

# Cardiac complications in people living with human immunodeficiency virus/acquired immunodeficiency syndrome and their association with CD4+ T-cell count – A cross sectional study

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## Abstract

**Introduction:** Cardiac complications of HIV infection tend to occur late in the disease or are associated with related therapies and are therefore becoming more prevalent as therapy and longevity improve.

**Materials and Methods:** The study was undertaken to study the common cardiovascular complications in Indian HIV patients and to their association with the CD4+ T-cell count. **Observations and Conclusion:** Prevalence of cardiac abnormality in our study was 24%. The abnormalities included LVDD (22%), pulmonary hypertension (12%), DCMP (12%), pericardial effusion (7%), left ventricular systolic dysfunction (5%), and right ventricular dysfunction (1%).

**Key words:** Dilated cardiomyopathy, infective endocarditis, left ventricular diastolic dysfunction, left ventricular systolic dysfunction, premature coronary artery disease, pulmonary artery hypertension

## INTRODUCTION

Since the first detection of acquired immunodeficiency syndrome (AIDS) cases in 1981 among homosexuals in the USA, the number of human immunodeficiency virus (HIV) positive individuals and AIDS cases have increased enormously.<sup>[1]</sup> The first case of HIV infection was reported in 1986 in India, and since then, the AIDS epidemic has advanced at an alarming rate till 2007 after which there has been a steady fall in the prevalence of cases.<sup>[2,3]</sup> Cardiac complications of HIV infection tend to occur late in the disease or are associated with related therapies and are therefore becoming more prevalent as therapy and longevity improve.<sup>[4]</sup>

The cardiac complications may include premature coronary artery disease, dilated cardiomyopathy, left ventricular systolic dysfunction, left ventricular diastolic dysfunction (LVDD), pulmonary artery hypertension, infective endocarditis, etc.

## Aims and objectives

The study was undertaken to study the common cardiovascular complications in Indian HIV patients and to their association with the CD4+ T-cell count.

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## MATERIALS AND METHODS

The study was conducted in the Department of Internal Medicine at LLRM Medical College, Meerut from July 2014 to March 2015. This was an observational cross-sectional type of study. The ethical clearance was obtained from the institutional ethics committee of LLRM Medical College, Meerut. Written informed consent was taken from all the participants. All previously diagnosed case of HIV infection >18 years willing to participate in the trial were included in the study. Patients with chronic renal failure, diabetes mellitus, hypothyroidism, patient on steroid therapy, history of myocardial infarction, and congenital heart diseases were excluded from the study.

All the patients were evaluated for cardiac involvement and their immunodeficiency evaluated with CD4 counts. A standard twelve-lead resting electrocardiogram was done for all patients. Cardiac structure, function, and cardiac abnormalities were assessed using standardized transthoracic echocardiographic examination, using Phillips echocardiography machine model HD 11XE. The presence of pericardial effusion, chamber dilatation, myocardial dysfunction, ejection fraction, pulmonary hypertension, and valvular lesions was noted.

## RESULTS

A total of 100 HIV patients were studied. They were divided into two groups based on the basis of the CD4 count.

In the present study, out of 100 cases studied, 55% of cases were males and 45% of cases were females. Male to female ratio was 1.2:1. Mean age of patient was 34.3 years.

The age and sex distribution of the population studied has been shown in Figures 1 and 2.

In this study, mean duration of HIV infection was 1.8 years. Mean duration of HIV infection in Group I (patients with CD4+ T-cell count <350) and Group II (patients with CD4+ T-cell count >350) was 1.51 and 1.94 years, respectively. There was statistically significant correlation was observed between duration of HIV infection and cardiac abnormalities in Group II who has lower CD4 count. Dyspnea was found in 23 patients. Nearly 4% of patients had edema. No patient complained of chest pain, palpitations, or syncope. There is a significant correlation between symptoms and cardiac abnormalities in patients who had lower CD4 count.

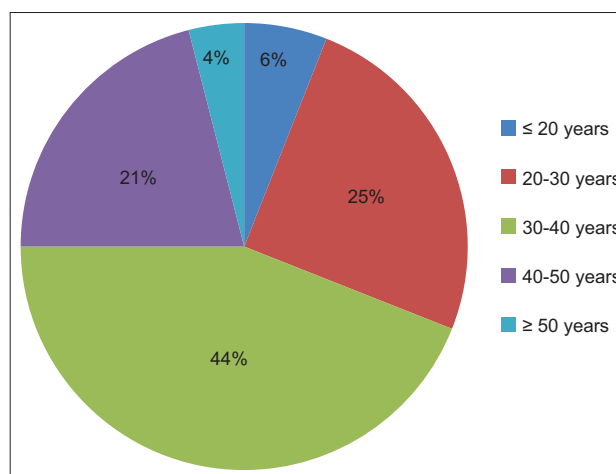


Figure 1: Age distribution

Out of 100 cases, 54% were having CD4+ Tcell count more than 350 cells/mm<sup>3</sup>, 46% had CD4+ Tcell count <350 cells/mm<sup>3</sup>. In the present study, out of 100 cases studied 89% patients had normal electrocardiography (ECG). The most common abnormalities were sinus tachycardia observed in 11% of cases. ECG was suggestive of P-wave abnormality in 1%, left ventricular hypertrophy in 2% of cases and it showed ST-T changes in 9% of cases only.

Prevalence of cardiac abnormality in our study was 24%.

LVDD was found to be the most common echocardiographic abnormality. It was seen in 22% of patients. Nearly 10% of patients had Grade I LVDD, 8% had Grade II LVDD, whereas 4% had Grade III LVDD.

Other echocardiographic findings were pulmonary hypertension (12%), pericardial effusion (7%), left ventricular systolic dysfunction (5%), right ventricular dysfunction (1%), and DCMP was noted in 12% of patients.

Out of the 7% of patients having pericardial effusion 1% patient had mild pericardial effusion, whereas 3% had moderate and 3% had severe pericardial effusion.

The mean age of patients with respective cardiac complications has been shown in Figure 3.

### The association of cardiovascular complications with CD4+ counts

Table 1 shows the various cardiac complications along with CD4+ counts of the patients. The low CD4+ T-cell count was found to be associated

with DCMP, pericardial effusion, and LV systolic dysfunction. The association was statistically significant.

Figure 4 shows the cardiac complications in HIV patients with CD4+ counts >350 and in patients with CD4+ counts <350.

Among 7% of cases with pericardial effusion, all cases had CD4+ T cell count was <350 cells/mm<sup>3</sup>. This is statistically significant.

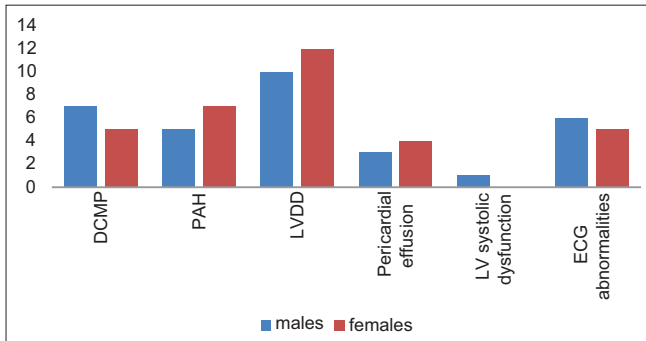


Figure 2: Sex distribution in patients suffering with cardiac complications

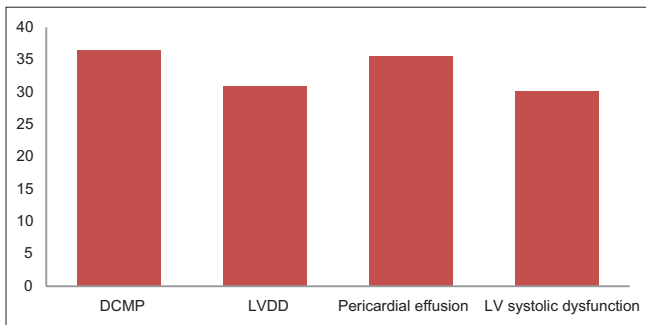


Figure 3: Mean age of patients suffering with cardiovascular complications

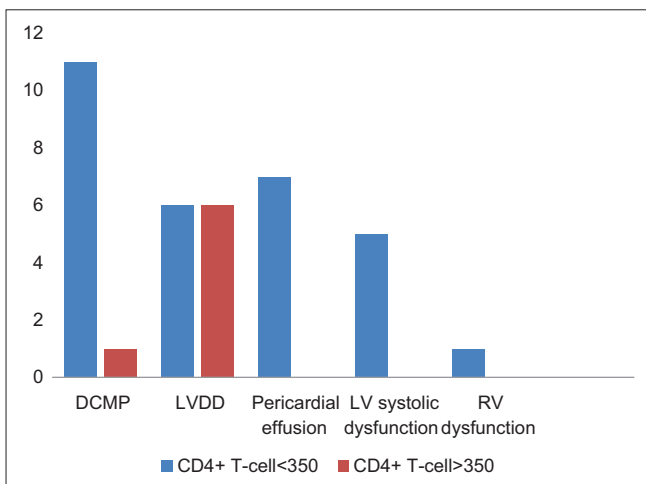


Figure 4: Cardiac complications in patients with CD4+ T-cell <350 and CD4+ T-cell >350

Two-dimensional echocardiography was within normal limits in 76% of cases.

Mean age of patients suffering with DCMP was 36.4167 ± 10.36128 years.

It was found to be associated with low CD4+ count (P < 0.001). However, there was no association with sex or duration of HIV.

Similarly mean age of patients suffering with DCMP was 30.2000 ± 6.64831 years. It was found to be associated with low CD4+ count (P < 0.001). However, there was no association with sex or duration of HIV. All the patients suffering with DCMP had CD4+ T-cell count <100.

Mean age of patients suffering with LVDD was 30.9545 ± 7.71194 years.

It was found to be associated with duration of HIV (P < 0.001). Patients with a longer history of disease were more likely to develop LVDD. However, there was no association with sex or low CD4+ count.

ECG abnormality found to be associated with low CD4+ count (P < 0.001). There was no association with sex or duration of HIV.

Pericardial effusion was found to be associated with low CD4+ count (P < 0.001). However, there was no association with sex or duration of HIV.

## DISCUSSION

In the present study, most of the patients (46%) belonged to age group 30–40 years. The age distribution has been depicted in Figure 1.

There was no significant correlation between age and cardiac abnormalities similar to the study conducted by Caggese *et al.*<sup>[5]</sup>

Table 1: Cardiac complications in HIV patients with CD4+ counts

Cardiac complications	CD4+		Total (n=100)	P
	<350 (n=46)	>350 (n=54)		
DCMP	11 (23.9)	1 (1.9)	12	0.001
LVDD	6 (13.0)	16 (29.6)	22	0.055
PAH	9 (19.6)	3 (5.6)	12	0.060
Pericardial effusion	7 (15.2)	0	7	0.003
LV systolic dysfunction	5 (10.9)	0	5	0.018
RV dysfunction	1 (2.2)	0	1	0.460

DCMP=Diagnosed dilated cardiomyopathy; LVDD=Left ventricular diastolic dysfunction; PAH=Pulmonary artery hypertension; LV=Left ventricular; RV=Right ventricular

Cardiac symptoms were found in 23 patients in which dyspnea was the most predominant symptoms. 4% of patients had edema.

There is a significant correlation between symptoms and cardiac abnormalities in Group II who had lower CD4 count. In a study conducted by Sudagar Singh *et al.*<sup>[6]</sup> at Sri Ramachandra Medical College and Hospital most patients were asymptomatic (55 patients), cardiac symptoms were found in 45 patients in which dyspnea was the most predominant symptoms. In a study by Ewig *et al.*,<sup>[7]</sup> nine out of 14 patients (64%) with cardiac abnormalities had symptoms.

Electrocardiographic abnormalities were seen in 11% of patients. In Joshi *et al.* study,<sup>[8]</sup> among 74 patients, 20.27% had electrocardiographic abnormalities. There was a significant correlation between CD4 count and ECG abnormalities.

Prevalence of echocardiographically diagnosed cardiac abnormality in our study was 24%. Echocardiographic findings were LVDD (22%), pulmonary hypertension (12%), DCMP (12%), pericardial effusion (7%), left ventricular systolic dysfunction (5%), and right ventricular dysfunction (1%). In a study by Mishra *et al.*,<sup>[9]</sup> 36.7% had diastolic dysfunction, and 23.3% had systolic dysfunction. In Mirri *et al.*<sup>[10]</sup> study, 17% had echocardiographic abnormalities.

There was a significant correlation between CD4 count and Echocardiographic abnormalities.

### **Dilated cardiomyopathy**

Etiology is multifactorial. It can be due to drugs, for example, Cocaine, AZT, IL-2 doxorubicin, interferon; infections such as HIV (direct effect), toxoplasma, coxsackievirus group B, EBV, CMV, adenovirus; Metabolic causes: selenium or carnitine deficiency, anemia, hypocalcemia, and hypophosphatemia, hyponatremia, hypokalemia, hypoalbuminemia; hypothyroidism, growth hormone deficiency, adrenal insufficiency, hyperinsulinemia, hemochromatosis, sarcoidosis, amyloidosis pheochromocytoma; cytokines: tumor necrosis factor-alpha (TNF- $\alpha$ ), nitric oxide, transforming growth factor beta, endothelin-I, interleukins; CD4+ T-cell count <100.

### **Left ventricular systolic dysfunction**

Patients with left ventricular systolic dysfunction can be asymptomatic or can present with New York Heart Association Class III or IV heart failure. Etiology is multifactorial. Possible causes can be myocarditis caused by either direct action of HIV

on the myocardial tissue or with coinfecting viruses such as coxsackievirus Group B, Epstein-Barr virus, cytomegalovirus, adenovirus, and *Toxoplasma gondii*.

Other causes could be cytokine alterations, i.e., increased production of TNF- $\alpha$ , increased nitric oxide production, transforming growth factor- $\beta$ , and endothelin-1 upregulation.<sup>[11]</sup> Deficiencies of trace elements have been associated with cardiomyopathy, for example, selenium deficiency.<sup>[12]</sup> Vitamin B<sub>12</sub>, carnitine, and growth and thyroid hormone can also be altered in HIV disease; all have been associated with LV dysfunction. Mortality in HIV-infected patients with cardiomyopathy is increased, independently of CD4 count, age, gender, and HIV risk group.

### **Left ventricular diastolic dysfunction**

Diastolic dysfunction is relatively common in long-term survivors of HIV infection. LV diastolic dysfunction may precede systolic dysfunction.<sup>[13-15]</sup>

The pathogenesis of LV diastolic dysfunction is likely multifactorial. Possible causes include hypertension associated with antiretroviral therapy, directly affect of HIV or other associated viral infection on myocardium or subclinical atherosclerosis

### **Pericardial effusion**

HIV-infected patients with pericardial effusions generally have a lower CD4 count than those without effusions, indicating more advanced disease. Effusions are generally small and asymptomatic.

HIV infection should be suspected whenever young patients have pericardial effusion or tamponade.

Pathogenesis of pericardial effusion in HIV infection is unclear. Numerous case reports have described Kaposi's sarcoma, mycobacteria, cytomegalovirus, prosthetic valve endocarditis, bacterial pericarditis, and lymphoma as the cause of pericardial effusion in HIV infection. Effusion markedly increases mortality. It was seen in the PRECIA study, where it almost tripled the risk of death among AIDS patient.

### **CONCLUSION**

Cardiac abnormalities in HIV are common. In our study 24% patients had cardiac abnormalities on echocardiography. The abnormalities included LVDD (22%), pulmonary hypertension (12%), DCMP (12%), pericardial effusion (7%), left ventricular systolic dysfunction (5%), and right ventricular dysfunction (1%). we recommend doing electrocardiography and echocardiography in all HIV

patients for early diagnosis and treatment of cardiac abnormalities.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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