ABSTRACT

Objective: To determine cardiovascular disease in different stages of HIV/AIDS and its associated risk factors in HIV-infected individuals. Methods: A observational study conducted with cardiovascular diseases at baseline. The information included data on HIV infection at various stages, echocardiography, demographic values, cumulative incidence and statistical significance. Results: The relative risk of cardiovascular disease was found to be 1.61 [95% confidence interval (CI) 1.43–1.81] among people living with HIV (PLHIV) without antiretroviral therapy (ART) compared with HIV-uninfected people and the relative risk was identified as 2.00 (95% CI 1.70–2.37) among PLHIV on ART compared with HIV-uninfected people. There was a positive correlation between low CD4 count and echocardiographic abnormalities. Other occurrences such as cardiomyopathy, pericardial effusion, and pulmonary hypertension were also noted. Conclusion: In conclusion, it is clear that cardiovascular complications are highly seen in HIV-infected patients and are increasing with the increase of the stages of HIV. PLHIV exhibit multiple known risk factors for cardiovascular disease.

KEYWORDS Cardiovascular disease, CD4 count, HIV, AIDS and risk factors.

Introduction

Acquired immunodeficiency syndrome (AIDS) is a chronic, life-threatening disease caused by the human immunodeficiency virus (HIV), which leads the patient to multiple opportunistic infections, malignant neoplasms, and progressive dysfunction of multiple organ systems. [1,2] Globally, 38 million people were living with HIV in 2018, with over half residing in Eastern and Southern Africa. Although highly active antiretroviral therapy (HAART) has emerged, which increased the survival rate of patients with HIV but sometimes severe treatment-associated metabolic side effects with this therapy are now developing the cardiovascular abnormalities in those individuals and are the immediate cause of death in some. [3-5] Cardiovascular disease (CVD) is a general term for diseases related to the heart and its respective blood vessels since it is being the number one cause of death worldwide. It is estimated that globally death by CVD will increase from 16.7 million in 2002 to 23.9 million by 2030. [6-10]

Due to the increased survival rate in HIV patients, they are at high risk of developing cardiac diseases, including coronary atherosclerosis, Dilated cardiomyopathy, Pericardial effusion, Human immunodeficiency virus-associated pulmonary hypertension, Endocarditis, Thrombosis, Embolism, left ventricular dysfunction myocarditis, coronary artery disease and drug-related cardiotoxicity, Vasculitis, Aneurysm, pulmonary hypertension, Cardiac involvement in AIDS-related tumours. The prevalence of cardiac involvement in AIDS patients has been reported to range between 28% and 73%. [11-15] Increased risk of HIV was connected with traditional CVD risk factors such as alcohol consumption, smoking, lesser physical activity, unhealthy diets, hypertension and diabetes in high-income countries. Anecdotal case evidence exists, but the patients with conspicuous impairment of cardiac manifestations have a poor prognosis. However, this needs to be confirmed by a larger survival study. [16-20]

In the present study, our aim was to determine cardiovascular disease in different stages of HIV/AIDS and its associated risk factors in HIV-infected individuals.
Table 1 Association of 2D echocardiographic findings with clinical staging according to WHO

<table>
<thead>
<tr>
<th>Cardiac manifestations</th>
<th>Clinical staging of HIV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
</tr>
<tr>
<td>Reduced ejection fraction (&lt;50%)</td>
<td>0</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>0</td>
</tr>
<tr>
<td>Pericardial effusions</td>
<td>0</td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Fractional shortening (&lt;30%)</td>
<td>2</td>
</tr>
<tr>
<td>Valvular regurgitations</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2 Cardiac dysfunction and their correlation demonstrating mean pattern of study parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group with echo findings Mean ± sd (n = 39)</th>
<th>Group without echo findings Mean ± sd (n = 31)</th>
<th>Statistical significance &quot;p&quot; value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>8.74 ± 2.008</td>
<td>8.49 ± 2.7</td>
<td>0.8421 (ns)</td>
</tr>
<tr>
<td>CD4 count/microL</td>
<td>101 ± 111</td>
<td>338.6 ± 206.4</td>
<td>&lt;0.0001 (s)</td>
</tr>
<tr>
<td>Total leukocyte count</td>
<td>7788.2 ± 2872.2</td>
<td>7652.6 ± 2471.8</td>
<td>0.836 (ns)</td>
</tr>
</tbody>
</table>

Materials and Methods

A clinical and observational study was conducted with patients having HIV. All patients being positive after the ELISA test and diagnosed with HIV infection/AIDS after ELISA were also included in the study. The exclusion criteria included patients with severe heart disease, i.e., congenital disease, rheumatic heart disease etc. The patients included were examined thoroughly, including patient history and clinical examination. Also, patients who had received ART were included in the study. CD4 count was identified in all patients using the flowcytometry technique. M Mode and Two-dimensional transthoracic echocardiography and colour flow doppler examination observe patients’ cardiac stability. CVD comprised stroke, myocardial infarction, ischaemic heart disease, coronary heart disease, and congestive heart failure as recorded on patient medical charts. The presence of cardiac abnormalities such as pericardial effusion and valve regurgitation was evaluated.

Statistical analysis

The prevalence of risk factors associated with HIV and cardiovascular diseases has been calculated. Statistical analysis was done using chi-square, PLINK, R, SAS version 9.2 (SAS Corporation, Cary, NC) and Stata version 12.0 (StataCorp LP, College Station, TX). In addition, multi-variable logistic regression was performed to identify parameters independently associated with the presence of CVD risk factors.

Results

All the patients were analysed for the CD4 count, cardiac stability, stage of the disease and the inclusion of their ART status. The patients included were classified according to WHO clinical staging of HIV/AIDS. The relative risk of cardiovascular disease was found to be 1.61 [95% confidence interval (CI) 1.43-1.81] among people living with HIV (PLHIV) without antiretroviral therapy (ART) compared with HIV-uninfected people, and the relative risk was identified as 2.00 (95% CI 1.70-2.37) among PLHIV on ART compared with HIV-uninfected people. There was a positive correlation between low CD4 count and echocardiographic abnormalities. Other occurrences such as cardiomyopathy, pericardial effusion, and pulmonary hypertension were also noted. A higher number of cases with diastolic dysfunction, pericardial effusions and pulmonary hypertension had CD4+ count <50.

Discussion

In our study cause of death due to cardiac abnormalities in HIV patients is most common. The increase in rates of immune suppression in HIV-infected groups persuades them to an increased inflammatory risk and cardiovascular disease. Cardiac manifestations are found to be 22% among HIV patients. The cardiac manifestations were higher in males (23.17%) compared to females (16.66%). Smoking addiction is well-established and is being a modifiable risk factor of cardiovascular abnormalities, with significantly higher prevalence rates in HIV-infected patients compared to the other risk factors of the general population. In addition, the preponderance of hypertension is identified to rise as the age of PLWH increases.

Comparing various cardiac manifestations, the most common one is dilated cardiomyopathy (22.72%), followed by pericardial effusion (18.18%). Incidence of other abnormalities includes coronary artery disease (13.63%), pulmonary hypertension (13.63%), left ventricular hypertrophy (9.09%), diastolic dysfunction 4.54%, another valvular heart disease 4.54%, pulmonary thromboembolism 4.54% and mediastinal mass (4.54%) was observed. Comparing different stages of HIV, a higher risk is associated with stage 4 (27.27%), followed by stage 3 (18%). This estimates that the increase in cardiovascular abnormalities increases as the disease stage increases. The incidence of pericardial effusion (75%) and cardiomyopathy (100%) is higher in stage 4. The present study noted that almost all manifestations occur when there is a lower CD4 count. Likewise, the instant reduction in the CD4+ count, i.e., CD4+ T-cell depletion during untreated HIV infec-
tion, can prolong, despite subsequent ART-induced viral defeat. For example, constant depletion of gut-associated lymphoid tissue occurs during acute infection, which never fully heals even with continuous treatment. The main risk factors for this cardiac disorder are alcohol consumption and smoking. The majority of subjects stated ART with lower CD4 counts, similar to other studies by Bijker et al.[4], Rotger et al.[6] and Sarah et al. [9].

The HIV-infected population corresponds to a vulnerable group of individuals facing challenges in systematic barriers, including economic and structural barriers to access services in healthcare. In general, HIV-infected women had higher risks and maximum rates of total cardiovascular disease compared to healthy and uninfected women as compared to uninfected women, Framingham risk factors, after adjustment for demographic characteristics and substance to use and abuse. Our results also coincide with previous studies reporting that HIV infection is defined as an independent risk factor for cardiovascular abnormalities in men, suggesting that increased cardiovascular manifestations in HIV infection is associated regardless of gender. Previous studies have demonstrated that cardiac manifestations in relation to HIV are often seen in a stage of severe immunosuppression with less CD4 Count (CD4+ < 200/microL) [18,20]. This study also observed that HIV patients with CD4+ count less than 200/microL (CD4+ < 200/microL) had a higher prevalence of echocardiographic abnormalities than those with CD4+ count more than 200/microL (CD4+ > 200/microL). It was clear that echocardiographic abnormalities were usually seen in HIV individuals. The present study reported it to 55%, while it slightly differed from other researchers. Diabetes mellitus also plays an important role in the cardiac abnormalities of HIV population, which was consistent with the study done by Kayya et al. [1]

However, quantitative M-mode and two dimensions were estimated to view the cardiac abnormalities as shown by Her skowitz et al. [14,15]. Antiretroviral therapy [ART] helps suppress HIV, but the side effects may result in cardiac abnormalities. Our present study showed the differences between the patient receiving the ART treatment and one more population without ART treatment. Establishing diagnostic criteria for HIV-associated heart failure should be a high priority. Diagnostic criteria should consider the degree of immunosuppression and stage of HIV because causes of HIV-associated heart failure likely vary depending on HIV clinical stage. This was similar to the study by Bloomfield et al. [18]. The observation of cardiac abnormalities in the HIV population should not be ignored. Hence, a keen understanding of cardiac manifestations in HIV infected patients should be taken care of, and proper diagnostic and therapeutic treatment. To reduce the discrepancy in the care of cardiovascular disease in people living with HIV, the medical technologies must be comprehensively addressed, with persistent monitoring of health outcomes. This will result in the improvement of cardiovascular disease-related outcomes and reduce the danger in the people living with HIV population.

Conclusion

HIV and AIDS always remain a growing challenge to both infected patients and healthcare providers in providing the right point of cure and support to ensure the best possible patient outcome. In India, HIV infection is transmitted more easily through heterosexual contact than other modes of transmission in other populated countries. The most common cardiac manifestations are generally associated with a reduction in ejection fraction, pericardial effusions, left fractional ventricular shortening, diastolic dysfunction and dilated cardiomyopathy. Since they are linked with low CD4+ count and occur in an advanced higher stage of the HIV disease, especially in Stage 4. The study concludes that cardiovascular abnormalities are now more common in HIV infected population. Since the new techniques help in increasing the survival rate of HIV patients, cardiovascular complications are also increasing. The increase in cardiovascular abnormalities increases as the disease stage increases. Echocardiography is the most useful technique for the early assessment and treatment of cardiac dysfunction in such individuals. Diabetes and systematic hypertension are other risk factors that further increase cardiac disease risk. Reducing the traditional risk factors can help prevent cardiovascular disease in HIV-infected patients. Measures should be observed and implemented to reduce the risk of cardiovascular abnormalities, such as smoking cessation programs, improved diet and increased exercise targeted at subjects with HIV. Early assessment and recognition are also needed to prevent significant morbidity from cardiac disorders. Further, larger assessment studies are needed to clarify the role of the HIV virus and opportunistic infections in the pathogenesis of cardiac pathology found in HIV-infected patients. Clinicians can also take action in the existing general risk stratification algorithms, such as the Framingham risk score, to identify the cardiac-associated risk in HIV patients.

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Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

References


8. HIV Infection and Cardiovascular Disease in Women


