International Journal of Research in Medical Sciences
Okechukwu AA et al. Int J Res Med Sci. 2024 Sep;12(9):3155-3163
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20242589

Original Research Article

Cardiovascular diseases in HIV infected children and adolescents on highly anti-retroviral therapy at the university of Abuja teaching hospital, Gwagwalada, Nigeria

Adaora A. Okechukwu[1]*, Juliana O. Lawson[2], Onalo Richard[1], Orji A. Okechukwu[3]

[1]Department of Paediatrics, University of Abuja Teaching Hospital, Gwagwalada, Abuja, FCT, Nigeria
[2]Department of Paediatrics, Zankli Medical Center, Abuja, FCT, Nigeria
[3]Paediatric Special Treatment Clinic, University of Abuja Teaching Hospital, Gwagwalada, Abuja, FCT, Nigeria

Received: 04 June 2024
Revised: 18 July 2024
Accepted: 25 July 2024

***Correspondence:**
Dr. Adaora A. Okechukwu,
E-mail: nebokest@yahoo.com

ABSTRACT

Background: Effect of prolong use of antiretroviral therapy and chronic HIV infection on cardiac performance of infected children and adolescents requires evaluation. We studied cardiac structure/functions, and troponin levels of these subjects on anti-retroviral therapy for > 6 months in our hospital.
Methods: A cross sectional survey was conducted in our facility for the above objectives. Bio-data, time and type antiretroviral drugs, mode of transmission, weight, height, body-mass-index, echocardiogram, electrocardiogram, CD4, viral load, and troponin were done for all subjects.
Results: Of a total of 126 subjects recruited, 66 (52.4%) were males. Their mean age, and duration on antiretroviral therapy was 14.1±3.1 (7, 18) years, and 7.2±2.9 (1, 14) years. Majority 69 (54.8%) were between 15-18 years, most 73 (57.9%) had BMI of <18 kg/m^2, and 99 (78.6%) had vertical transmition. Their mean troponin-1 level was 2.0±1.6ng/ml. Abnormal echocardiogram and electrocardiogrm was detected in 41.3% and 38.1% of the subjects, with mild-systolic-dysfunction (11.9%), pulmonary-hypertension (11.1%) and left-ventricular-dysfunction (10.3%) as the commonest abnormal echocardiogram findings, and sinus-tachycardia 16 (12.7%), non-specific-ST-T abnormality 12 (9.5%), mild-right and left-ventricular-hypertrophy 4 (3.2%) as the commonest electrocardiogram abnormalities detected. Significant relationship was seen between troponin and the following variables; echocardiogram, chi^2 36.95, p=0.0001; electrocardiogram, chi^2 59.07, p=0.0001; body-mass-index chi^2 13.63, p=0.001; 1st line antiretroviral therapy, chi^2 21.187, p=0.001, 2nd line, chi^2 19.978, p=0.002; CD4, chi^2 6.896, p=0.032; and viral-load, chi^2 7.515, p=0.023.
Conclusions: There is high prevalence of cardiac abnormalities among the study subjects. Echocardiogram and electrocardiogram to be included in their baseline and follow-up care for early disease detection, and initiation of measures to halt its progression.

Keywords: Adolescents, Children, Echocardiogram, Electrocardiogram, HIV, Troponin

INTRODUCTION

Sub-Sahara Africa alone is responsible for over 71% burden of Human Immuno-deficiency Virus (HIV) across the globe.[1,2] Nigeria which ranks second in this world burden has 3.3 million of its population living with the virus out of which 360,000 were children <15 years.[3] With increasing access to highly active antiretroviral therapy (HAART), perinatal infected children are living into adulthood now. Such children are exposed to higher

risk of cardiovascular events from chronic HIV infection itself, and prolong use of HAART.[4] HIV is transmitted to children vertically from their infected mothers in 90% of paediatric HIV.[2] Cardiovascular disease (CVD) remains the leading cause of non–HIV related deaths in infected persons, and is the 1^0 cause of acquired heart disease in this group of people for both children and adults.[4] Cardiovascular complications result from direct myocardial invasion by HIV, chronic inflammatory response from the infection, endothelial dysfunction, autoimmunity to the virus, pulmonary hypertension (PH) from recurrent parenchymal lung disease, and derugrelated cardiotoxicity.[4] HAART has remained the standard treatment for HIV infection. Cardiovascular risk following its prolong use is dependently associated with increased risk of heart failure, cardiomyopathies, premature atherosclerosis, stroke, and myocardial infarction in both pre and HAART eras.[4] Inflammation with complex immune interaction in HIV infection is associated with endothelial dysfunction in both HIV treated and untreated patients.[5] Hsue et al reported carotid intima media thickness and elevated C-reactive proteins (CRP) that remained elevated in all HIV groups, irrespective of the level of viraemia suggesting persistent inflammation, key etiology for early atherosclerosis in these patients.[6] Several studies have also shown that despite the control of HIV replication below the assay threshold (20, 40 or 50 copies/ml), HIV replication persists along with immune activation from; evolving HIV production, co-pathogen load of cytomegalovirus (CMV) and herpes viruses, the loss of immune-regulatory T cells, the translocation of lipopolysaccharide across a damaged gut mucosa, and the irreversible fibrosis of the lymphoid infrastructure.[5-8]

Cardiac troponin 1 (cTcI), a cardio-myocyte injury marker, and specific for diagnosing acute myocardiac infarction, is a globular protein complex involve in muscle contractility.[9,10] Together with troponin T (cTcT) and C form a troponin complex in the heart for transmission of intracellular calcium signal actin-tropomyosin interaction. In children, serum measurements are sensitive and specific for detecting myocardial injury in a variety of settings.[9-11] HAART, the triple drug regimen used for the treatment of HIV infection is associated with clinical cardiovascular concerns. Triant et al, showed a significantly higher prevalence of hypertension (21.2% vs 15.9%), diabetes (11.5% vs 6.6%) and dyslipidaemia (23.3% vs 17.6%) in HIV-infected patients than in the non-HIV cohort ($p<0.0001$ for each comparison).[12] The lipoatrophic and lipohypertrophic changes typically start to manifest after 6-12 months of anti-retroviral (ARV) therapy.[13,14] According to Nigeria guideline, the preferred 1st line HAART for children 20 to 30kg or 6-10 years during the period of the study was nucleoside reverse transcriptase inhibitors (NRTI) backbone, [zidovudine (AZT), or Abacavir (ABC), + lamivudine (3TC) and integrase inhibitors, dolutegravir (DTG).[15] Alternative 1st line was AZT or ABC +3TC+ protease inhibitor (PIs), (LPV/r). Preferred 1st line HAART for adolescents was tenofovir (TDF)+3TC+DTG. Preferred 2nd HAART for children and adolescents was AZT or ABC or TDF+3TC or FTC + atazanavir (ATV)/r or LPV/r or DTG or darunavir (DRV)/r.

Electrocardiography (ECG), echocardiography (ECHO), troponin I, are all highly sensitive parameters that can be used in identifying at risk group for CVD. There is dearth of information on the type of CVD associated with chronic HIV infection, and prolong use of HAART in our environment. This study was therefore structured for that aim. It is envisaged that the result will provide the baseline information on CVD in HIV positive children and adolescents on treatment in our environment, for better management.

METHODS

We carried out a cross sectional survey at the Paediatric Out-patient Special Treatment Clinic (POSTC) of the University of Abuja Teaching Hospital (UATH) between August to December 2023. POSTC is an out-patient clinic service area of the health institution where HIV infected children and adolescents, and exposed babies were followed up for treatment and monitoring. It has consulting rooms for the doctors, nurses, and adherence counselors. Record clerks, pharmacists, and nutritionists and home base-care providers are also at their disposal on week days (Monday-Friday, from 7.30 am to 4 pm.). UATH is a 500 bed capacity referral hospital, sub-serving the people of Federal Capital Territory (FCT) Abuja and five neighbouring states. Is one of the first centers in the country to start offering free HIV/AIDS services through the President Emergency Plan for AIDs Relief (PEPFAR) since 2005. Ethics clearance was obtained from the ethics committee of the health institution before the commencement of the study.

Inclusion criteria

Inclusion for the study subjects were; stable HIV infected children and adolescents with no signs or symptoms of infection such fever, painful urination, cough, difficulty with swallowing, etc, not having any chronic diseases such diabetics, sickle cell disease, asthma, will be ≤18 years, started on ARV therapy for not less than six months.

Exclusion criteria

Excluded were those with signs and symptoms of infection, those with chronic diseases, and those unwilling to participate in the study.

Consecutive eligible subjects were recruited and enrolled into the study after caregivers has provided written informed consent, and children ≥7 years provide assent. All the enrolled were evaluated clinically, their weight, height was measured, body mass index calculated and

classified according to WHO classification (underweight <18.0, normal is 18.5-24.9, overweight is ≥25.0, obesity is ≥30.0. CD4 cell count, VL, ECG, ECHO, troponin was also carried out for all subjects. CD4 cell count was measured using automated Partec Cyflow easy count kit (Partec code no. 05-8401 Western Germany), while VL measurement was with (Roche Smp/prep/cobs Taqman 96, USA). CD4 cell count and VL were done at enrollment into the study if there was no recent one. Seca beam weighing scale accurate to the nearest 0.01 kg was used for measuring their weight, while standiometer also by Seca was used for the height. The socio-economic class (SEC) of the parents was assessed using Olusanya two factor index classification (father's occupation and mother's level of education).[16]

ECHO (2-Dimesional, M-mode, and Doppler evaluation) were carried out by the paediatric cardiologist using the general electric vivid echo machine in accordance with the criteria of the American Society of Echocardiography.[17] The transducer frequency of 3.5 or 5 MHz was used depending on the need. Left ventricular systolic dysfunction (LVSD) was defined as left ventricular fractional shortening <28%. Dilated cardiomyopathy (DC) was defined as LVSD with bi-ventricular or left ventricular enlargement. Pericardial effusion (PE) was diagnosed when the effusion measured more than 4mm. Prolapsed mitral valve was diagnosed on the basis of: thickening of the valve; and left atrial systolic dislocation of one or both mitral leaflets from the mitral valve ring plane. A 12-lead standard ECG using the Hewlett Packard M1700A3412A08047 was used for ECG evaluation. cTc1 assayed was done using a test method that was based on immunoassay technology that employs the sandwich immune detection method. Concentrations and clinical references: 0-0.3ng/ml is normal level, >0.3ng/ml indicates risk of acute myocardial infarction.[18]

Data analysis

Data analysis was computed using SPSS version 23.0 computer software packages. Tests of significance were the Chi-square or Fisher exact test (whenever the expected frequency in one of the cells was less than 5. Differences between groups were considered significant at $p<0.05$.

RESULTS

Table 1 showed the characteristics of the study population according to the mode of HIV transmission. Of the 126 participants recruited, 66 (52.4%) were males, with male to female ratio of 1.1:1. Their mean age was 14.1±3.1 [7, 18] years, majority 69 (54.8%) were between 15-18 years, while the least 15(11.9) were <10 years. Most 82 (65.1%) came from a low SEC, and 73 (57.9%) were underweight (BMI of <18 kg/m^2) with mean of 17.6±3.5 [8.2, 29.6] kg/mm^2. There was statistically significant difference in BMI of vertically and non-vertically transmitted subjects, chi^2 5.91, p=0.053. While 99 (78.6%) got their HIV infection through vertical means, 27(21.4%) acquired theirs non-vertically. Most 90 (71.4%) had both parents alive, 7 (5.6%) and 29 (23.0%) has lost either both parents or lost only one. Parent survival for the two groups also showed significant difference, chi^2. 4.65, p =0.043. Their mean troponin 1 was 2.0±1.6ng/ml, with 90 (71.4) having normal value of <0.3ng/ml. Again, no significant difference was also observed in troponin levels for the two groups, p values >0.05. Most 92 (92.9%) of the vertical transmitted subjects were on 2nd line HARRT, while 15 (55.6%) of the non-vertical were on 1st line medication. Though the mean duration on HARRT for the subjects was 7.2±2.9 [1, 14] years, statistically significant difference was observed between the vertical and the non-vertical transmitted subjects for the 2nd line HARRT, Chi^2 5.08, p=0.020. There was also statistically significant in their mean CD4 cell count, and VL at enrollment for the two groups, chi^2 3.768, p=0.0003 for CD4 cell count, and chi^2 1.609, p=0.046 for the VL.

Table 1: Characteristics of the study population.

Variables	Vertical transmission (%), n=99. Mean±SD	Non-vertical transmission (%), n=27, Mean±SD	Total (%), n=126 Mean±SD [range]	Chi^2	P value
Age (in years)					
Mean age	13.7±3.2	15.9±2.3	14.1±3.1 [7, 18]	4.76	0.080
<10	14 (14.1)	1 (3.7)	15 (11.9)	1.09	0.581
10-<15	38 (38.4)	4 (14.8)	42 (33.3)		
15-18	47 (47.5)	22 (81.5)	69 (54.8)		
Sex					
Male	51 (51.5)	15 (55.6)	66 (52.4)	0.018	0.894
Female	48 (48.5)	12 (44.4)	60 (47.6)		
Socio-economic class					
Upper	12 (12.1)	1 (3.7)	13 (10.3)	4.23	0.122
Middle	27 (27.2)	4 (14.8)	31 (24.6)		
Low	60 (60.6)	22 (81.5)	82 (65.1)		

Continued.

Variables	Vertical transmission (%), n=99. Mean±SD	Non-vertical transmission (%), n=27, Mean±SD	Total (%), n=126 Mean±SD [range]	Chi²	P value
Parent survival status					
Both parents alive	77 (77.8)	13 (48.2)	90 (71.4)	4.65	0.043
Both parent dead	1 (1.0)	6 (22.2)	7 (5.6)		
One parent dead	21 (21.2)	8 (29.6)	29 (23.0)		
BMI (kg/m²)					
Mean BMI	17.3±3.4	17.9±38	17.6± 3.5 [8.2, 29.6]	0.21	0.351
<18	62 (62.6)	11 (40.7)	73 (57.9)	5.91	0.053
18-24.9	34 (34.4)	16 (59.3)	50 (39.7)		
25- <30	3 (3.0)	0 (0.0)	3 (2.4)		
.>30	0 (0.0)	0 (0.0)	0 (0.0)		
Troponin level (ng/ml)					
Mean troponin level (ng/ml)	2.51±20.21	0.09±0.024	2.0±1.6		
0-0.3	70 (70.7)	20 (74.1)	90 (71.4)	0.619	0.537
≥ 0.3	29 (29.3)	7 (25.9)	36 (28.6)	0.83	0.360
1st line HAART	7 (7.1)	15 (55.6)	22 (17.5)	1.86	0.532
2nd line HAART	92 (92.9)	12 (44.4)	104 (82.5)	4.02	0.032
Duration on HAART (yrs)	*15.7±1.7	*1.1±0.20	* 7.2±2.9 [1, 14]	5.08	0.020
CD4 at enrollment (cell/mm³)	*763.5±612.48	*312.6±193.4	*538.05±375.89	3.768	0.0003
VL at enrollment (copies/ml)	*1013.4±286.9	6868.5±111.6	*3940.5±255.4	1.609	0.046

Table 2: ECHO, ECG and, HARRT Used by the study population.

Variables	Vertical transmission (%), n=99	Non-vertical transmission (%), n=27	Total (%), n=126	Chi²	P value
ECHO findings					
Normal	61 (65.7)	13 (66.7)	74 (58.7)	6.59	0.581
Mild Rt and LV-systoli-dysfunction	10 (9.1)	5 (7.4)	15 (11.9)		
Cardiomyopathy	3 (2.0)	1 (3.7)	4 (3.2)		
Mild LIV-diastolic-dysfunction	1 (1.0)	0 (0.0)	1 (0.8)		
Pulmonary hypertension	11 (8.1)	3 (11.1)	14 (11.1)		
Dilated cardiac chambers	4 (4.0)	1 (3.7)	5 (4.0)		
LV dysfunction	9 (10.1)	4 (11.1)	13 (10.3)		
ECG findings					
Normal	63 (63.6)	15 (55.6)	78 (61.9)	16.45	0.052
ST elevation	2 (6.1)	1 (11.1)	3 (2.4)		
Lt ventricular hypertrophy	2 (12.1)	2 (14.8)	4 (3.2)		
Rt ventricular hypertrophy	2 (0.0)	1 (3.7)	3 (2.4)		
Non-specific ST segment abnormality	10 (6.1)	2 (3.7)	12 (9.5)		
T wave abnormality	2 (2.0)	1 (3.7)	3 (2.5)		
Sinus-tachycardia	12 (1.0)	4 (0.0)	16 (12.7)		
Bi-ventricular hypertrophy	2 (5.1)	0 (3.7)	2 (7.8)		
First degree heart block	3 ()	0 (0.0)	3 (1.6)		
Sinus-arrhythmias	1 (1.0)	1 (3.7)	2 (1.6)		
Types of 1st line HAART					
AZT+3TC+NVP	0 (0.0)	0 (0.0)	0 (0.0)	18.76	0.002
AZT+3TC+EFV	0 (0.0)	0 (0.0)	0 (0.0)		
ABC+3TC+LPV/r	1 (1.0)	2 (7.4)	3 (2.4)		
AZT+3TC+LPV/r	0 (0.0)	2 (7.4)	2 (1.6)		
TDF+3TC+DTG	4 (4.0)	8 (29.6)	12 (9.5)		
ABC+3TC+DTG	2 (2.0)	3 (11.1)	5 (4.0)		
Total (%)	7 (7.1)	15 (55.6)	22 (17.4)		

Continued.

Variables	Vertical transmission (%), n=99	Non-vertical transmission (%), n=27	Total (%), n=126	Chi^2	P value
Type of 2nd line HAART					
ABC+3TC+LPV/r	12 (12.1)	1 (3.7)	13 (10.3)		
AZT+3TC+LPV/r	7 (7.1)	0 (0.0)	7 (5.6)		
TDF+3TC+DTG	46 (46.5)	8 (29.6)	54 (42.9)		
ABC+ FTC+ATV/r	4 (4.0)	0 (0.0)	4 (3.2)		
ABC+3TC+DTG	20 (20.2)	3 (11.1)	23 (18.3)		
TDF+3TC+ATV/r	3 (3.0)	0 (0.0)	3 (2.4)	14.21	0.03
Total (%)	92 (92.9)	12 (44.4)	104 (82.5)		

Table 3: Cardiac troponin 1 levels Vs age, sex, BMI, ECHO, and ECG findings.

Variables	Troponin 0-0.3 ng/ml, n=90	Troponin >0.3 ng/ml, n=36	Total (%) n=126	Chi ^{2}	P value
Age (in years)					
<10	13 (14.4)	2 (5.6)	15 (11.9)		
10-15	30 (33.3)	12 (33.3)	42 (33.3)	3.89	0.143
16-18	47 (52.2)	22 (61.1)	69 (54.8)		
Sex					
Male	50 (55.6)	16 (44.4)	66 (52.4)	4.21	0.235
Female	40 (44.4)	20 (55.6)	60 (47.6)		
BMI (kg/m^2)					
<18	54 (60.0)	19 (52.8)	73 (57.9)		
18-24.9	34 (37.8)	16 (44.4)	50 (39.7)	13.63	0.001
25-<30	2 (2.2)	1 (2.8)	3 (2.4)		
>30	0 (0.0)	0 (0.0)	0 (0.0)		
ECHO findings					
Normal	74 (82.2)	0 (0.0)	74 (58.7)		
Mild Rt and LV-systolic-dysfunction	5 (5.6)	10 (27.8)	15 (11.9)		
Dilated cardiomyopathy	0 (0.0)	4 (11.1)	4 (3.2)		
Mid-diastolic-dysfunction	0 (0.0)	1 (2.8)	1 (0.8)	36.95	<0.0001
Pulmonary hypertension	3 (3.3)	8 (22.2)	14 (11.1)		
Dilated cardiac chambers	2 (2.2)	2 (5.6)	5 (4.0)		
LV-dysfunction	3 (3.3)	5 (13.9)	13 (10.3)		
ECG findings					
Normal	78 (86.7)	0 (0.0)	78 (61.9)		
ST segment elevation	1 (1.1)	2 (5.6)	3 (2.4)		
Lt ventricular hypertrophy	1 (1.1)	3 (8.3)	4 (3.2)		
Rt ventricular hypertrophy	1 (1.1)	2 (5.6)	3 (2.4)		
Non-specific ST-T abnormality	2 (2.2)	10 (27.8)	12 (9.5)	59.07	<0.0001
T wave abnormality	1 (1.1)	2 (5.6)	3 (2.4)		
Sinus-tachycardia	3 (3.3)	13 (36.1)	16 (12.7)		
Bi-ventricular hypertrophy	0 (0.0)	2 (5.6)	2 (1.6)		
First degree heart block	2 (2.2)	1 (2.8)	3 (2.4)		
Sinus-arrhythmias	1 (1.1)	1 (2.8)	2 (1.6)		

Table 2 showed the ECHO, ECG findings, and HARRT use by the study population. The prevalence of abnormal ECHO, and ECG were 41.3%, and 38.1% with mild Rt and Lt ventricular-systolic-dysfunction 15 (11.9%), pulmonary hypertension (PH) 11 (8.7%), and left ventricular (LV) dysfunction 13 (10.3%) as the commonest ECHO abnormalities, and sinus-tachycardia 16 (12.7%), non-specific ST-T abnormality 12 (9.5%), and LV hypertrophy 4 (3.2%) for common ECG abnormalities. Most of the abnormal findings were seen with the vertically transmitted subjects. No statistically significant difference was observed between the two groups for ECHO, chi^2 5.95, p= 0.581, but significant difference was seen with ECG, chi^2 16.45, p=0.052, 1st

line HAART, chi^2 18.76, p=0.002, and 2nd line HARRT, chi^2 14.21, p= 0.03.

Table 3 shows cTcI levels Vs age, sex, BMI, ECHO, and ECG findings for the study subjects. Thirty-six (28.6%) had higher troponin levels of >0.3ng/ml, with statistical significant relationship seen between troponin and BMI, chi^2 13.63, p=0.001, ECHO, chi^2 36.95, p =0.0001, and ECG, chi^2 59.07, p=0.0001. No significant relationship was seen for other variables; their p values were >0.05. Most of the abnormal ECHO and ECG was among the subjects with elevated troponin.

Table 4: Cardiac troponin 1 levels Vs mode of transmission, SEC, parent survival, CD4, VL, and HARRT.

Variables	Troponin 0-0.3ng/ml, n=90 (%)	Troponin >0.3ng/ml, n=36 (%)	Total, n=126 (%)	Chi^2	P value
Mode of transmission					
Vertical	80 (88.9)	19 (52.8)	99 (78.6)	2.743	0.452
Non-vertical	10 (11.1)	17 (47.2)	27 (21.4)		
Socio-economic class					
Upper	10 (11.1)	2 (5.6)	12 (9.5)	1.649	0.648
Middle	21 (22.2)	10 (27.8)	31 (24.6)		
Low	59 (65.6)	24 (67.7)	83 (65.1)		
Parent survival status					
Both parent alive	81 (90.0)	9 (25.0)	90 (71.4)	9.152	0.010
Both parent dead	1 (1.1)	6 (16.7)	7 (5.6)		
Only one parent alive	8 (8.9)	21 (58.3)	29 (23.0)		
CD4 cell count (ml/mm^3)					
<200	0 (0.0)	8 (22.2)	8 (6.3)	6.896	0.032
200-<500	1 (1.1)	16 (44.4)	17 (13.5)		
>500	89 (98.9)	12 (33.3)	101 (80.2)		
Viral load (copies/ml)					
<20	58 (64.4)	2 (5.6)	60 (47.6)	7.515	0.023
20-<1000	26 (28.9)	4 (11.1)	30 (23.8)		
>1000	6 (6.7)	30 (83.3)	36 (28.6)		
Types of 1st line HAART					
AZT+3TC+NVP	0 (0.0)	0 (0.0)	0 (0.0)	21.187	0.001
AZT+3TC+EFV	0 (0.0)	0 (0.0)	0 (0.0)		
ABC+3TC+LPV/r	0 (0.0)	3 (8.3)	3 (2.4)		
AZT+3TC+LPV/r	2 (2.2)	0 (0.0)	2 (1.6)		
TDF+3TC+DTG	10 (11.1)	2 (5.6)	12 (9.5)		
ABC+3TC+DTG	1 (1.1)	4 (11.1)	5 (4.0)		
Types of 2nd line HAART					
ABC+3TC+LPV/r	6 (6.7)	7 (19.4)	13 (10.3)	19.978	0.002
AZT+3TC+LPV/r	7 (7.8)	1 (2.8)	7 (5.6)		
TDF+3TC+DTG	51 (56.7)	3 (8.3)	54 (42.9)		
ABC+ FTC+ATV/r	1 (1.1)	3 (8.3)	4 (3.2)		
ABC+3TC+DTG	9 (10.0)	13 (36.1)	22 (17.5)		
TDF+3TC+ATV/r	3 (3.3)	0 (0.0)	4 (3.2)		

Table 4 showed cTcI levels Vs mode of transmission, SEC, parent survival, CD4, VL, and HARRT for the study subjects. Parent survival, CD4, VL, 1st and 2nd line HARRT had statically significant relationship with levels of troponin, chi^2 9.152, p=0.01 for parental survival; chi^2 6.896, p=0.032 for CD4; chi^2 7.515, p=0.023 for VL; chi^2 21.187, p=0.001 for 1st line, and chi^2 19.978, p =0.002 for 2nd line. Other variables did not show any relation with troponin, p<0.05.

DISCUSSION

Cardiac toponin I, the gold standard for assessing the myocardial injury, together with cardiac performance using ECHO and ECG were evaluated for HIV infected children and adolescents on ART overtime in our health facility. High cTc1 of >0.3ng/ml, was documented in 28.6% of the subjects. This was lower than 48%, 51%, and 86.4% reported by Bello et al from Nigeria among HIV children, Wilkinson et al from USA also in HIV childen, and Bello et al from Sokoto, Nigeria among adult population.[19-21] These high values from other studies could be attributed not only to the higher number of HAART naïve subjects in their study, but also to the differences in age group of their participants, as earlier studies have reported cTcI to be higher in younger age groups in both humans and animals.[22] The recorded lower prevalence in this study was however similar to the 20%

by Buiten et al among adult population.[23] This lower finding in this study could be due their adequate viral suppression in 71.4% of the subjects, and good immunity in 80.2%, both of which will reduce viral replication, and minimizing inflammatory damage to the cardiac structures.

The prevalence of abnormal ECHO findings in the present study was 41.3%. This was also lower than 75.9% reported by Okoromah et al from Nigeria among HIV children, 76.9% by Shah et al, from India, and 76.9%, 74% and 73%, by Fink et al, from USA.[24-26] Published reports showed lower cardiac dysfunction similar to the findings from the present study; 36.9%, 40%, and 44% from India and two sub-Saharan African countries.[27-29] The wide variation on prevalence of abnormal ECHO findings from different countries may be from differences in the methodology, definition of cardiac dysfunction, inclusion criteria, and HIV disease severity. There is also varied reports on the prevalence of ECG changes in HIV-infected children, with the present study reporting 38.1%. This compared favourablely to 26.5% by Lubega et al in Uganda, 34.5% by Attamah et al, in Nigeria, and 47% by Badal from India.[30,31,27] It was however much lower than 88% by Pongprot et al from Thailand, and 65% by Sani et al among adults from Jos, Nigeria.[5,32] The lower prevalence of abnormal ECHO and ECG in this study might be from the clinical, immunology, and virology stability of the subjects. Combine ECHO and ECG abnormality prevalence was however high 79.4% in this study and compared to 62.0% by Badal et al, but lower than 93% by Shah et al.[27,25] This high combine prevalence justifies the earlier suggestion by other researchers of inclusion of ECHO and ECG in the screening for cardiovascular abnormalities at baseline, and follow-up care of children with HIV for early detection, and institutition of early measures to ameliorate or halt the disease progression.[27,31,33]

ECHO abnormalities in this study were: mild Rt and Lt ventricular-systolic-dysfunction (11.9%), PH in 11.1%, LV-dysfunction (10.3%), dilated cardiac chambers (5.0%), and dilated cardiomyopathy (3.2%). These specific cardiac abnormalities compared favourabely with other reports elsewhere.[25-29,33] But differ from findings by Okoroma et al from Nigeria who reported heart failure, dilated cardiomyopathy (33.7%), decreased LVSF (33.7%), increased LV-mass (20.5%) and pericardial effusion (14.5%) in their HIV HARRT naïve subjects.[24] While Badal et al documented LV-systolic-dysfunction (26%) as their commonest ECHO findings, the present study recorded same pathology in 10.3% of their subjects.[27] Systolic-dysfunction is associated with wall thinning and cavity dilatation, from interstitial fibrosis, ischemia, infarction, and small vessel disease, worsened in the presence of LV-systolic-dysfunction which is one of the predictor of mortality in HIV infected individuals. PH is also one of the chronic complications associated with HIV infection that may result in right ventricular failure. As reported by Idris et al, 13% of ART-exposed, and 8% of ART-naïve infected children had ECHO evidence of PH.[34] This compared favourabely to 11.1% recorded in this study, and raises concerns of the possible effects of ART on the pulmonary vasculature. Ritonavir, a protease inhibitor used widely as 1st and 2nd line ART in this study has been suggested to inhibit bradykinin-dependent vasorelaxation. Other ART drugs, especially abacavir significantly increases the odds of elevated cTnT that signifies myocardical injury. This in turn decreases the synthesis of nitric oxide, a potent pulmonary vasodilator, thus increasing the risk of PH.[34,35] Cardiomyopathy is also a common aftermath of HIV infection in the cardiac muscles.[28] It was documented 3.2% of the subjects in this study. This was similar to 3.0% reported by Lubega et al from Uganda, but lower than 14.8% by Nzuobontane et al from Cameroon, 16% by Lipshultz et al from USA, and 33.7% by Okoroma et al from Nigeria.[30,35,36,24] Inspite of the documented high prevalence of cardiovascular abnormalities in children with HIV, most of these anomalies remain asymptomatic.[27,31] For example, asymptomatic children with significant pericardial effusion may be picked at routine ECHO or ECG, and not clinically.[31] By performing them at baseline and follow-up visits, provides opportunity for early detection, and thus prevent progression to massive effusion and cardiac tamponade. The above scenario is supported by the association of HIV with dilated cardiomyopathy, a condition commonly complicated by pericardial effusion. The commonest ECG abnormalies in this study were sinus-tachycardia (12.7%), non-specific ST-T abnormality (9.5%), and LV hypertrophy 4 (3.2%). Badal et al also reported 29% sinus-tachycardia among his subjects, while other reported similar ECG findings.[27,31,32]

BMI contributes to drug metabolism, and efficacy of HAART.[38] In the present study, 57.9% of the study subjects had BMI of <18kg/m^2. Manafe et al from Mozambique also uncovered 80% of their study population to had BMI <18.5 kg/m^2.[33] Malnutrition is associated with decrease LV-mass, LV-volume and ventricular function. Its aggressive correction is advocated because of increased risk of LV-dysfuction.[38] The high prevalence of underweight in this study might not only be from inadequate nutrition as 65.1% of the study subjects were from low SEC, but also from prolong use of HARRT. Some ART, especially regimens containing didanosine/stavudine and nelfinavir or efavirenz plus dual nucleosides were associated with greater loss of limb fat, while protease inhibitors are associated with lean body mass from lipoatrophy/dystrophy.[13-15]

Using bivariate model, ECHO, ECG, BMI, HARRT, CD4 cell count, and VL had significant association with cTcI level in this study. Several other studies, has documented similar findings.[19-21] Infact, Wilkinson et al found cTcI to be correlated with increased LV thickness-to-dimension ratio (r=0.21, p=0.04); LV end-diastolic posterior wall thickness (p=0.04); and abacavir with

(aOR=2.33, p=0.04).[20] Buiten et al also reported serum cTcI levels to have a stronger association with LV- mass-index, and LV-ejection fraction.[23] However, Khair et al did not report such significant association in their adult study subjects (p>0.05).[39]

The cross sectional nature of the study was the limitations of this study.

CONCLUSION

There is high prevalence of cardiac abnormalities among HIV positive children and adolescent on HARRT overtime in our center. The findings also supports the clarion call for ECHO and ECG to be included in the baseline and follow-up care of these patients for early disease detection, and institutition of measures to ameliorate or halt their progression.

ACKNOWLEDGEMENTS

Authors would like to thank the cooperation of staff of the Special Treatment Clinic of University of Abuja Teaching Hospital for their cooperation during the data collection.

Funding: This study funded by TETFUND (Tertiary Education Trust Fund)
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organisation. Global Health Observatory Report, 2015. Available at: http://www.who.int/gho/hiv/en/. Accessed 28 December 2015.
2. AVERT. HIV and AIDS in Sub-Saharan Africa, 2014. Available at: http://www.avert.org/hiv-aids-sub-saharan-africa.htm. Accessed 31 May 2015.
3. United Nations General Assembly Special Session Country Progress Report-2010. Available at: http://data.unaids.org/pub/report/Nigeria_2010_country_progress_report. Accessed 10 July 2013.
4. Lipshultz SE, Mas CM, Henkel JM, Franco VI, Fisher SD, Miller TL. HAART to heart: highly active antiretroviral therapy and the risk of cardiovascular disease in HIV-infected or exposed children and adults. Expert Revi. 2012;10:661-74.
5. Pongprot Y, Sittiwangkul R, Silvilairat S, Sirisanthana V. Cardiac manifestations in HIV-infected Thai children. Ann Trop Paediatr. 2004;24(2):153-9.
6. Hsue PY, Hunt PW, Schnell A, Kalapus SC, Hoh R, Ganz P, et al. Role of viral replication, antiretroviral therapy, and immunodeficiency in HIV-associated atherosclerosis. Aids. 2009;23(9):1059-67.
7. Ostrowski SR, Katzenstein TL, Pedersen BK, Gerstoft J, Ullum H. Residual viraemia in HIV-1-infected patients with plasma viral load ≤20 copies/ml is associated with increased blood levels of soluble immune activation markers. Scandin J Immunol. 2008;68(6):652-60.
8. Baumeister D, Akhtar R, Ciufolini S, Pariante CM, Mondelli V. Childhood trauma and adulthood inflammation: a meta-analysis of peripheral C-reactive protein, inetleukin-6 and tumour necrosis factor-α. Mol Psych. 2016;21(5):642-9.
9. Lipshultz SE, Wong JC, Lipsitz SR, Simbre VC 2nd, Zareba KM, Galpechian V, et al. Frequency of clinically unsuspected myocardial injury at a children's hospital. Am Heart J. 2006;151(4):916-22.
10. Soongswang J, Durongpisitkul K, Nana A, Laohaprasittiporn D, Kangkagate C, Punlee K, et al. Cardiac troponin T: a marker in the diagnosis of acute myocarditis in children. Pediatr Cardiol. 2005;26:45-9.
11. Newby LK, Rodriguez I, Finkle J, Becker RC, Hicks KA, Hausner E, et al. Troponin measures during drug development-considerations for monitoring and management of potential cardiotoxicity: an educational collaboration among the Cardiac Safety Research Consortium, the Duke Clinical Research Institute, and the US Food and Drug Administration. Am Heart J. 2011;162(1):64-73.
12. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab. 2007;92(7):2506-12.
13. Guaraldi G, Stentarelli C, Zona S, Santoro A, Beghetto B, Carli F, et al. The natural history of HIV-associated lipodystrophy in the changing scenario of HIV infection. HIV Med. 2014;15(10):587-94.
14. Dubé M, Parker RA, Pablof T, Grinspoon, SK, Zackin RA, Robbins GK, et al. Glucose metabolism, lipid, and body fat changes in antiretroviral-naive subjects randomized to nelfinavir or efavirenz plus dual nucleosides. AIDS. 2005;19(16):1807-18.
15. Federal Ministry of Health, National AIDS and STIs Control Programs. National Guidelines for HIV Prevention, Treatment and Care, 2020. Available at: https://naco.gov.in/sites/default/files/National_Guidelines_for_HIV_Care_and_Treatment_2021.pdf. Accessed 01 January 2024.
16. Olusanya O. The importance of social class in voluntary fertility control in developing country. West Afr J Med. 1985;4:205-12.
17. Committee Members, Cheitlin MD, Armstrong WF, Aurigemma GP, Beller GA, Bierman FZ, et al. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical

Application of Echocardiography). Circulation. 2003;108(9):1146-62.
18. Fred S, Apple FS. Cardiac Troponin I, Cardiac Markers. Humanna Press Inc.; 1998:229-243.
19. Bello SO, Abdulkadir MB, Ogunkunle TO, Popoola GO, Ernest SK. Serum cardiac troponin i as a diagnostic marker of myocardial injury among human immunodeficiency virus infected children in Ilorin Kwara State Nigeria. MJPCH. 2022;28(2):98-104.
20. Wilkinson JD, Williams PL, Leister E, Zeldow B, Shearer WT, Colan SD, et al. Cardiac biomarkers in hiv un-infected children: the paediatric HIV/AIDS cohort study (PHACS). AIDS. 2013;27:1099-108.
21. Bello A, Mainasara AS, Liman HM, Hayatu U, Abubakar AF, Saidu K, et al. Troponin I as marker of subclinical cardiac injury in human immunodeficiency virus-seropositive patients in Sokoto, Nigeria., J HIV Hum Reprod. 2016;4(1):20-6.
22. Undhad V V, Fefar DT, Jivani BM, Gupta H, Ghodasara DJ, Joshi BP, et al. Cardiac troponin: an emergingcardiac biomarker in animal health. Vet World. 2012;5(8):508-11.
23. Buiten MS, de Bie MK, Rotmans JI, Dekker FW, van Buren M, Rabelink TJ, et al. Serum cardiac troponin-I is superior to troponin-T as a marker for left ventricular dysfunction in clinically stable patients with end-stage renal disease. PLoS One 2015;10(8):1-13.
24. Okoromah CAN, Ojo OO, Ogunkunle OO. Cardiovascular dysfunction in HIV-infected children in a sub-saharan African country: comparative cross-sectional observational study. J Trop Pediatr. 2012;58 (1):3-11.
25. Shah I, Prabhu SS, Sumitra V, Shashikiran HS. Cardiac dysfunction in HIV infected children: a pilot study. Indian Pediatr. 2005;42(2):146-9.
26. Fink L, Reicheck N, Sutton MG. Cardiac abnormalities in acquired immunodeficiency syndrome. Am J Cardiol. 1984;54(8):1161-3.
27. Badal S, Gupta R, Kumar P, Sharma M, Chhajta DS. Cardiac manifestations in HIV infected children. are they under diagnosed? HIV/AIDS Res Treat Open J. 2015;2(1):21-6.
28. Schuster C, Mayer FJ, Wohlfahrt C, Marculescu R, Skoll M, Robert Strass R, et al. Acute HIV infection results in subclinical inflammatory cardiomyopathy. JID. 2018;218(3):466-470.
29. Longo-Mbenza B, Segheri LV, Vita EK. Assessment of ventricular diastolic function in AIDS patients from Congo: a Doppler echocardiographic study. Heart. 1998;80(2):184-9.
30. Lubega S, Zirembuzi GW, Lwabi P. Heart disease among children with HIV/AIDS attending the paediatric infectious disease clinic at Mulago hospital. Afr Health Sci. 2005;5(3):219-26.
31. Attamah CA, Sadoh WE, Ibadin MO, Omoigberale AI. Electrocardiographic Findings in Human Immunodeficiency Virus-Infected Children in Benin City, Nigeria. Niger Postgrad Med J. 2020;27(4):357-64.
32. Sani MU, Okeahialam BN, Ukoli CO. Electrocardiographic abnormalities in Nigerian AIDS patients. Trop Cardiol. 2004;30(117):3-33.
33. Manafe N, Ngale A, Biquiza N, Zimba I, Majid N, Mocumbi AO. Need for active cardiovascular screening in HIV-infected children under antiretroviral therapy in Africa. Cardiovasc Diagn Ther. 2019;9(1):68-72.
34. Idris NS, Uiterwaal CSP, Burgner DP, Grobbee DE, Kurniati N, Cheung MMH. Effects of HIV infection on pulmonary artery pressure in children. Global Hrt. 2019;14(4):367-72.
35. Nzuobontane D, Blackett KN, Kuaban C. Cardiac involvement in HIV infected people in Yaounde. Postgrad Med J. 2002;78(925):678-81.
36. Lipshultz SE, Easley KA, Orav EJ, Kaplan S, Starc TJ, Bricker JT, et al. Cardiac dysfunction and mortality in HIV-infected children: the prospective P2C2 HIV multicenter study. Circulation. 2000;102(13):1542-8.
37. Eleazar ES, Eleazar CI, Nwachukwu DC, Nwagha UI. ECG abnormalities among HIV infected children placed on ART at Enugu, South East of Nigeria. Afri Heal Sci. 2020;20(4):1742-8.
38. Li X, Ding H, Geng W, Liu J, Jiang Y, Xu J, et al. Predictive effects of body mass index on immune reconstitution among HIV-infected HAART users in China. BMC Infecti Dis. 2019;19(373).
39. Khair U, Mappangara I, Katu S, Bakri S, Rasyid H, Kasim H, et al. Profile of CD4 count and troponin I level in HIV Patient obtaining triple fixed dose combination (FDC) anti-retroviral therapy. Int J Med Rev Case Rep. 2019;3(5):216-20.

Cite this article as: Okechukwu AA, Lawson JO, Richard O, Okechukwu OA. Cardiovascular diseases in HIV infected children and adolescents on highly anti-retroviral therapy at the university of Abuja teaching hospital, Gwagwalada, Nigeria. Int J Res Med Sci 2024;12:3155-63.