

Original Research Article

Cardiac manifestations in HIV patients and their correlation with CD4 count

Santosh Kumar Maurya*, Sarita Bajaj, Piyush Saxena,
Kamlesh Kumar Sonker, Sujit Kumar Verma

Department of Medicine, Moti Lal Nehru Medical College, Allahabad, Uttar Pradesh, India

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*Correspondence:

Dr. Santosh Kumar Maurya,
E-mail: santoshkmr280@gmail.com

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ABSTRACT

Background: The introduction of highly active antiretroviral therapy (HAART) has significantly improved the clinical evolution of human immunodeficiency virus (HIV)/AIDS disease, with an increased survival of infected patients. With advances in the management of patients living with HIV and AIDS, not only survival has increased but manifestations of late stage HIV infection are encountered more often including cardiovascular complications. Objectives were to determine the prevalence and characteristics of cardiac manifestations in patients with HIV infection, and to correlate the cardiac manifestations with CD4 count.

Methods: 115 HIV-positive cases and 30 healthy control subjects were evaluated by detailed history and general physical examination. CD4 was done for all patients using flowcytometry using a BD FACS Count system. All patients were evaluated using M Mode and two-dimensional transthoracic echocardiography and colour flow doppler examination.

Results: Male to female ratio was 1.6:1 in cases. The most common symptoms were cough (54.78%), palpitations (10%), shortness of breath (52%), chest pain on exertion (18.0%) and ankle swelling (21.0%). Echocardiographic abnormalities were found in 63% of the cases compared with 6% in the controls. 18 (15.65%) patients had dilated cardiomyopathy, 17 (15%) pericardial effusion, 16 (14%) pulmonary artery hypertension, 17 (15%) mitral valve prolapses and 25 (22%) had reduced ejection fraction compared with none of controls. 54 (47%) cases had diastolic dysfunction compared with 3 (10%) controls and 40 (35%) cases had reduced fractional shortening ($\leq 27\%$) compared 4 (13%) controls. Significant statistical positive correlation was not observed between low CD4 count and echocardiographic abnormalities. Pericardial effusion was seen more in patients with CD4 count below 200.

Conclusions: Cardiovascular abnormalities in HIV infected patients are common and can occur without any clinical manifestation. There was no significant association between CD4 count and any cardiac manifestation.

Keywords: HIV, AIDS, CD4 count, Echocardiographic findings

INTRODUCTION

The Joint United Nations Program on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) estimated that 5.7 million people in India were infected with the human immunodeficiency virus (HIV).¹ In developing countries, where HAART is not widely available, an increase in the prevalence of

cardiomyopathy and pericardial effusion, with a related high mortality rate for congestive heart failure occur.²

In the context of these new clinical findings, it has been observed in developed countries that some HAART regimens, especially those including protease inhibitors, may cause an iatrogenic metabolic syndrome (HIV-associated lipodystrophy syndrome) that is associated

with an increased risk for cardiovascular events (myocardial infarction and stroke) because of a process of accelerated atherosclerosis.

According to reports of clinical and autopsy studies, the reported prevalence of cardiomyopathy in HIV-positive patients constitutes a broad range from about 4% to as high as 75% in different studies.^{3,4} Mortality in HIV patients has also been reported to be substantially due to cardiomyopathy with up to 6 fold higher rate of death in HIV+ children.⁵ Minimal left ventricular dysfunction in children was associated with 55% mortality in 5 years follow up.⁶ The same rates have been reported in adult populations.⁷ The effect of antiretroviral therapy (ART) on the incidence and prevalence of HIV-related cardiovascular disease has also been not well demonstrated. A large study of over 23 thousand HIV positive patients reported that use of ART is associated with increased risk of acute cardiovascular and cerebrovascular events.^{8,9} In chronic HIV infection, cardiomyopathy seems to benefit from ART with declining the incidence and mortality of HIV-related mortality in these patients.⁵

METHODS

Patients of age ≥ 18 years diagnosed for HIV infection by ELISA test included in this study. The patients were yet to commence antiretroviral therapy.

Clinical assessment, electrocardiography (ECG), chest radiography, and Doppler echocardiographic examination done. Haemoglobin measurement, CD4 count, ESR and routine serum biochemistry analysis were done. Patients with hypertension, ischemic heart disease, cardiomyopathy and chronic bronchopulmonary disease were excluded. Dyspnoea alone was not a reason for exclusion, because it is a relatively common complaint in AIDS.

Thirty healthy, HIV-negative individuals served as controls. They were recruited after voluntary screening in the HIV clinic side laboratory to confirm their negative status. They were recruited to match the age, gender and weight and height profile of the HIV cases.

Transthoracic echocardiography was performed using a Siemens Sonoline S1-450 in the cardiovascular laboratory with a 3.5-MHZ transducer probe. Two-dimensional (2D), M-mode, pulse-wave, continuous-wave and colour Doppler echocardiography assessment was done with the subject in the left lateral decubitus position.¹² The two-dimensional images were obtained in the parasternal long and short-axis views, apical and subcostal views.^{10,11}

Left atrial diameter (LA), aortic size (AO), right ventricular outflow tract (RVOT), left ventricular end-systolic (LVEDs) and end-diastolic (LVEDd) diameters,

interventricular septum (IVS), left ventricular posterior wall thickness (LVPW), estimated right ventricle (ERV), and end-point septal separation (EPSS) measurements were obtained from 2D directed, M-mode recordings from the parasternal long axis.¹¹ Measurements were taken (in cm) according to the American Society of Echocardiography guidelines.¹² The mean of three measurements was recorded.

Doppler studies included pulmonary velocity (PV), aortic velocity (AV), transmitral flow, and deceleration time (DT) measurements. Isovolumetric relaxation time (IVRT) was obtained from pulse-wave Doppler studies.¹¹ Echocardiographic abnormalities, e.g. pericardial effusion, thickening, separation, valvular lesions such as stenosis, and regurgitations and regional wall-motion abnormalities were also looked for.

RESULTS

115 consecutive patients with HIV infection who were hospitalized to in patients and attending ART centre were studied. 30 healthy control subjects were recruited for the study. There was a gender predominance with male to female ratio 1.6:1. The age of the patients studied ranged between 18 and 56 years, with a mean age of 35.89 (± 7.30) years in cases and 34.56 (± 6.60) years in controls respectively. Majority of the patients, 76% cases and 70% controls were young and were in the age group of 20 to 40 years.

The CD4 count ranged from 17.00 to 800.0/ μ l with a mean of $200.37 \pm 160.4/\mu$ l. CD4 count was less than 50/ μ l in 28%, 35% of cases had CD4 count between 50 to 200/ μ l while 19% had CD4 Count 200-400/ μ l and 18% cases had CD4 count $\geq 400/\mu$ l.

The most common symptoms were cough (54.78%), palpitations (10%) and shortness of breath (52%), chest pain on exertion (18.0%) and ankle edema (21.0%). Only two patients had overt symptoms of heart failure (dyspnoea at rest, orthopnoea, paroxysmal nocturnal dyspnoea, ankle edema, tender hepatomegaly), while one had features of massive pericardial effusion. All three had a CD4 count less than 100/ μ l.

Echocardiographic abnormalities were found in 63% of the cases compared with 6% in the controls ($\chi^2=4.99$; $p=0.025$). The echocardiographic abnormalities are summarized in Table 1. Of the 115 cases studied, 18 (15.65%) had dilated cardiomyopathy ($p=0.0002$), 17 (15%) pericardial effusion ($p=.025$), 16 (14%) pulmonary artery hypertension ($p=0.030$), 17 (15%) mitral valve prolapses ($p=0.025$) and 25 (22%) have reduced ejection fraction ($p=0.004$) compared with none of controls. 54 (47%) cases had diastolic dysfunction compared with 3 (10%) in controls ($p=0.0002$) and 40 (35%) cases had reduced fractional shortening ($\leq 27\%$) compared with 4 (13%) in controls ($p=0.022$).

Table 1: Echocardiographic abnormalities in cases and controls.

Echocardiographic abnormalities	Cases (n=115)	Controls (n=30)	χ^2	P-value
Pericardial effusion	17	0	5.02	0.025
Diastolic dysfunction	54	3	13.62	0.002
Dilated cardiomyopathy	18	0	5.361	0.020
Pulmonary Artery Hypertension	16	0	4.69	0.030
Mitral valve prolapsed	17	0	5.02	0.025
↓ Left Ventricular Ejection Fraction	25	0	7.88	0.004
↓ Left Ventricular Fractional shortening	40	4	5.17	0.022
Patients having cardiac manifestation	72	7	4.99	0.025

Table 2: Echocardiographic dimensions in cases and controls.

Parameter	Cases (n=115)	Controls (n=30)	P-value
LA (cm)	3.116±0.2	3.22±0.3	0.085
AO (cm)	2.799 ±0.462	2.606±0.285	0.0031
IVST (cm)	0.95±0.3	0.78 ±0.2	0.0007
LVPWT (cm)	0.934±0.28	0.783±0.13	0.0024
LVMI (g/m ²)	88.02±17.23	73.7±17.3	0.0001
RV DIMENTION	3.061±0.41	2.98±0.25	0.113

Values are mean±SD. LA: left atrial diameter; AO: aortic root diameter; IVS: interventricular septum; LVPW: posterior wall thickness; p<0.05 is statistically significant.

Table 3: Association of 2D echocardiographic findings with CD4 count in cases.

Cardiac manifestations	CD4 count in /μL			Total
	<50	50-199	>200	
Pericardial effusion	12	5	0	17
Diastolic dysfunction	29	14	11	54
Dilated cardiomyopathy	10	5	3	18
PAH	8	4	4	16
Mitral valve prolapsed	12	4	1	17
Reduced LV ejection fraction	10	8	7	25
Reduced LV fractional shortening	21	12	7	40

As presented in Table 2, HIV-positive patients had significantly increased IVST, LVPWT as compared with the controls and reach the level of statistical significance (p=0.002 and p=0.0007 respectively) LA diameter and RV dimension also increased in cases but not reached to significant level (p=0.08 and p=0.11 respectively).

As presented in Table 3, maximum number of echocardiographic findings were seen in patients with CD4 count less than 200. Out of the total 17 patients with pericardial effusion, 12 patients had CD4 count less than 50. Similarly, reduction in FS, 21 patients out of total 40 had CD4 count less than 50, 10 out of 18 cases of dilated cardiomyopathy had CD4 count less than 50, 12 out of total 17 patients of mitral valve prolapse had CD4 count less than 50 and 10 patients out of total 25 of reduced ejection fraction had CD4 count less than 50. Maximum number of cases with pericardial effusions, diastolic dysfunction and pulmonary artery hypertension, reduced ejection fraction, reduced LV fractional shortening and

mitral valve prolapse have CD4 count less than 50. There was significant association between echo finding and increased ESR (erythrocyte sedimentation rate) (p=0.006). There was no correlation of echo finding with CD4 count haemoglobin and TLC.

DISCUSSION

115 patients with HIV infection and registered in ART centre and 30 controls were included in this study. Majority of the patients, 78% males and 70% females, belonged to the young age group of 20 to 40 years. It was in concordance with NACO annual report 2009-2010.¹³ The NACO report has shown that most HIV in India were young adults. Men were more affected than females by a ratio of 1.61:1. 71 patients (62%) were males and 44 patients (38%) were females. The gender difference was also as with NACO report.

Clinical features such as palpitation- 10%, cough- 54.78%, breathlessness- 52% respectively is different to other studies from India due to non-specific symptoms and could be attributable to secondary pulmonary infections.¹⁴ diastolic dysfunction was frequently seen in HIV-infected patients (47%), signifying ventricular filling abnormalities due to a noncompliant ventricle. Diastolic dysfunction was also observed to be more frequent and worsening with disease progression. The findings in this study compare with the 46.95% prevalence noted by Jain et al.¹⁵ in their work. Diastolic dysfunction has also been reported in other studies.^{16,17}

DCM is a well-documented cardiac abnormality in HIV/AIDS and was found in 15.65% of cases, with none in the control group.^{18,22-24} All patients with DCM had more advanced immunosuppression with a mean CD4 count of 69/ μ l. This result correlates well with several reports that dilated cardiomyopathy in HIV is associated with advanced immunosuppression and lower CD4 lymphocyte counts <100/ μ l.¹⁸⁻²¹ Nzuobotane et al demonstrated a similar relationship between the degree of immunosuppression and the likelihood of cardiomyopathy (18%).¹⁸ Interestingly, a CD4 count of 100/ μ l proved to be the important threshold in that study as well. whereas studies published by Moreno et al and Hakim et al.^{25,26} had detected 6% and 5% respectively. It is due to that in this study the mean CD4 count of cases is less than other study.

Pericardial effusion was seen in 15% of cases which is as par with Indian studies done by Aggarwal et al.²⁷ and studies done at United States by Himelman et al.²⁸ The pericardial effusion detected was often small in amount and without any hemodynamic significance.

CONCLUSION

Cardiovascular abnormalities in HIV infected patients are common and can occur without any clinical manifestation. The most common cardiac manifestations were reduction in ejection fraction, reduction in fractional shortening, pericardial effusion, dilated cardiomyopathy and diastolic dysfunction. There was no significant association between CD4 count and any cardiac manifestation. There was significant association between echo finding and increased ESR (erythrocyte segmentation rate). It suggests that echo finding occur due to myocarditis not directly associated with CD4 count. Though echocardiography seems to be a useful technique for the early recognition and treatment of cardiac dysfunction in such patients; clinic pathological studies may help to clarify the role of HIV virus and opportunistic infections in the pathogenesis of cardiac abnormalities found in HIV infected patients.

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