Myocardial Dysfunction in Human Immunodeficiency Virus Infection: An Echocardiographic Study
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Abstract
Objectives: To determine the prevalence and characteristics of myocardial dysfunction and other cardiac manifestations in patients with human immunodeficiency virus (HIV) infection
Methods: Fifty-two patients with HIV infection were examined and screened for various opportunistic infections. CD4 cell count was done and two dimensional echocardiography was performed.
Results: Echocardiographic findings were identified in 22 of 52 patients (42.3%). Eighteen patients (34.6%) were having reduction in fractional shortening, 10 patients (19.2%) left ventricular diastolic dysfunction, 8 patients (15.4%) global hypokinesia and 6 patients (11.5%) pericardial effusion. Nineteen out of 22 patients having CD4 cell count <100 cells/mm3 had high prevalence of echocardiographic abnormalities. Patients with opportunistic infections had more frequent echocardiographic abnormalities than those without opportunistic infections (P<.001 for TB, candidiasis and various pneumonias).
Conclusion: Although often not diagnosed clinically, cardiac involvement in patients with HIV infection is a clinical reality with pericardial effusion, left ventricular diastolic dysfunction, reduction in fractional shortening and global hypokinesia appearing to have a high prevalence. These echocardiographic findings are associated with clinically apparent opportunistic infections and low CD4 cell count.

Introduction
Although not fully recognized in the early days of HIV epidemic, cardiac involvement has been reported with increasing frequency in recent years. The prevalence of cardiac involvement in AIDS patients has been reported to range between 28% and 73%. The cardiac diseases include pericardial effusion, myocarditis, dilated cardiomyopathy, endocarditis, pulmonary hypertension, malignant neoplasm, coronary artery disease, left ventricular dysfunction, and drug related cardiotoxicity. When patients are examined by echocardiography, cardiac abnormalities are detected more often than would be expected from clinical symptoms and physical examination. Echocardiography is very helpful in detecting cardiac dysfunction at an early stage, even if clinically unclear, probably because all patients had coexistent opportunistic infections and the usual stigmata of dysfunction could be alternatively explained by infection. The most common sign of cardiac damage is impairment of LV fractional shortening. This could be explained by reduction of myocardial contractility. There are many causes of myocarditis in HIV infection including HIV itself and infection with other organisms such as Toxoplasma gondii and cytomegalovirus. Myocardial dysfunction in HIV infection could also be an effect of anti-retroviral drugs particularly zidovudine. We examined 52 patients infected with HIV by echocardiography. The principal aims were to establish the prevalence of myocardial dysfunction and determine its association with variables such as the extent of HIV disease and opportunistic infections.

Materials and Methods
Fifty-two HIV infected patients were studied. We excluded patients that had a history or a physical examination suggestive of ischemic, rheumatic, congenital or hypertensive heart disease previous to diagnosis of HIV infection.

The patients were assessed clinically by relevant history, general physical examination and specific investigations were undertaken to establish diagnosis and screening for opportunistic infections. CD4 cell count was done by fluorescent activated cell sorter system. All patients studied using quantitative M-mode and two dimensional transthoracic echocardiography and flow Doppler examination. Each two-dimensional study consisted parasternal long and short axis, and apical two and four chamber views.

The conventions of American Society of Echocardiography were followed in obtaining left atrial dimensions, left ventricular end systolic and end diastolic dimensions, right ventricular end diastolic dimensions and left ventricular fractional shortening. Left ventricular volumes were measured with the Biplane Simpson's rule, and ejection fraction was subsequently calculated. The presence of pericardial effusion, any valve regurgitation and any regional valve motion abnormalities were also looked for.

Statistical analysis
All results are reported as the percentage of patients found to have the given abnormality or as mean ± standard deviation. The number of patients manifesting an echocardiographic abnormality with and without opportunistic infections were compared using chi-square analysis. Mean CD4 cell count of patients with and without echocardiographic abnormality was compared using unpaired student t test. For all analyses, a p value <0.05 was considered significant.

Results
A total of 52 patients studied, comprising 40 males and 12 females. Mean age for male patients was 34 years and for female patients 31.4 years. All male patients were heterosexual and none admitted to intravenous drug use. No patient had received zidovudine or any other antiretroviral agent. The common
opportunist infections found were tuberculosis in 33 patients (63.5%), oropharyngeal candidiasis in 16 patients (30.8%) and pneumonias in 12 patients (23.1%). The most common form of tuberculosis found was disseminated tuberculosis in 20 patients, followed by tuberculous meningitis in 5 patients, sputum positive pulmonary tuberculosis in 4 patients and tubercular pleural effusion and ascites in 3 patients each. Out of 12 patients with pneumonia, 10 were having lobar pneumonia and 2 patients were suffering from Pneumocystis carinii pneumonia. Out of these 52 patients CD4 count of 37 patients (71%) was found to be <100/mm3.

**Echocardiography**

Echocardiographic abnormalities were noted in 22 patients (42.3%). Most common echocardiographic abnormality found was reduction in fractional shortening (18 patients, 34.6%), followed by left ventricular diastolic dysfunction (10 patients, 19.2 %), global hypokinesis (8 patients, 15.4%) and pericardial effusion (6 patients, 11.5%).

Mean CD4 count in patients with echocardiographic abnormalities was found to be 61.68 + 34.16, whereas in patients without echocardiographic abnormalities it was 116±95.89 (P<.001).

Out of these 22 patients, tuberculosis was found in 20 patients (91%), oropharyngeal candidiasis in 11 patients (50%) and pneumonias in 6 patients (27.3%). When these opportunistic infections were compared with those found in patients without echocardiographic abnormalities, they were highly significant (P < 0.001).

**Discussion**

The study showed that echocardiographic abnormalities are very common in HIV infected patients. Commonest manifestation found is reduction in fractional shortening which is consistent with study done by Corrallo et al. Left ventricular diastolic dysfunction is found in 19.2% of patients; consistent with study done by Hakim et al. Global hypokinesis is seen in 15.4% of patients, consistent with study done by Herskowitz et al. Impairment of LV fractional shortening can be explained by reduction of myocardial contractility. Asymptomatic LV hypokinesis by echocardiography could either represent a mild form of primary cardiac muscle disease that will progress to a clinically evident form of dilatated cardiomyopathy. Pericardial effusion is seen in 11.5% of patients, consistent with study done by Himelman et al. The pericardial effusion is often small and without any haemodynamic consequence. Pericardial effusion in HIV patients may be a marker of end-stage HIV infection, because it is associated with low CD4 count and is often caused by opportunistic infections and malignant neoplasms seen in advanced stages of AIDS. In our study the investigations for identifying the cause of pericardial effusion were not done.

In spite of presence of significant pathology in the heart, overt cardiac manifestations are infrequently seen in AIDS. In a autopsy study done by Lanjewar et al. in India on 52 AIDS patients, 48 patients showed microscopic changes in heart, the most common being myocardial atrophy, but only one patient had clinical presentation of cardiac involvement (pericardial effusion). Involvement of myocardium by Toxoplasma gondii is also seen in AIDS patients. Incidence of Toxoplasma myocarditis in patients dying with AIDS is 8.3% as reported by Sahasarabudhe et al.

Studies have shown that HIV related heart muscle disease is often seen in a state of severe immunosuppression with low CD4 counts (<100 cells/mm³) and poor prognosis. Our results also showed that patients with CD4 count <100/mm³ had a high prevalence of echocardiographic abnormalities than those with CD4 counts > 100/mm³. In addition our results indicate that cardiac involvement in HIV patients is commonly associated with opportunistic infections that occur in later stages of disease. This is in keeping with the findings of De Castro et al. who found a good correlation between opportunistic pathogens and cardiac abnormalities. Absence of endocardial involvement in this study may be related to, that no patient was abusing intravenous drug.

**Conclusion**

Our results indicate that cardiovascular abnormalities in HIV infected patients are more common in the presence of opportunistic infections and can occur without any clinical manifestation. However, cardiac dysfunction occurs late in the course of AIDS and hence it becomes likely that better treatment of opportunistic infections and HIV disease will result in more patients surviving to develop such pathology. Echocardiography is a useful technique for the early recognition and treatment of cardiac dysfunction in such patients. Further clinicopathological studies are required to clarify the role of HIV virus and opportunistic infections in the pathogenesis of cardiac pathology found in HIV infected patients.

**References**