Prevalence of Cardiac Manifestations in HIV Infected Patients Correlating with CD4 Count

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Abstract- HIV affects all the systems of the body which may be due to HIV infection itself or due to opportunistic infections or malignancies. The clinical and pathologic findings in various organ systems including the pulmonary, integumentary, gastrointestinal, hematologic and neurologic systems have been well described. Reports of cardiac abnormalities in HIV and AIDS patients, however, have been less well documented. The cardiovascular diseases in HIV/AIDS are increasing in the developing world. The Present study is to evaluate Cardiac abnormalities in HIV infected adult patients with noninvasive investigations like electrocardiography, echocardiography and correlating with cd4 count.

The cardiac disorders that were identified in our study were diastolic dysfunction (33%), pericardial effusion (12%), systolic dysfunction (9%), pulmonary hypertension (8%), dilated cardiomyopathy (5.5%), mitral regurgitation (3.5%), clot (1%) and vegetation (0.5%).

Index Terms- HIV, echocardiography NACO, (National AIDS control organization), cardiomyopathy, pericardial effusion.

I. INTRODUCTION

According to Global Summary of the AIDS Epidemic / 2013 Number of People living with HIV in 2013, Total 35.0 million; Adults are 31.8 million; women are 16.0 million; Children (< 15 years) are 3.2 million. People newly infected with HIV in 2013, Total 2.1 Million in whom Adults are 1.9 million; Children (< 15 years) are 2,40,000. No of deaths due to AIDS in 2013 are Total 1.5 million; Adults are 1.3 million and Children (< 15 years) 1,90,000.

Infection with human immunodeficiency virus (HIV) is a leading cause of acquired heart disease worldwide and specifically of accelerated atherosclerosis, symptomatic heart failure, and pulmonary arterial hypertension (PAH). Cardiac complications of HIV infection tend to occur late in the disease in those with acquired immunodeficiency syndrome (AIDS) or prolonged viral infection and are therefore becoming more prevalent as longevity improves.

Clinical criteria Cardiac disease was identified clinically as per the standard clinical examination.

Radiological criteria

Standard radiological criteria were used to diagnose the lung disorders and cardiomegaly. The diagnosis of cardiomegaly was considered when the cardiac-to-thoracic width ratio was above 50 percent.

ECG criteria

Standard electrocardiographic criteria were used to detect abnormalities in ECG

Echo Cardiographic criteria

2D echocardiography is an ideal imaging modality for assessing left ventricular (LV) size and function. A qualitative assessment of the ventricular cavity and systolic function can be made directly from the 2D image by experienced observers. 2D echocardiography is useful in the diagnosis of LV hypertrophy and is the imaging modality of choice for the diagnosis of hypertrophic cardiomyopathy. Other chamber sizes are assessed by visual analysis, including the left atrium and right-sided chambers. 2D echocardiography is the imaging modality of choice for the detection of pericardial effusion, which is easily visualized as a black echolucent ovoid structure surrounding the heart.

Echocardiographic Definition dilated Cardiomyopathy

**Diagnostic criteria (or major criteria; both must be present)**

1. LV ejection fraction <45% and/or fractional shortening <25%, diagnosed by echocardiogram, isotopes or ventriculography
2. Left ventricular end-diastolic diameter >117% of the predicted value corrected for age and body surface area, which corresponds to 2 standard deviations from the expected normal limit + 5% (applying Henry's formula)

Echocardiographic Definition of systolic dysfunction

The most common denominator of LV function continues to be the ejection fraction (EF) which is the stroke volume divided by end diastolic volume. The most common method for determining EF is Modified Simpsons method. The value above 50% is considered normal but according to recommendations of American Society of Echocardiography (ASE), a value above 55% is normal, 45% to 54% is mildly abnormal, 30% to 44% moderately abnormal and below 30% severely abnormal.

Echocardiographic definition of diastolic dysfunction
Advanced diastolic dysfunction can lead to isolated diastolic heart failure, now referred to as heart failure with normal ejection fraction (HFNEF).

Diagnosis of HFNEF is based on following criteria:
1) Presence of clinical syndrome of heart failure, 2) Presence of normal ejection fraction (>50%), 3) Presence of diastolic dysfunction, 4) E/E’ (ratio of mitral Doppler E wave velocity to tissue Doppler) 5) early diastolic velocity, i.e. E’ greater than 15:1 indicative of increased LV filling pressure, and 6) Usually non-dilated heart. Echocardiography can confidently assess diastolic functions by evaluating mitral inflow Doppler, tissue Doppler, pulmonary vein, LA volume index etc.

Echo cardiographic diagnosis of pulmonary hyper tension

Common echo cardiographic features of PAH include right atrial enlargement, right ventricular enlargement and dysfunction, small under filled left-sided heart chambers, interventricular septal flattening, tricuspid regurgitation with elevated velocity, and reduced tricuspid annular plane systolic excursion (TAPSE).

All patients were evaluated for their CD4 counts and for the presence of opportunistic infections.

II. MATERIALS AND METHODS

The study was done prospectively from November 2011 to October 2013 at Osmania General Hospital, Hyderabad a tertiary care referral centre. Two hundred patients who were seropositive for HIV infection were selected for this study. Sero positivity was determined by the established NACO guidelines. The ethics clearance was obtained from the appropriate authority appointed by the institution (ethics committee).

Inclusion Criteria
1. All patients, above 18 years who are HIV seropositive by NACO criteria and willing for cardiac evaluation. Both symptomatic and asymptomatic patients were included in the study.
2. Patients below 18 years, with congenital or pre-existing heart disease diagnosed before the diagnosis of HIV infection, HIV positive patients with diabetes or hypertension. Patients on ART were excluded from the study.

Methods
A detailed history, general physical examination and systemic examination was done for each patient with special emphasis on cardiovascular system. Routine investigations done on HIV infected patients were obtained for all the patients. All patients were subjected to non-invasive cardiovascular investigation like chest x-ray, ECG and ECHO. Angiograms were not done due to the cost considerations.

The following features were used to diagnose cardiac conditions.

Clinical criteria, Radiological criteria, ECG criteria, Echocardiographic Criteria

III. RESULTS AND OBSERVATIONS

Mean CD4 count in the study population less than 200 in 129 patients (64.5%), CD4 count between 201-350 in 51 patients (25.5%) and CD4 count more than 350 in 20 patients (10%).

In the study group 134 patients had AIDS (129 patients with CD4 count <200 and 5 patients with CD4 count more than 200 but with AIDS-defining opportunistic illnesses) and 66 patients did not have AIDS.

Components of Cardiac manifestations

<table>
<thead>
<tr>
<th>Cardiac disorder</th>
<th>Clinically detected</th>
<th>Detected by Investigation</th>
<th>Detected by both</th>
<th>Total Number (n=200)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic dysfunction</td>
<td>6</td>
<td>18</td>
<td>6</td>
<td>18</td>
<td>9.0</td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td>0</td>
<td>66</td>
<td>0</td>
<td>66</td>
<td>33</td>
</tr>
<tr>
<td>Mitral Regurgitation</td>
<td>4</td>
<td>7</td>
<td>4</td>
<td>7</td>
<td>3.5</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>1</td>
<td>24</td>
<td>1</td>
<td>24</td>
<td>12.0</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>6</td>
<td>11</td>
<td>6</td>
<td>11</td>
<td>5.5</td>
</tr>
<tr>
<td>Hypertrophic Cardiomyopathy</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>0</td>
<td>16</td>
<td>0</td>
<td>16</td>
<td>8.0</td>
</tr>
<tr>
<td>Clot</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td>Vegetation</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

ECG AND X- RAY findings

<table>
<thead>
<tr>
<th>ECG Findings</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>160</td>
<td>80</td>
</tr>
</tbody>
</table>
ECG findings

80 percent of our patients had normal ECG. Commonest abnormalities were Sinus Tachycardia (16%), Low voltage complexes (0.5%), IHD changes (3%), LVH (0.5%).

Of the clinical and biochemical parameters low hemoglobin level is significantly associated with the presence of the cardiac disorders.

<table>
<thead>
<tr>
<th>CD4 Counts</th>
<th>Total number of patients</th>
<th>Pericardial effusion</th>
<th>Pulmonary HTN</th>
<th>Cardiomyopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 200</td>
<td>129 (64.5%)</td>
<td>21 (16.3%)</td>
<td>9 (56.25%)</td>
<td>10 (7.8%)</td>
</tr>
<tr>
<td>201 – 350</td>
<td>51 (25.5%)</td>
<td>2 (3.9%)</td>
<td>6 (37.5%)</td>
<td>2 (3.9%)</td>
</tr>
<tr>
<td>&gt; 350</td>
<td>20 (10%)</td>
<td>1 (5%)</td>
<td>1 (6.25%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>24</td>
<td></td>
<td>16</td>
</tr>
</tbody>
</table>

IV. DISCUSSION

Prevalence of cardiac involvement in HIV disease varies from 5% to 50% but symptomatic involvement occurs in 5% to 7% of patients only. Most common clinically significant cardiac abnormality due to direct HIV infection is HIV-associated dilated cardiomyopathy. There is evidence of myocarditis and HIV has been isolated from myocardial cells. Diagnosis can be supported by chest radiograph and electrocardiogram and confirmed by echocardiography and elevated serum NTproBNP. CD4+ count in these patients is generally >200/cumm. HIV associated cardiomyopathy has poor prognosis. Other findings on echocardiography may be diastolic dysfunction, pericardial effusion, right ventricular hypertrophy, pulmonary arterial hypertension and non-bacterial thrombotic endocarditis.

In HIV-infected patients, concurrent pulmonary infections, pulmonary hypertension, anemia, portal hypertension, malnutrition, or malignancy can alter or confuse the characteristic signs that define heart failure in other populations. Thus patients with LV systolic dysfunction can be asymptomatic or have New York Heart Association Class III or IV heart failure.

Echocardiography is useful for assessing LV systolic function in these patients and, in addition to diagnosing LV dysfunction, often reveals either low to normal wall thickness or LV hypertrophy and dilation, as well as left atrial dilation. Dilated cardiomyopathy can be related to the direct action of HIV on myocardial tissue or to proteolytic enzymes or cytokine mediators induced by HIV alone or in conjunction with co-infecting viruses. Diastolic dysfunction is common in long-term survivors of HIV infection. Such dysfunction may precede systolic dysfunction and signal an early manifestation of HIV-associated cardiac disease.

Pulmonary Hypertension is rare in the general population, occurring in approximately 0.5% of HIV-infected patients. Its prevalence has not changed with the introduction of HAART. Before the HAART era, pericardial effusions occurred in up to 11% of patients with AIDS. The prevalence reaches a mean of approximately 22% in asymptomatic patients after 25 months. Cardiac abnormalities associated with HIV infection include premature myocardial infarction (MI) or stroke, pericardial effusion, lymphocytic interstitial myocarditis, dilated cardiomyopathy (frequently with myocarditis), left ventricular (LV) diastolic dysfunction, infective endocarditis, and malignancy (myocardial Kaposi sarcoma and B-cell immunoblastic lymphoma). Symptomatic cardiac disease was present in patients with AIDS (CD4 count less than 200).

Most common opportunistic infection tuberculosis found in n=41, cryptococcal meningitis in n=6, candidial infections in n=4 CMV retinitis in n=2, chronic diarrhea in n=3 pneumocystic jirovecii pneumonia in n=2 and Herpes Zoster in 2 patients.

V. CONCLUSIONS

In our study Male to Female ratio 1.7:1. Most patients are in the younger age group. Only 1% of the patients were above 60 years. Prevalence of cardiac involvement was 48%. Only 5.5% patients were symptomatic. Mean CD4 count is significantly lower in patients with cardiac disorder than in patients without cardiac disorder. Lower CD4 count was significantly associated with the presence of pericardial effusion. 20% of patients had ECG abnormalities from sinus tachycardia 16%, IHD 3%, LVH and low voltage complex 0.5%. Of the noninvasive investigations 24.5% had chest x-ray abnormalities commonest being pulmonary tuberculosis 9%, cardiomegaly 6.5%, pneumonia 5% and pleural effusion 3%. The cardiac disorders that were identified by 2D Echo in our study were diastolic dysfunction (33%), pericardial effusion (12%), systolic dysfunction (9%), pulmonary hypertension (8%), dilated cardiomyopathy (5.5%), mitral regurgitation (3.5%), clot (1%) and vegetation (0.5%). Cardiac disorders in HIV patients are common, only small percentage are symptomatic and non invasive investigation like Echo cardiology is helpful in early diagnosis of asymptomatic cardiac disorders.
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