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Myocardial Dysfunction in HIV: An Echocardiographic Study

[1]Joel Quadros Piedade, [2]Bolivia Fernandes, [3]Warren Fernandes, [4]Manjunath Desai, [5]Rahul Mahadik
` [1,5]Assistant Professor, [2,3]Junior Resident, [4]Associate Professor
[1,3,4,5]Department of Cardiology, [2]Department of Medicine
Goa Medical College, Goa, India

***Corresponding Author:**
Warren Fernandes
Department of Cardiology, Goa Medical College, Goa, India

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Abstract

Background

It is estimated that there are more than 36 million people living with HIV/AIDS. The spectrum of cardiovascular involvement in HIV/AIDS is diverse. This study aims to determine the prevalence and characteristics of myocardial dysfunction. We also aim to study the correlation with echocardiography, electrocardiography and chest x-ray.

Materials and Methods

50 cases of newly detected HIV patients diagnosed according to NACO guidelines were selected for the study. A detailed clinical profile including detailed history, general physical examination and systemic examination was done for each patient with special emphasis on cardiovascular system. Routine line of investigations was obtained for all the patients. All patients were evaluated for CD4 counts and subjected cardiovascular investigations like ECG, ECHO and chest x-ray.

Results

In our study 80% of the patients were males and 20% were females and majority were in the age group of 31 to 50 years. 48% of patients had an abnormal ECG. Commonest abnormalities were sinus tachycardia. Commonest abnormalities noted were cardiomegaly (16%), bilateral pulmonary infiltrates suggestive of pulmonary TB (10%) and bronchiectatic lesions (8%). In this study 17 patients (34%) had pericardial effusion on echocardiography. Overall, 78% of patients were found to have cardiac dysfunction.

Conclusion

Dilated cardiomyopathy is an independent adverse prognostic factor in patients with HIV and is strongly associated with low CD4 count. Patients with CD4 count less than 200 had high prevalence of echocardiographic abnormalities than those with CD4 count more than 200. There is a high percentage of subclinical involvement of cardiovascular system as seen in our study which should be taken into consideration when evaluating any patient with HIV.

Keywords: HIV/AIDS, Myocardial dysfunction, Echocardiography

INTRODUCTION

In the 30 years since HIV/AIDS was first discovered, the disease has become a devastating pandemic, taking lives of 30 million people around the world.

India is one of the largest and most populated countries in the world, with over one billion inhabitants. Of this number, it's estimated that around 38 million people are currently living with HIV [1].

At the beginning of 1986, despite over 20,000 reported AIDS cases worldwide, India had no reported cases of HIV or AIDS [2].

Because individuals in their most productive years (15-49 years old) are most commonly infected with HIV/AIDS, the disease has a wide socioeconomic impact that threatens development progress in many poor countries, especially those in sub-Saharan Africa.

Cardiac involvement in AIDS/HIV infected persons occurs frequently but may be quiescent clinically and may be a direct cause of death [3].

The spectrum of cardiovascular involvement includes dilated cardiomyopathy, pericardial effusion, pulmonary hypertension, endocarditis, thrombosis, embolism, vasculitis, coronary artery disease, aneurysm, and cardiac involvement in AIDS related tumors.

Present study is carried out to determine the prevalence and characteristics of myocardial dysfunction and other cardiac manifestations in newly detected HIV patients. We also aim to study the correlation with non-invasive investigations like echocardiography, electrocardiography and chest x-ray.

MATERIALS AND METHODS

This study was carried out in Goa Medical College. The ethical committee clearance was obtained from the appropriate authority. 50 cases of newly detected HIV patients diagnosed according to NACO guidelines were selected for the study. A detailed clinical profile including detailed history, general physical examination and systemic examination was done for each patient with special on cardiovascular system. Routine line of investigations was obtained for all the patients. All patients were subjected to cardiovascular investigations like ECG, ECHO and chest x-ray. All relevant findings of echocardiography like LV internal dimension in systole [LVIDs], LV internal dimension in diastole [LVIDd], interventricular septal thickness in systole and diastole, fractional shortening [FS] and ejection fraction were studied.

All patients were evaluated with their CD4 counts and were analyzed for different cardiac manifestations

Inclusion criteria: The study included patients newly diagnosed to have HIV infection.

Exclusion criteria: Those with the following were excluded

1) Congenital heart disease
2) Pre-existing valvular heart disease
3) Hypertension
4) Diabetes Mellitus
5) Patients on antiretroviral therapy
6) Pregnant patients; postdelivery up to 6 months
7) Alcoholic liver disease

RESULTS AND OBSERVATION

Fifty ELISA positive HIV infected individuals were recruited for this study over a period of two years. Following are the results and observations made during this study.

Table 2: Age and Sex distribution

Age Category	Male	%	Female	%
20-30	9	18	2	4
31-40	13	26	4	8
41-50	17	34	3	6
>51	1	2	1	2
Total	40		10	

In our study 80% of the patients were males and 20% were females and majority were in the age group of 31 to 50 years.

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Table 3: ECG Findings

ECG Findings	Number	%
Normal	26	52
Tachycardia	10	20
Low voltage complexes	2	4
Ischemic heart disease	3	6
Left ventricular hypertrophy	1	2
Right axis deviation	4	8
Left anterior hemiblock	1	2
Right bundle branch block	1	2
P pulmonale	1	2
Generalized ST-T changes	1	2

In our study of 50 patients 52% of patients had normal ECG and 48% of patients had an abnormal ECG. Commonest abnormalities were sinus tachycardia (20%), right axis deviation (8%) and ischemic heart disease (6%).

Table 4: Chest X-Ray Findings

X-Ray Findings	Number	%
Normal	25	50
Cardiomegaly	8	16
Pleural effusion	3	6
Bilateral pulmonary infiltrates suggestive of pulmonary TB	5	10
Lobar pneumonia	3	6
Bronchiectatic lesion	4	8
Fibrosis	1	2
Nodular infiltrates	1	2

In this study 25 patients (50%) had normal chest x-ray while 25 patients (50%) had abnormalities on chest x-ray. Commonest abnormalities noted were cardiomegaly (16%), bilateral pulmonary infiltrates suggestive of pulmonary TB (10%) and bronchiectatic lesions (8%).

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Table 5: Cluster differentiation (CD4+) T-cell counts

CD4+ T-cell counts	Total Number	%
<50	13	26
51-200	13	26
201-350	11	22
>351	13	26

Table 6: Association of CD4+ T cell counts with cardiac dysfunction in HIV/AIDS

Cardiac dysfunction	CD4+ T-cell counts				
	<50	51-200	201-350	>351	Total (%)
Pericardial effusion	6	3	4	4	17 (34%)
Dilated cardiomyopathy	2	2	1	0	5 (10%)
Systolic Dysfunction	6	7	4	2	19 (38%)
Diastolic dysfunction	4	5	5	4	18 (36%)
Mitral regurgitation	0	0	1	0	1 (2%)
Tricuspid regurgitation	3	1	0	0	4 (8%)
Pulmonary hypertension	5	3	1	0	9 (18%)
Clot	0	0	0	0	0
Vegetation	0	0	0	0	0

Table 7: Severity of pericardial effusion

Pericardial Effusion	Number	%
No PE	33	66
With PE	17	34
Mild PE	14	28
Moderate PE	3	6
Large PE	0	0

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In this study 17 patients (34%) had pericardial effusion on echocardiography. Most of them had mild pericardial effusion (28%) while moderate pericardial effusion was seen in 3 patients (6%). None of the patients had large pericardial effusion.

Table 8: Association of pericardial effusion with CD4+ T-cell counts.

Pericardial Effusion	CD4+ T-cell Counts				
	<50 (n=13)	50-200 (n=13)	201-350 (n=11)	>351 (n=12)	Total
Without PE	6 (18.88%)	10 (30.30%)			33
With PE					
Mild	5 (29.41%)	3 (17.64%)	3 (17.64%)	2 (11.76%)	14
Moderate	2 (11.76%)			15 (5.88%)	3
Large					

Table 9: Cardiac Dysfunction

Cardiac Dysfunction	Number	%
Present	39	78%
Absent	11	22%

DISCUSSION

The effects of HIV virus are protean and all major organs are potential targets of infection. There is no definitive assessment of the natural history and associations of cardiac dysfunction in the entire range of adult groups infected with HIV. Cardiac involvement includes pericardial effusion (index presentation in countries like Africa [4]); dilated cardiomyopathy; infective endocarditis; infiltrative lymphoma; Kaposi's sarcoma; pulmonary hypertension; coronary artery disease.

This study was conducted in Goa Medical College to determine myocardial dysfunction in newly detected HIV patients. 50 adult patients were taken into the study of which 40 were males and 10 were females. Their clinical profile, electrocardiography, echocardiography, chest x-ray was done and correlated. The commonest symptoms were fever 70%, cough 42%, breathlessness 30%. The commonest cardiovascular finding in our study was systolic murmur in mitral area. Work conducted by Herdy G. V. et al. demonstrated that common examination findings in such patients were systolic murmur at left sternal border and decreased intensity of heart sounds [5].

Our study showed low incidence of infectious complications as 48% of patients were asymptomatic newly detected HIV positive patients at the outpatient clinic. However, work conducted elsewhere showed that diarrhea, tuberculosis and oral candidiasis were frequent infectious complications [5]

In the present study sinus tachycardia was the commonest observation on ECG which was also corroborated by a study conducted by Anita B. et al. [3].

Commonest abnormality noted in chest x-ray was cardiomegaly, probably due to pericardial effusion. Findings are comparable to study by Anita B et al. [3].

Echocardiographic abnormalities were noted in 72% of our study population. There was a significant percentage of cardiac dysfunction as noted in above chart based on echocardiography. The picture in our country is still dominated by opportunistic infection, as such cardiovascular abnormalities are not given importance. The most common abnormality detected

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in our study was left ventricular systolic dysfunction followed by diastolic dysfunction and pericardial effusion.

The incidence of dilated cardiomyopathy in our study was 10%. Other studies showed the prevalence of dilated cardiomyopathy that ranged from 5-20% [4, 5, 6]. HIV related heart muscle disease is often seen in a state of severe immunosuppression with low CD4 counts and poor prognosis [7]. In our study 4 out of 5 patients of dilated cardiomyopathy had CD4 counts less than 200. Currie et al. [7] reported similar findings.

The pathogenesis of myocardial disease in HIV infection is not known in most cases. Factors incriminated are; role of opportunistic infection [8] like toxoplasmosis; cytomegalovirus; Cryptococcus; due to HIV virus itself or immunologically mediated, due to antiretroviral therapy; even though some studies do not implicate zidovudine [6], post viral cardiac autoimmunity. Others like selenium deficiency, which is associated with malnutrition. Selenium deficiency is documented to be a cause of dilated cardiomyopathy in china – Keshan disease [9].

Limitation of our study was that no endomyocardial biopsies were done as they were technically not feasible. Although serological test for toxoplasma were performed, none were positive.

Involvement of myocardial cell is complex and multifactorial. Feature of advanced HIV is isolated dilation of either ventricle at earlier stage which later progresses to dilated cardiomyopathy [10]. Presence of left ventricular dysfunction on single echocardiographic measurement doesn't necessarily imply a poor prognosis.

Isolated right ventricular dilation was found in two patients in our study. It was secondary to pulmonary hypertension. The etiology of isolated right ventricular dilatation is multifactorial. It could be a part of myopathic process; due to pulmonary hypertension; recurrent chronic pulmonary infections; tricuspid regurgitation due to valvular endocardial damage.

Role of myocarditis in development of dilated cardiomyopathy is not fully characterized [11]. Lymphocytic myocarditis was found at autopsy in 46.52% patients of AIDS [12]. Study conducted by Barbaro et al. [13] showed histologic diagnosis of myocarditis was made in 83% of patients with dilated cardiomyopathy. This shows that there is a pathogenetic relationship between myocarditis and dilated cardiomyopathy. Limitation of our study is that no pathological post mortem examination was conducted.

During infection some patients developed congestive heart failure and echocardiographic manifestations suggestive of dilated cardiomyopathy, as during infection there is an increase in blood levels of interleukin 1 which correlates to severity of disease [14]. Interleukin 2 produced by T lymphocytes increases the toxicity of killer cells that promote the synthesis of tumor necrosis factor. Interleukin 2 and tumor necrosis factor decrease ejection fraction of left ventricle.

Pericardial effusion was the third most common abnormality in our study. Spectrum of involvement ranged from asymptomatic effusion to cardiac tamponade. Pericardial disease in India is largely due to tuberculosis. Low incidence of pericardial effusion in study conducted by Himelman et al was probably due to low incidence of tuberculosis in California where this study was conducted [15]. Other causes include: mycobacterium avium complex, Cryptococcus, nocardia, pyogenic organisms like streptococcus, Kaposi sarcoma, lymphoma, viral, probably HIV itself [12].

Our study had 28% mild pericardial effusion where in pericardial tap was not possible to ascertain the cause. 6% had moderate effusion which was tapped: results were inconclusive as no definitive organisms were found. Our study had 28% patients infected with tuberculosis. Specific identifiable cause of pericardial effusion in AIDS is not always possible.

Moreno et al [16] reviewed echocardiographic studies in 141 HIV patients and 55 (39%) had pericardial effusion. Most of 34/35 were small (61%). This percentage was higher than found in our study possibly could be because of small sample size in our study. Heidenreich et al [17] studied the incidence of pericardial effusion and its relation to mortality in HIV patients. 231 patients were recruited and 74 had AIDS. 15 patients with HIV infection had pericardial effusion and 12 effusions were small. Only 3 patients had moderate to large pericardial effusion which caused tamponade. In our study 2 patients had moderate effusion.

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Our study did not find any patient with infective endocarditis. Infective endocarditis was mostly described in intravenous drug abusers and none of our patients were IV drug abusers. Marantic endocarditis was seen in chronically ill and wasted patients. None of our study patients had this finding.

The prevalence of pulmonary hypertension in India is reported to be 20%. Our study had similar results which was 18%. Work done by Hadadi et al. [18] and Singh et al. [19] reported prevalence of pulmonary hypertension to be 12.68% and 11.42% respectively.

The pathogenesis of pulmonary hypertension associated with HIV infection is unclear. Mette et al. [20] were unable to demonstrate the presence of HIV in pulmonary arterial endothelial cells by electron microscopy, immunohistochemistry, DNA in situ hybridization and PCR. These findings allude to an indirect mechanism of HIV associated pulmonary hypertension.

Our study did not have any patients with Kaposi sarcoma or lymphomas. None of our patients had involvement of coronary arterial involvement. We speculate that this could be the case as none of our patients were on antiretroviral treatment. Increased incidence of myocardial infarction in HIV patients has been described by Mary Krause M et al. [21] and Klein et al. [22]. Both these studies related it to the use of protease inhibitors.

CONCLUSION

The course of asymptomatic echocardiographic myocardial dysfunction and its relevance to overall long-term prognosis remains undetermined.

Furthermore, studies of etiology of pericardial effusion, myocardial dysfunction in HIV with biopsy evaluation is required.

Follow-up echo is required as regression in left ventricular dysfunction may be seen if the process was a self- limiting myocarditis.

Dilated cardiomyopathy is an independent adverse prognostic factor in patients with HIV and is strongly associated with low CD4 count.

Conventional treatment with digoxin, diuretics, ACE inhibitors may help improve cardiac dysfunction even in asymptomatic HIV patients.

Dilated cardiomyopathy occurs late and is associated with signs and symptoms which may be attributed mistakenly to other disease processes.

Direct effects of HIV virus causing cardiac dysfunction requires further evaluation as zidovudine does not seem to be related to cardiac dysfunction.

Decision on treatment of HIV patients should take into account both the trend of serology results and clinical factors (including presence of heart disease).

Present study showed that patients with CD4 count less than 200 had high prevalence of echocardiographic abnormalities than those with CD4 count more than 200/

There is a high percentage of subclinical involvement of cardiovascular system as seen in our study which should be taken into consideration when evaluating any patient with HIV.

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