: A prospective case-control study involving one hundred HIV- seropositive adult patients of age range 18 – 60 years (mean: 44.9 ± 10.09 years) comprising 79 females and 21 males. Echocardiography was performed to assess the interventricular septal wall, left ventricular posterior wall thickness, left ventricular ejection fraction and diastolic function abnormalities. SPSS was used for univariate, bivariate and multivariate data analysis with statistical significance set at p-values of <0.05 .

Results: The interventricular septum and left ventricular posterior wall thicknesses were increased, whilst the ejection fraction values were reduced with diastolic function abnormalities. Additional cardiac abnormalities detected included dilated cardiomyopathy and a calcified tricuspid valve.

Conclusion: Echocardiographic imaging of persons with HIV infection showed an increase in the interventricular septal thickness, left ventricular posterior myocardial wall thickness with reduced ejection fraction and presence of diastolic function abnormalities.

Keywords: Human Immunodeficiency Virus Infection; Cardiac; Echocardiography.

INTRODUCTION

Human immunodeficiency virus (HIV) infection affects the immune system leading to the acquired immune deficiency syndrome (AIDS) in advanced stages.¹ AIDS is characterized by an acquired, irreversible, immune suppression that predisposes the patient to multiple opportunistic infections, malignant neoplasms and a progressive dysfunction of multiple organ systems.² From the beginning of the AIDS epidemic, it was recognized, first at autopsy and later by non-invasive techniques, that HIV can cause cardiac abnormalities, some of which may be subclinical in nature.^{3,4}

Improved survival of persons living with HIV (PLWH) from the availability of highly active antiretroviral therapy (HAART) has led to the manifestations of late stage HIV infection, which includes HIV related cardiac disease.^{2,5,6} Several studies have demonstrated the presence of high rates of traditional cardiovascular risk factors in patients with HIV infection³. Some of these, such as dyslipidaemia (11.9%),^{3,7} hypertension (33.3%),³ diabetes mellitus and the metabolic syndrome may be related to HIV infection or to HIV therapies, while others such as smoking (70% - 80%),³ are independent of HIV infection.³ Other factors that may contribute independently to cardiovascular risk include, uncontrolled HIV

replication, the effects of HIV and antiretroviral therapy (ART) on vascular endothelial function and inflammatory cytokines.⁸

Cardiac diseases in HIV infection include pericardial effusion, pericarditis, endocarditis, myocardial involvement (myocarditis, dilated cardiomyopathy, left ventricular dysfunction, diastolic dysfunction, pulmonary hypertension, malignant neoplasm, coronary artery disease and drug related cardiotoxicity.^{2, 3, 9}

Cardiac ultrasound, otherwise known as echocardiography can be used to assess abnormalities of cardiac structure and function in patients with HIV. It is useful, safe, available, easily accessible and does not involve the use of ionizing radiation. Furthermore, it can be used to monitor cardiac abnormalities over time to evaluate patients' response to therapy/intervention, as well as prevent deterioration into cardiac failure.

The aim of this study was therefore to evaluate the echocardiographic patterns in patients with HIV infection with the purpose of detecting and managing cardiac complications.

METHODS

Research Design

This was a prospective case control study. One hundred HIV-seropositive adult patients of age range 18 – 60 years of both sexes were selected at random from the HIV clinic of the Haematology Department of the Lagos State University Teaching Hospital between October 2017 and August 2018. One hundred apparently healthy age and sex matched controls without any evidence of cardiac disease were selected from other clinics in the hospital for comparison.

Inclusion Criteria

Adult patients with confirmed HIV infection via positive antibody levels detection in serum using Rapid test strips.

Exclusion Criteria

Patients with hypertension, diabetes mellitus and cardiac disease were excluded.

Echocardiographic technique¹⁰

Transthoracic echocardiography was performed on each patient using grayscale and Doppler imaging technique using the VIVID e ultrasound machine equipped with a 2-5MHz curvilinear probe. Two-dimensional (2D), M mode, pulse-wave and color Doppler echocardiography assessment were done on each patient.

Measurements of the interventricular septum (IVS) thickness, left ventricular posterior wall (LVPW) thickness and left ventricular ejection fraction values were obtained in the parasternal long axis from 2D derived M-mode recordings. Measurements were taken (in cm) according to the American Society of Echocardiography guidelines (leading edge methodology). The mean of three recordings was used for computation.

Doppler studies included pulmonary velocity, transmitral flow, Deceleration time (DT) and Isovolumetric relaxation time (IVRT). The following definitions were used: A dilated left ventricle is a left ventricular end-diastolic diameter (LVEDd) > 5.5cm. The ejection fraction was calculated using the formula: $\frac{LVEDV - LVESV}{LVEDV} \times 100$, where LVEDV = Left ventricular end-diastolic volume (LVEDd) and LVESV = Left ventricular end-systolic volume (LVESd). Dilated cardiomyopathy was diagnosed using three criteria: Left ventricular end-diastolic diameter (LVEDd) > 5.5 cm, global hypokinesia and fractional shortening (LVFS) < 28%. Left ventricular diastolic dysfunction was diagnosed and graded into three types based on the following criteria: Type I = impaired relaxation with an E/A ratio < 1, IVRT > 100 ms (milisecond) and DT > 220 ms (millisecond); Type II = pseudonormalization resembling the normal transmitral configuration, but with low or normal DT; Type III = restrictive pattern with E/A ratio > 2, IVRT < 70 ms and DT < 160 ms. Echocardiographic abnormalities such as pericardial effusion and thickening, valvular lesions like stenosis, calcifications and

regional wall motion abnormalities were sought for.

Ethical considerations

Ethical approval to carry out the study was obtained from the research and ethics committee of the Lagos State University Teaching Hospital, Ikeja (LREC. 06/10/1050). A written informed consent was obtained from each participant, having filled a data form with the following information: age, sex, history of diabetes and hypertension, weight, height, BMI (body mass index) and duration of HIV infection.

Data Analysis

Data obtained was entered into the Statistical Package for Social Sciences Software (SPSS) version 20, Chicago, Illinois, USA (2011) and the results documented using tables, graphs and charts. Association between variables were explored using independent samples *t* – test and correlations for comparison at 95% confidence interval. Associations were considered significant if *p* value < 0.05. Fischer's exact test was used to determine the significance level between proportions. Cardiac measurements were expressed as mean \pm -standard deviation (SD). Other cardiac abnormalities were expressed as percentages of HIV patients.

Outcome Measures

The outcome measures were interventricular septum thickness, left ventricular posterior myocardial wall thickness, ejection fraction and diastolic function abnormalities.

RESULTS

The study subjects comprised of 79% females and 21% males, while the controls were made up of 83% females and 17% males. The gender distribution of the study population was without statistical significance (*p* = 0.589). The mean age of the subjects was 44.96 \pm 10.09 years, while that of the controls was 42.46 \pm 8.92 years with a range of 20 – 60 years for both groups. The age group with the highest involvement were those in the above 36 years age category (table 1). Educational level of participants ranged from

primary to post-tertiary, with 118 (59%) out of 200 having attained secondary education.

Table 1: Sociodemographic characteristics of subjects

Variable	Category	Case	Control	Total
Age Group (years)	≤ 20	2	3	5
	21- 35	11	14	25
	≥ 36	87	83	170
Gender	Male	21	17	38
	Female	79	83	162
Educational Level	Primary	14	6	20
	Secondary	57	61	118
	Tertiary	22	29	51
	Post	7	4	11
	Tertiary			

Table 2: Mean Comparison of cardiac parameters in cases and controls

Cardiac parameters (cm)	Case (100)	Control (100)	p-value
Interventricular septum	0.96 \pm 0.28	0.86 \pm 0.17	0.002
Left ventricle posterior wall	1.14 \pm 0.27	1.02 \pm 0.17	0.001
Ejection Fraction %	53.25 \pm 8.70	61.46 \pm 6.90	0.001

Cardiac parameters such as the interventricular septum (IVS) thickness, left ventricle posterior wall (LVPW) thickness, ejection fraction (EF) values and diastolic function abnormalities in the subjects were compared to that of the controls and showed statistical significance (table 2).

The interventricular septum thickness and left ventricular posterior wall thickness were increased in subjects as compared to controls (figures 1 and 2).

The interventricular septum (IVS) thickness was increased ($> 1.20\text{cm}$) in 16 subjects, while 38 subjects had increased left ventricular posterior wall (LVPW) thickness (figure 3).

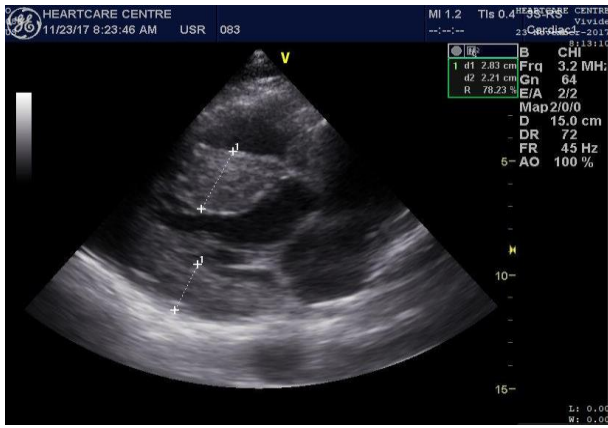


Figure 1: Grayscale parasternal long axis 2D image showing thickened interventricular septum (IVS) and left ventricular posterior wall (LVPW) in a 49-year male with HIV

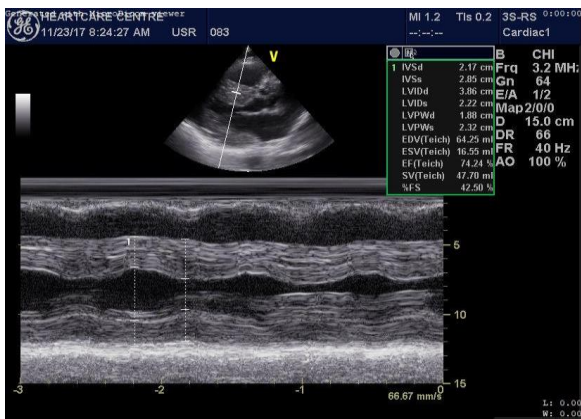


Figure 2: Parasternal long axis image 2D M-mode image showing increased interventricular septum (2.17cm) and left ventricle posterior wall thickness (1.88cm) in the same patient as depicted in figure 1.

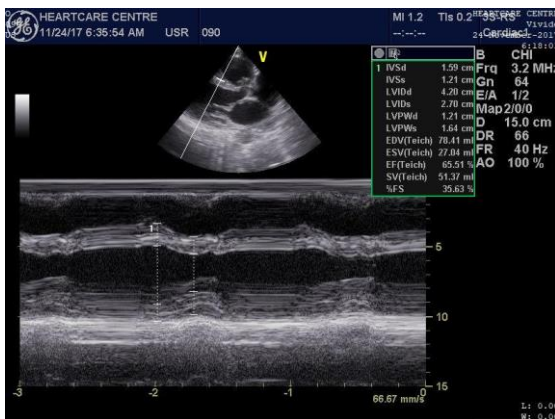


Figure 3: Parasternal long axis image 2D M-mode image showing increased interventricular septum (1.59cm) and left ventricle posterior wall thickness (1.21cm) in a 28-year-old female patient with HIV

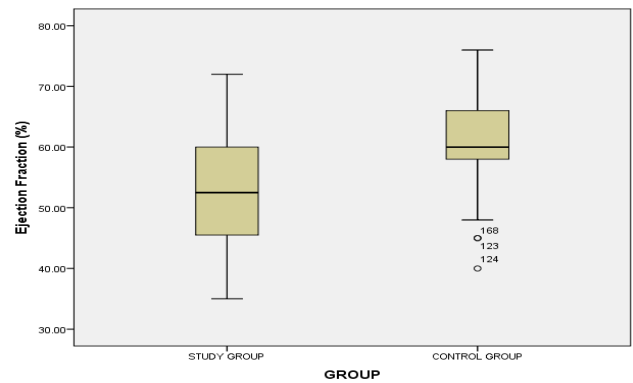


Figure 4: Boxplot of ejection fraction in cases and controls showing a wider range and variability among the cases as compared to the controls.

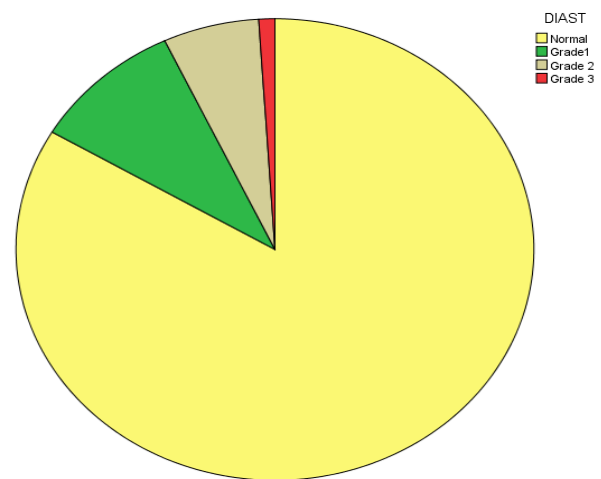


Figure 5: Piechart showing diastolic grades in cases.

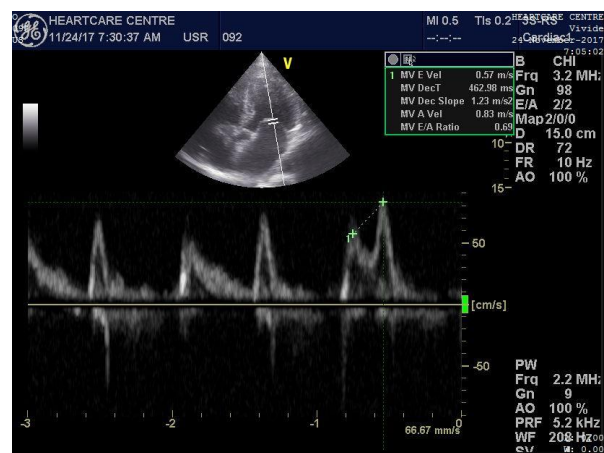


Figure 6: Pulsed wave echocardiogram of mitral inflow velocity showing type 1 diastolic dysfunction with reversal of E (green arrow) and A (orange arrow) velocities. The E/A ratio is < 1 (0.69), isovolumetric relaxation time (IVRT) > 100 ms and deceleration time (DT) > 220 ms. Cursors show fusion of the E/A velocities.

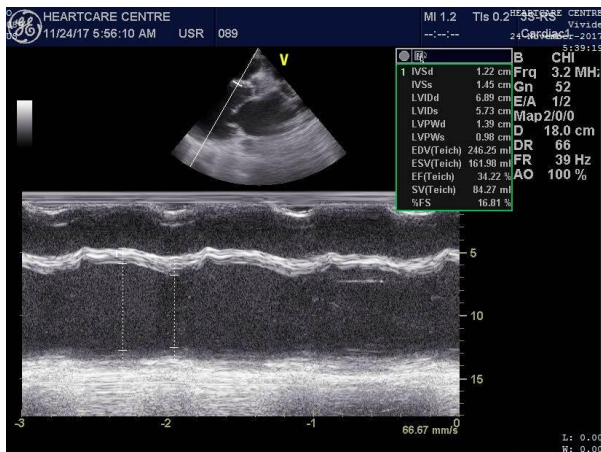


Figure 7: Two-dimensional echocardiogram left parasternal long axis showing dilated left ventricle with poor systolic function in a 57 year old man with dilated cardiomyopathy. Left ventricular end diastolic diameter (LVEDd) of 6.89cm, global hypokinesia, reduced ejection fraction of 30% and reduced fractional shortening of 16%. The IVS (1.22cm) and LVPW thicknesses (1.39cm) are also increased.

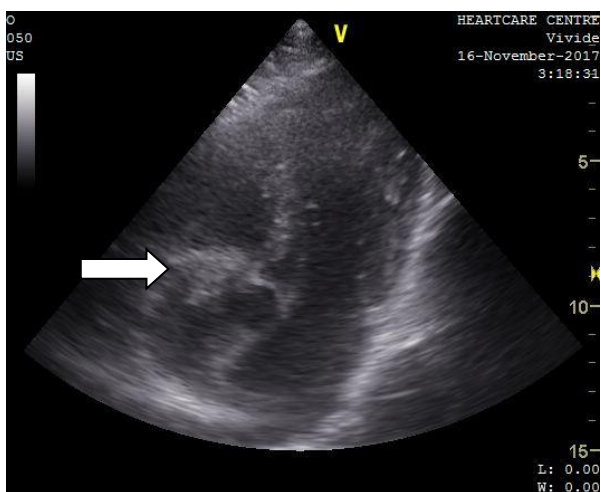


Figure 8: Two-dimensional echocardiogram apical four chamber view showing calcified tricuspid valve (white arrow) in a 50 year old female with HIV

Twenty-nine (29%) subjects had reduced ejection fraction (<50%). The variation of the ejection fraction distribution between cases and controls is shown in boxplot distribution (figure 4). Twenty-eight (28%) subjects had diastolic dysfunction abnormalities of varying grades, shown in a pie chart distribution (figure 5). Fourteen (14%), twelve (12%) and two (2%) subjects had diastolic dysfunction of grades 1, 2 and 3 respectively (figure 6).

Additional cardiac abnormalities detected in this study were dilated cardiomyopathy (DCM) shown in figure 7 and calcified tricuspid valves (figure 8).

DISCUSSION

Cardiac ultrasound (echocardiography) is a reliable, affordable and non-invasive diagnostic tool that can be used to evaluate for cardiac abnormalities in persons infected with HIV infection. Cardiovascular manifestations of HIV infection include cardiomyopathy, pericarditis with or without pericardial effusion, pulmonary hypertension, coronary vasculopathy and cardiac neoplasms. Echocardiographic findings in this study include increased interventricular septum (IVS) thickness, left ventricular posterior wall (LVPW) thickness, reduced ejection fraction and increase diastolic dysfunction in cases as compared to controls. Other abnormalities detected include dilated cardiomyopathy and tricuspid valve calcification.

The results obtained in this study suggest that the interventricular septum thickness and left ventricular posterior wall thickness are increased in HIV infected persons as compared to controls. A total of 16% and 38% of HIV patients had increased interventricular septum and left ventricular posterior wall thickness respectively when compared to 2% and 12% of controls. This difference in left ventricular wall dimension was significant, a finding that is in agreement with those of other studies that found an increase in left ventricular wall indices in HIV patients as compared to controls.^{8,11-15} The values of the mean left ventricular wall dimensions obtained in this study were similar to those of Meng *et al.*¹⁵ who reported mean IVS and LVPW dimensions of $(1.1 \pm 0.3$ vs 1.0 ± 0.2 , $p = 0.049$) and $(1.1 \pm 0.2$ vs 1.0 ± 0.2 , $p = 0.027$) in subjects and controls respectively, similar to those obtained in this study of IVS (0.96 ± 0.28 vs 0.86 ± 0.17 , $p < 0.002$) and LVPW (1.14 ± 0.27 vs 1.04 ± 0.19 , $p < 0.003$).

Several studies such as those of Reinsch *et al.*⁸, Hsue *et al.*¹⁶, Ogunmodede,¹² Olusegun-Joseph,¹⁷ Maurya,¹¹ and Adebola,¹⁴ have

reported that structural dimensions of the cardiac chambers and walls are increased in persons infected with HIV as compared to controls. The left ventricular mass indexed to body surface area (LVMI) has also been observed to be increased in persons with HIV when compared to controls.^{12, 15-18}

Reasons that have been postulated for this increase in the structural dimensions of the heart in this population group include inflammatory changes.^{12, 16, 19} Similar increases in left ventricular mass have been observed in patients with chronic inflammatory conditions such as systemic lupus erythematosus (SLE) and rheumatoid arthritis, hence its occurrence in HIV with higher levels of inflammation. Other reasons include subclinical atherosclerosis,^{12, 16, 20} (studies have shown an association between nadir CD4 count and subclinical atherosclerosis as assessed by the carotid intima media thickness; the virus causes inflammatory reaction in the coronary vessels which is believed to promote endothelial dysfunction and atherosclerosis) and long term use of protease inhibitors,¹⁵ which has also been linked to an increased incidence of myocardial infarction in persons with HIV.²

The results of the ejection fraction (EF) obtained in this study suggest the presence of increased left systolic dysfunction in persons with HIV. A total of 29% and 71% of HIV patients had EF below and above 50% respectively as compared to 4% and 96% of controls ($p < 0.001$). This was similar to the findings of Olusegun-Joseph and coworkers who found systolic dysfunction in 30% of their patients.¹⁷ Other similar findings were those of Sachdeva (26%),²¹ Singh (23%),² and Maurya (22%), while Isiguzo,²² and Ogunmodede,¹² reported lower values of 10.5% and 2.7% respectively. The reasons for this observation in the Ogunmodede study group could probably be explained by the short duration of disease (only HIV patients newly diagnosed within less than or equal to 3 months were recruited into the study), while for the Isiguzo study population, only a sizeable number of the patients (84 of 200) (42%) had HIV related cardiac disease with

left ventricular systolic dysfunction (10.5%) being the commonest abnormality followed by diastolic dysfunction (10%) and pericardial disease (8.5%).

Reduction in ejection fraction without global hypokinesia or chamber enlargement in the absence of any other symptom may represent an early form of cardiac disease that may later progress to a clinically evident dilated cardiomyopathy (DCM).^{2, 17} Systolic dysfunction implies a reduction in myocardial contractility and has been documented as part of the echocardiographic abnormalities seen in persons with HIV, that worsens with disease progression.¹⁷

Diastolic dysfunction (DD) was noted in some of the patients in the present study. A total of 28% and 5% of subjects and controls respectively had diastolic dysfunction (DD), when compared to 72% and 95% of cases and controls without DD. This finding is in agreement with those of Olusegun-Joseph and Sachdeva who reported the presence of DD in 32% and 26% of their patients respectively,^{17,21} while Maurya and Hsue *et al.* reported slightly higher values of 47% and 49% in their patients respectively.^{11,16} Isiguzo however reported lower values of 10%.²² Diastolic dysfunction was seen in 28% of the patients and was categorized as mild (14%), moderate (12%) and severe (2%). Most of the patients had a grade 1 DD, an observation that was also reported by other studies.^{16,17,21}

Diastolic dysfunction is usually indicative of ventricular filling abnormalities due to a non-compliant ventricle which worsens with disease progression.^{11,17} Possible causes of DD include chronic inflammation and increased cytokine expression, which worsen with disease progression.¹³ The pathogenesis of HIV related DD is said to be multifactorial.¹⁶ Several possible reasons that have been advanced for DD in persons with HIV include use of protease inhibitors, hypertension with prolonged use of antiretroviral therapy, increase in LVMI underlying development of mild DD and HIV or other associated viral infection directly affecting the myocardium (HIV-1 has been

detected in endomyocardial biopsy specimens of HIV patients with left ventricular dysfunction; also genomic sequences of HIV-1 have been detected in the myocytes of HIV patients at autopsy). Studies have also shown that individuals with HIV infection have high rates of inflammation which may predispose the HIV patients to myocardial fibrosis and DD.^{16,23} Furthermore, a lower CD4 count and longer duration of nucleoside reverse transcriptase inhibitor (NRTI) use was associated with DD, suggesting that advanced immunodeficiency and/or side effects from medication may mediate the development of this abnormality¹⁶. NRTI use has previously been associated with cardiomyopathy and mitochondrial damage.¹⁶ Another possible mechanism underlying DD in persons with HIV may be ischemic heart disease and increased arterial stiffness secondary to subclinical atherosclerosis.¹⁶ Other cardiac abnormalities detected include dilated cardiomyopathy (DCM) and calcification of the tricuspid valve.

One (1%) patient in this study had DCM as compared to none in the controls. Similar findings of 2-8.5% have been reported.^{2,12,17,21,24} Maurya found DCM in 15.65% of patients,¹¹ while Twagirumukiza found DCM in 17.7%,²⁵ a finding that may be attributed to a larger sample size of 416 subjects in a patient population not receiving highly active antiretroviral therapy (HAART).

Dilated cardiomyopathy (DCM) is a well documented cardiac abnormality in patients with HIV infection and is associated with advanced levels of immunosuppression and reduced CD4 lymphocyte counts of < 100 u/l. The patient with DCM in this study had HIV RNA viral copies of < 20 copies/ ml of blood, which correlates with higher CD4 lymphocyte counts > 500/ul. The ART combination he was using included lamivudine, zidovudine and nevirapine, a combination he took twice daily for the past 10 years, however he appeared to be malnourished. Probable factors for DCM in this patient may include cardiotoxic effect of zidovudine and nutritional deficiency. The actual cause of

cardiomyopathy in HIV patients remains unclear and is multifactorial. Reasons that have been elucidated for DCM in PLWH include myocarditis, direct HIV invasion of myocardial tissue and co-infection with other cardiotropic viruses such as coxsackie virus, cytomegalovirus and Epstein-barr virus.^{13,17} Other causes include the duration of HIV infection, low socio-economic factors,²⁵ endothelial dysfunction, abnormal lipid metabolism,²⁴ cardiotoxic effects of antiretroviral drugs such as zidovudine, autoimmunity and nutritional factors such as deficiency of selenium and other trace elements.¹⁷ Selenium deficiency as a cause of heart muscle disease is said to be of interest in Africa considering that most patients present with multiple nutritional deficiencies^{17,25}.

One patient in this study (a 60 year old female) had calcified tricuspid valve. This observation might be attributed to the effects of aging.

CONCLUSION

Echocardiographic evaluation of persons with HIV disease revealed a range of abnormalities which included increased thickness of the interventricular septum and left ventricular posterior wall, as well as systolic and diastolic dysfunction abnormalities. Regular echocardiographic evaluation of persons with HIV infection should be encouraged early in the course of the disease to enable timely detection of abnormalities, thus reducing mortality and morbidity and also provide a baseline for monitoring and followup.

Acknowledgements

The staff and patients of the Department of Haematology and Blood Transfusion of LASUTH, Ikeja are appreciated for their cooperation at the HIV clinic during the study.

Conflict of interest: None declared

Funding support: Nil

REFERENCES

1. Falutz J. Pathophysiology of HIV/AIDS. Managing the Older Adult Patient with HIV. 1st Edition ed. Springer International Switzerland: AIDI; 2016. p. 7-18.
2. Singh A, Das S, Dalai RK. Study of cardiac manifestations in patients with HIV infection and their correlation with CD4 count in Indian population. *International Journal of Clinical Medicine*. 2012; 3(03):178.
3. Nina Rakhlin PH, Cheitlin MD. Cardiac Manifestations of HIV. HIV Insite Knowledge Base Chapter October 2005. Available from: www.hivinsite.ucsf.edu (Date Accessed: 10 October 2017)
4. Liao CT, Toh HS, Chang WT, Yang CT, Chen ZC, Tang HJ, et al. Assessment of subclinical cardiac dysfunction by speckle-tracking echocardiography among people living with human immunodeficiency virus. *Frontiers in Cardiovascular Medicine*. 2023; 10:1200418.
5. Fisher SD, Lipshultz SE. Epidemiology of cardiovascular involvement in HIV disease and AIDS. *Annals of the New York Academy of Sciences*. 2001; 946(1):13-22.
6. Mishra TK, Mishra SK, Singh S. Cardiovascular manifestations of people living with HIV/AIDS: Report from a hot spot in eastern India. *Indian heart journal*. 2019; 71(4):338-343.
7. Sud K, Argulian E. Echocardiography in patients with HIV infection. *Current Cardiology Reports*. 2020; 22:1-7.
8. Reinsch N, Kahlert P, Esser S, Sundermeyer A, Neuhaus K, Brockmeyer N, et al. Echocardiographic findings and abnormalities in HIV-infected patients: results from a large, prospective, multicenter HIV-heart study. *American journal of cardiovascular disease*. 2011; 1(2):176.
9. Magula NP, Mayosi BM. Cardiac involvement in HIV-infected people living in Africa: a review. *Cardiovascular Journal of South Africa*. 2003; 14(5):231-237.
10. Spencer B, Gay RJW Jr. Imaging Techniques: Doppler Ultrasound. *Radiology Recall*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 43.
11. Maurya SK, Bajaj S, Saxena P, Sonker KK, Verma SK. Cardiac manifestations in HIV patients and their correlation with CD4 count. *International Journal of Advances in Medicine*. 2017; 4(3):783.
12. Ogunmodede JA, Kolo PM, Katibi IA, Salami AK, Omotoso A. Structural echocardiographic abnormalities seen in HIV/AIDS patients are independent of cd4 count. *Nigerian journal of clinical practice*. 2017; 20(6):716-723.
13. Olusegun-Joseph AD, Ajuluchukwu JN, Okany CC, Mbakwem AC, Oke DA, Okubadejo NU. Echocardiographic abnormalities and disease severity (based on CD4 count) in treatment-naïve HIV positive patients. *HIV & AIDS Review International Journal of HIV-Related Problems*. 2017; 16(3):169-175.
14. Adebola AP, Akinbo AA, Daniel FA. Relationship between CD4 cell count and left ventricular dimension and function in treatment-naïve human immunodeficiency virus-infected patients. *Nigerian Journal of Cardiology*. 2019; 16(1):11.
15. Meng Q, Lima J, Lai H, Vlahov D, Celentano DD, Strathdee S, et al. Use of HIV protease inhibitors is associated with left ventricular morphologic changes and diastolic dysfunction. *Journal of acquired immune deficiency syndromes (1999)*. 2002; 30(3):306-310.
16. Hsue PY, Hunt PW, Ho JE, Farah HH, Schnell A, Hoh R, et al. Impact of HIV infection on diastolic function and left ventricular mass. *Circulation: Heart Failure*. 2010; 3(1): 132-139.
17. Olusegun-Joseph D, Ajuluchukwu J, Okany C, Mbakwem A, Oke D, Okubadejo N. Echocardiographic patterns in treatment-naïve HIV-positive patients in Lagos, south-west Nigeria: cardiovascular topic-online article. *Cardiovascular journal of Africa*. 2012; 23(8):1-6.
18. Doria de Vasconcellos H, Post WS, Ervin AM, Habermen SA, Budoff M, Malvestutto C, et al. Associations between HIV serostatus and cardiac structure and function evaluated by 2-dimensional echocardiography in the Multicenter AIDS Cohort Study. *Journal of the American Heart Association*. 2021; 10(7):e019709.

19. Robbertse PPS, Doubell AF, Steyn J, Lombard CJ, Talle MA, Herbst PG. Altered cardiac structure and function in newly diagnosed people living with HIV: a prospective cardiovascular magnetic resonance study after the initiation of antiretroviral treatment. *The International Journal of Cardiovascular Imaging*. 2023; 39(1):169-182.
20. Athanasiadi E, Bonou M, Basoulis D, Kapelios CJ, Masoura C, Skouloudi M, et al. Subclinical left ventricular systolic dysfunction in HIV patients: prevalence and associations with carotid atherosclerosis and increased adiposity. *Journal of Clinical Medicine*. 2022; 11(7):1804.
21. Sachdeva S, Kaur S, Khurana T, Singh G. A Study of Cardiac Manifestations of HIV/AIDS. *Annals of International Medical and Dental Research*. 2017; 3(3):18.
22. Isiguzo G, Okeahialam B, Danbauchi S, Odili A, Iroezindu M. Determinants of HIV-related cardiac disease among adults in north central Nigeria. *Heart Asia*. 2014; 5(1):130-135.
23. Butler J, Greene SJ, Shah SH, Shah SJ, Anstrom KJ, Kim RJ, et al. Diastolic dysfunction in patients with human immunodeficiency virus receiving antiretroviral therapy: results from the CHART study. *Journal of cardiac failure*. 2020; 26(5):371-380.
24. Bendwal K, Bendwal S, Gawarikar S, Dhawale R. Cardiac manifestation of HIV infection. *Journal of medical science and clinical research (JMSCR)*. 2019; 07(08):298-302.
25. Twagirumukiza M, Nkeramihigo E, Seminega B, Gasakure E, Boccara F, Barbaro G. Prevalence of dilated cardiomyopathy in HIV-infected African patients not receiving HAART: a multicenter, observational, prospective, cohort study in Rwanda. *Current HIV research*. 2007; 5(1):129-137.