Original Article

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Paediatrics Section

Cardiac Involvement among HIV-positive Individuals less than 18 years of Age on Antiretroviral Therapy- An Observational Study from a Rural Tertiary Care Hospital, West Bengal, India

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ABSTRACT

Introduction: With advancement of medical science, individuals diagnosed with Human Immunodeficiency Virus (HIV) infections are getting treated earlier and a fewer of them develop Acquired Immunodeficiency Syndrome (AIDS)-related complications. But the downside is that, there is an earlier onset and higher relative risks for different chronic diseases including cardiovascular diseases.

Aim: To determine the proportion and pattern of cardiac involvements among children undergoing treatment for HIV infection and to correlate various cardiac findings with duration of Antiretroviral Therapy (ART) among them.

Materials and Methods: An observational cross-sectional study was conducted among 136 HIV infected patients attending Paediatrics and General Medicine Outpatient Departments of North Bengal Medical College and Hospital (NBMCH) from October 2019 to March 2021. All patients were assessed clinically and underwent two dimensional (2D) Echocardiography, Motion mode (M mode) and colour doppler for assessing cardiac involvement. Collected data were analysed using Statistical Package for the Social Sciences (SPSS) software version 22.0 and Pearson's correlation test was applied to test association between duration of ART and different echocardiographic parameters.

Results: The mean age of the study participants was 10.14 years and the mean duration of ART was 49.18 months. Almost 1/2 (48.5%) of the HIV-positive individuals had cardiovascular findings. The most common echocardiographic change noted in patients was diastolic dysfunction 39 (28.7%) followed by Pericardial Effusion (PE) 29 (21.3%) and systolic dysfunction 28 (20.6%). Statistically significant positive correlation between changes in the values of Left Ventricular Internal Diameter in Diastole (LVIDD) (r=0.982), Left Atrium (LA) (r=0.634), mean Pulmonary Artery Pressure (mPAP) (r=0.200) with duration of ART was noted. Negative correlation was seen between duration of ART with ejection fraction (r=-0.984) and Tricuspid Annular Plain Systolic Excursion (TAPSE) (r=-0.438). This indicated that, all these important cardiological parameters became worser with advancement of treatment.

Conclusion: Cardiac involvements among HIV-positive individuals undergoing ART were still high. There was definite correlation between cardiac involvement and duration of ART.

Keywords: Diastolic dysfunction, Human immunodeficiency virus, Pericardial effusion, Systolic dysfunction

INTRODUCTION

Medical therapy has transformed HIV from a terminal illness into a chronic, manageable condition. But as people with HIV live longer, they also find themselves at higher risk for heart attack, stroke and other types of cardiovascular disease. With advances in the treatment of HIV, unfortunately the affected individuals experience heart disease and its complications at faster rates than people without the infection [1].

The risk of heart disease and stroke for people who have HIV is about 1.5 to two times greater than for people not infected with the virus. HIV-related cardiovascular disease accounts for 2.6 million years of healthy life lost around the world each year. That's expected to increase as an ageing population of people with HIV develop risks for ailments and diseases other than AIDS [2].

Long-term HIV infections are at higher risk of developing plaque in their coronary arteries, regardless of other risk factors for coronary artery disease. The coronary arteries of the people infected with HIV, who had not yet developed plaque react abnormally to stress. This abnormal stress response was similar to people with severe coronary artery disease and is itself a predictor of future adverse cardiovascular events such as heart attack and sudden death. Heart failure and abnormal heart rhythms may be more likely in people living with HIV [3].

The present study was intended to evaluate cardiac manifestations among HIV infected individuals in a rural tertiary care centre of North-eastern India and their correlation with duration of antiretroviral treatment.

MATERIALS AND METHODS

An observational cross-sectional study was conducted among 136 HIV infected patients attending paediatrics and general medicine outpatient departments of North Bengal Medical College and Hospital (NBMCH) from October 2019 to March 2021. NBMCH is a tertiary care teaching hospital located in Darjeeling district of West Bengal, which caters populations from difficult and hilly terrains of eastern Himalayas with cases also attending from bordering nations.

Diagnosis of HIV was based on positive serology and western blot test. Ethical clearance was obtained from Institutional Ethics Committee of NBMCH (memo number- IEC/NBMC/2019-2-/109)

prior to initiation of the study. Informed consent was taken from the parents, guardians or care givers of the children beforehand.

Sample size estimation: It was predecided that all the patients attending the above-mentioned wards and fulfilling the inclusion/exclusion criteria will be enlisted for the study. So, complete enumeration technique was followed to select those 136 individuals.

Inclusion criteria: Participants whose age was in between 1 to 18 years were included.

Exclusion criteria: Patients with congenital heart disease, rheumatic heat disease, cardiomyopathy, pulmonary hypertension etc., were excluded.

Study Procedure

Standard pretested questionnaire was applied to them to collect the basic socio-demographic and clinicotherapeutic data like age, sex, and duration of ART etc. All participants were thoroughly examined physically before echocardiographic examination. Echocardiography was done maintaining standard protocol and all measurements were based on the criteria of the American Society of Echocardiograph [4].

Two-dimensional transthoracic Echocardiography, including M mode, colour doppler pulse wave and continuous wave doppler was done [4]. The 2D Echo was performed by a person expert in cardiology using an agilent image point ultrasound instrument with age appropriate transducers. For each study participant, the following views were obtained: parasternal long axis, parasternal short axis, apical 2-chamber, and apical 4-chamber. Transmitral flow was assessed in the apical 4-chamber view with the pulsed doppler sample volume at the leaflet tips [4]. The following variables were measured: cardiac chambers, valves, Right Ventricular Outflow Tract (RVOT), ejection fraction of Left Ventricle (LV), Tricuspid Annular Plane Systolic Excursion (TAPSE), mean Pulmonary Artery Pressure (mPAP), PE and LV systolic function (categorised by EF 40-50% mild, 30-40% moderate, less than 30% severe form).

Features of Right Ventricle (RV):

a) Systolic dysfunction was defined as:

- Mild=14-17 mm,
- Moderate=11-13 mm and
- Severe=<11 mm [4].

b) Diastolic dysfunction was categorised into grade I to grade III:

- Grade I=E/A ratio <0.75,
- Grade II=E/A ratio >1, Deceleration Time (DT) <140 ms, and
- Grade III as E/A ratio >2, DT <140ms

(E means early diastolic transmitral flow velocity, A means late/atrial diastolic transmitral flow) [4].

c) Increase in mPAP was defined as:

- Mild- <40 mmHg,
- Moderate- 40-50 mmHg and
- Severe- >50 mmHg

d) Pericardial effusion was graded as:

- Mild- 4-10 mm,
- Moderate- 11-20 mm and
- Severe- >20 mmHg [4].

In case any cardiac abnormality was detected, expert consultation was taken from Cardiology Department for further management.

STATISTICAL ANALYSIS

Collected data was entered in Microsoft Excel sheet and further analysis was done with the help of the software IBM SPSS for windows, version 22.0, Armonk, NY: IBM Corporation. Data were organised and presented using the principles of descriptive statistics, where quantitative data was presented as mean and Standard Deviation (SD). Statistical significance was considered as p-value <0.05. Calculation of correlation coefficient was done to find the significance between various parameters. The statistical test was used at 95% confidence interval.

RESULTS

Out of 136 subjects recruited for the present study, 67.6% were males and 32.4% were females [Table/Fig-1]. Mean age of the study participants was 10.14 years and the majority of them belonged to 6 to 12 years age group (58.8%). Duration of illness varied from less than one month to 156 months with mean duration 49.18 months [Table/Fig-1].

Clinical parameters	n (%)
Age group (years)	
Upto 10	69 (50.7)
≥10	67 (49.3)
Range	2 to 18
Mean±SD	10.14±3.15
Gender	
Male	92 (67.6)
Female	44 (32.4)
Duration of ART (months)	
Up to 12	26 (19.1)
13-59	65 (47.8)
60-120	41 (30.2)
>120	4 (2.9)
Range	1 to 156 months
Mean±SD	49.18±32.71

[Table/Fig-1]: Distribution of study participants according to their age, gender and duration of illness (N=136).

Cardiac involvement was noted among 66 (48.5%) study subjects, either LV/RV systolic function in terms of decrease in left ventricular EF and decrease in TAPSE or LV diastolic function or both systolic and diastolic dysfunction were noted among a significant proportion of the HIV-affected individuals. Diastolic dysfunction (measured by abnormal E/A ratio) was noted among 39 (28.7%) of the subjects with 27 (19.7%) subjects having grade I, 11 (8%) had grade II and one subject had grade III form of diastolic dysfunction. Total 28 individuals (20.6%) were found with systolic dysfunction (measured by decreased ejection fraction) in the present study, 17 (12.5%) of them had LV systolic dysfunction and 11 (8.1%) of them had RV systolic dysfunction (measured by decreased values of TAPSE). PE was observed among 29 (21.3%) individuals with 23 of them (16.5%) having mild and 6 of them (4.8%) had moderate PE [Table/Fig-2].

Cardiac parameters	n (%)
Cardiac involvement	66 (48.5)
Diastolic dysfunction	39 (28.7)
Grade I	27 (19.7)
Grade II	11 (8)
Grade III	1 (1)
Systolic dysfunction	28 (20.6)
LV dysfunction	17 (12.5)
RV dysfunction	11 (8.1)
Pericardial effusion	29 (21.3)
Mild	23 (16.9)
Moderate	6 (4.4)

[Table/Fig-2]: Distribution of study participants according to pattern of cardiac involvements (N=136).

Mean values for some of the important echocardiographic parameters found in the present study were- RVOT proximal value was 17.49 mm, LVIDD value was 42.32 mm, LA was 25.43 mm, ejection fraction was 56.45%, TAPSE value was 21.43 and mPAP was 21.44 mmHg [Table/Fig-3].

Echocardiographic parameters (mm or mmHg)	Minimum	Maximum	Mean±SD
RVOT proximal	12	32	17.49±4.56
LVIDD	33	56	42.32±6.25
LA	13	39	25.43±6.75
EF %	25	76	56.45±13.11
TAPSE	10	31	21.43±3.94
mPAP	11	58	1.44±10.04

[Table/Fig-3]: Measures of central tendency and range for some of the relevant Echocardiographic parameters (N=136).
RVOT: Right ventricular outflow tract; LVIDD: Left ventricular internal diameter in diastole; LA: Left atrium; EF: Ejection fraction; TAPSE: Tricuspid annular plain systolic excursion; mPAP: mean Pulmonary artery pressure

Correlation test between duration of treatment and Echocardiographic parameters revealed that there was statistically significant positive correlation between changes in the values of LVIDD (r=0.982, p-value=0.001), LA (r=0.634, p-value=0.001) and mPAP (r=0.200, p-value=0.001) and duration of ART, which indicated there was increment in the values of these parameters with advancement of treatment, making condition of the heart worser. There was negative correlation between duration of ART with ejection fraction (r=-0.984, p-value=0.001) and TAPSE (r=-0.438, p-value=0.001) which indicated with progression of treatment, values of these two parameters were found to be decreased which was considered as worsening of cardiac chambers. Though, there was some positive correlation between RVOT value and duration of ART (r=0.051, p-value=0.406), but this finding was statistically insignificant. The magnitude or strength of association between duration of ART and LVIDD and ejection fraction was observed very high (r>0.9) [Table/Fig-4].

Echocardiographic parameters	Duration of treatment	
	Correlation coefficient	p-value
RVOT proximal	0.051	0.406
LVIDD	0.982	0.001
LA	0.634	0.001
EF%	-0.984	0.001
TAPSE	-0.438	0.001
mPAP	0.200	0.001

[Table/Fig-4]: Correlation of Echocardiographic parameters with duration of ART of the subjects (N=136).
Statistical significance at p-value <0.05

DISCUSSION

The present study was conducted among 136 HIV infected patients with an aim to describe various cardiac abnormalities and to see the association between duration of ART with Echocardiographic changes. Cardiac involvement was noted among 48.5% of the study subjects, either LV/RV systolic dysfunction or diastolic dysfunction or both in the present study. Almost similar proportion (51%) cardiac abnormalities were reported by Lubega S et al., in their study conducted among children attending in a tertiary care hospital of Africa [5]. Jain N et al., in their study had found much higher proportion (67%) of cardiac abnormalities [6]. Okoromah CA et al., had also reported much higher prevalence (75.9%) of cardiac abnormalities than the present study [7]. Possible reason might be variation in the age group of the study subjects, smaller sample size and different time frame (conducted long before) from the present study.

Proportion of diastolic dysfunction (28.7%) was found in higher side than systolic dysfunction (20.6%) in the present study. Similar to this finding, Jain N et al., in their study reported much higher percentage of diastolic dysfunction (42.8%) than any other cardiac abnormality [6]. Nayak G et al., and Reinsch N et al., in their study also reported 37% and 48% of the patients respectively had diastolic dysfunction [8,9]. But in contrary to this, Singh A et al., had found much lower percentage (8.5%) of diastolic dysfunction in respect to other cardiac abnormalities [10]. Diastolic dysfunction rather than systolic dysfunction is the predominant form of heart failure in the era of ART.

Pericardial effusion was observed among 21.3% of subjects in the present study, with 16.5% mild, 4.8% moderate PE. Almost similar proportion of PE (21%) was reported by Estok L and Wallach F in their study done at New York City [11]. Singh A et al., in a study done at Cuttack had shown slightly lesser proportion of PE (17.4%) among the AIDS patients [10]. Okoromah CA et al., in their study recorded prevalence of PE among 14.5% of the patients, of which mild effusions were predominant, which was same as findings of present study [7]. Prevalence of PE was documented much higher (58%) in preART era, in some studies [12].

Mean values of some of the echocardiographic parameters as recorded in the present study. [Table/Fig-3] corroborates with the existing knowledge and findings of some of the previous studies. Mean value for LV ejection fraction was noted 56.45% in the present study. Higher mean values for LV ejection fraction were reported in the studies done by Okoromah CA et al., reported 67.43%; Badal S et al., reported 60.7%; and Hsue PY et al., reported 63% LV ejection fraction in their studies [7,13,14]. Mean value of LVIDD in the present study was 42.32 mm. Almost similar mean value (44%) of LV internal diameter in end diastole was noted by Hsue PY et al., and lower mean values (33 mm and 35.1 mm) were reported by Badal S et al., and Okomorah CA et al., [7,13,14].

Statistically significant correlation observed between increase in duration of ART and changes in cardiac parameters, like LVIDD, RVOT, LA, mPAP (increasing trend) and ejection fraction, TAPSE (decreasing trend). There was dearth in data showing the relationship between duration of ART and cardiac changes among HIV-affected individuals. Okoromah CA et al., in their study had reported, there was

increased occurrence of cardiovascular abnormalities in subjects on ART medications for longer duration [7].

Limitation(s)

It would have been more informative, if the researchers could collect the data related to various types of drugs used in ART, CD4 cell count of the individuals and draw the relationship between cardiological changes with these parameters.

CONCLUSION(S)

Cardiac involvements among HIV infected patients are significant. There was definite correlation between cardiac involvement and duration of ART. Cardiologic check-up should be regular among these patients, so that due care can be taken in the early stage of involvement.

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