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Original Research Article

Evaluation of cardiac abnormalities in HIV patients and its relation with WHO staging, duration of infection and opportunistic infections

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Abstract: Infection with the human immunodeficiency virus (HIV) is one of the leading causes of acquired heart disease. Cardiac complications of HIV infection tend to occur late in the disease and associated with related therapies. Therefore becoming more prevalent as therapy and longevity improve. The main Aim of the Study is to assess the cardiac abnormalities in HIV patients and its relation with WHO staging, duration of HIV infection and opportunistic infections. We had study population of 150 HIV patients who were divided into two groups depending on the CD4 count. Group I included 51 (34%) patients with CD4 count ≤ 350 cells/mm^3 and Group II included 99 (66%) patients with CD4 count > 350 cells/mm^3. Among them 62 (41.3%) were males and 88 (58.7%) were females. Study population were divided according to the WHO stages 1,2,3,4 and found to be 50%, 28%, 20% and 2% respectively. All patients underwent clinical examination, chest X-ray, ECG, and 2D echocardiography. Cardiologic data were correlated with WHO staging, duration of HIV infection and opportunistic infections. In results in our study population, mean age was 30.87± 6 years and mean duration of HIV infection was 3.18 years. Twenty three patients (15.3%) had opportunistic infections and Oral candidiasis was the most common. Prevalence of cardiac abnormalities was 16.7% in our study. Low voltage complex and pericardial effusion were the most common ECG and echo abnormalities respectively. In conclusion Cardiac abnormalities were specifically correlated with WHO staging, duration of HIV infection and opportunistic infections.
Keywords: HIV infection, Cardiac abnormality, WHO staging, opportunistic infection

INTRODUCTION:

HIV infection/AIDS is a global pandemic, with cases reported from every country. 95% of people living with HIV/AIDS reside in low- and middle-income countries. Cardiovascular disease may be associated with classic risk factors such as smoking, a direct consequence of HIV infection, or a complication of HAART. Patients with HIV infection have higher levels of triglycerides, lower levels of high-density lipoprotein cholesterol. The finding that the rate of cardiovascular disease events was lower in patients on antiretroviral therapy identified a clear association between HIV replication and risk of cardiovascular disease. In developed countries, most common form of heart disease is coronary heart disease [1]. Cardiovascular problems associated with advanced immunodeficiency, such as heart muscle disease, pericardial effusion and pulmonary hypertension; continue to predominate in resource-poor countries [2].

MATERIALS AND METHODS:

This cross sectional study was conducted from January 2008 to June 2008 in the Department of Medicine along with ART Centre and Department of cardiology, Kilpauk Medical College and Hospital, Chennai, Tamilnadu. Total of 150 HIV patients were selected after excluding 50 patients. Among them 62 (41.3%) were males and 88 (58.7%) were females .They were divided into two groups depending on the CD4 count. Group I included 51 (34%) patients with CD4 count ≤ 350 cells / mm^3. Group II included 99 (66%) patients with CD4 count > 350 cells / mm^3.Majority of the HIV patients in South Indian population with CD4 counts of 200 - 350 cells / mm^3 have high viral road than North Indian and Western counter parts. [3]Patients were distributed as per WHO staging 1, 2, 3 and 4.

Inclusion criteria

Patients who have been diagnosed as HIV positive by ELISA method

Exclusion criteria

1. Age less than 18 years and more than 55 years
2. Treatment with anti-retroviral drugs or any cardio toxic drugs
3. Diabetes
4. Hypertension
5. Previous congenital or acquired heart disease
6. Neoplastic diseases
7. Family history of cardiovascular diseases
8. Patients having lipid profile abnormalities.

Clinical examination focused in the study:

All patients were meticulously examined for the presence of anemia, jaundice, cyanosis, clubbing, pedal edema, dyspnea, generalized lymphadenopathy and skin and mucous membrane lesions. Respiratory rate, pulse rate, jugular venous pressure, blood pressure (both in supine and erect posture) were also recorded. A thorough clinical examination of the cardiovascular system, respiratory system, abdomen and central nervous system was done. Patients were distributed as per WHO staging 1, 2, 3 and 4.

Laboratory investigations: (CD4 Count Assay)

The standard method for enumerating CD4 T cells, a flow cytometer was used. Computer calculates the number of CD4 T cells by analyzing the size of the cell and which of the antibodies it has been tagged with. The overall process is called Fluorescence Activated Cell Sorting (FACS). A standard 12 lead resting electrocardiograms and chest skiagram were taken for all individuals in this study. Two dimensional echocardiography was done for all patients.

Statistical analysis:

Statistical analysis was done by using windows SPSS software (version 11.5). Chi square test was applied for significance. "P.values less than 0.05 were considered as significant.

Table: 1 Analysis of Study Population

	GROUP I CD 4 COUNT ≤350 Cells/mm^3	GROUP II CD4 COUNT >350 Cells/mm^3	TOTAL
Number of patients	51 (34%)	99 (66%)	150
Male/female	30/21	32/67	62/88
Mean age (years)	31.43±6.23	30.58±6.06	30.87±6.11
Mean duration of infection (years)	2.95	3.3	3.18
Mean CD4 count (cells/mm^3)	261.08±83.25	582.69±191.24	473.34±223.20
WHO STAGE 1,2,3,4 (number of patients)	16,15,17,3	59,27,13,0	
OPPORTUNISTIC INFECTIONS			
Oral candidiasis	9	4	13
Tuberculosis	4	2	6
Herpes zoster	2	2	4
ECG ABNORMALITIES			
Low voltage complex	5	1	6
Poor progression of 'R' wave	3	1	4
Atrial ectopy	1	2	3
ST/T abnormality	2	1	3
Sinus tachycardia	-	2	2
Ventricular ectopy	2	-	2
Conduction abnormality	-	2 (RBBB)	2
ECHO ABNORMALITIES			
Pericardial effusion	7	2	9
Dilated cardiomyopathy	4	1	5
Septal hypokinesia	1	-	1
Infective endocarditis	1	-	1

Table 2: cardiac abnormalities

CARDIAC ABNORMALITIES	GROUP I	GROUP II	TOTAL
PRESENT	16 (10.7%)	9 (6%)	25 (16.7%)
ABSENT	35 (23.3%)	90 (60%)	125 (83.3%)
TOTAL	51 (34%)	99 (66%)	150 (100%)

Out of 150 patients 25 patients had cardiac abnormalities.

Table: 3 WHO staging in relation to cardiac abnormalities

WHO STAGING	GROUP I			GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
STAGE 1	3 (5.9%)	13 (25.5%)	16 (31.4%)	4 (4%)	55 (55.6%)	59 (59.6%)
STAGE 2	3 (5.9%)	12 (23.5%)	15 (29.4%)	2 (2%)	25 (25.3%)	27 (27.3%)
STAGE 3	7 (13.7%)	10 (19.6%)	17 (33.3%)	3 (3%)	10 (10.1%)	13 (13.1%)
STAGE 4	3 (5.9%)	0 (0%)	3 (5.9%)	0 (0%)	0 (0%)	0 (0%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.024 P value for Group II was 0.169

There was a statistically significant difference noted between WHO staging and cardiac abnormalities in Group I ($P < 0.05$) in contrast to Group II ($P > 0.05$) which was insignificant.

Table: 4 Duration of HIV Infection In Relation To Cardiac Abnormalities

DURATION OF HIV	GROUP I			GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
< 1 year	3 (5.9%)	7 (13.7%)	10 (19.%)	1 (1%)	8 (8.1%)	9 (9.1%)
1- 3 years	4 (7.8%)	26 (51%)	30 (58.8%)	1 (1%)	68 (68.7%)	69 (9.7%)
>3 years	9 (17.6%)	2 (3.9%)	11 (21.6%)	7 (7.1%)	14 (14.1%)	21 (21.2%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.0001 P value for Group II was 0.000

There was a statistically significant increase in cardiac abnormalities observed as the duration of HIV infection increases in both the groups ($P < 0.05$).

Table: 5 opportunistic infections in relation to cardiac abnormalities

OPPORTUNISTIC INFECTIONS	GROUP I			GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
PRESENT	8 (15.7%)	7 (13.7%)	15 (29.4%)	2 (2%)	6 (6.1%)	8 (8.1%)
ABSENT	8 (15.7%)	28 (54.9%)	36 (70.6%)	7 (7.1%)	84 (84.8%)	91 (91.9%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.029 P value for Group II was 0.103

There was a statistically significant correlation noted between opportunistic infections and cardiac abnormalities in Group I ($P < 0.05$) in contrast to Group II ($P > 0.05$) which was insignificant.

DISCUSSION

Some form of heart disease is demonstrable at autopsy in approximately 40 percent of cases and by echocardiography in approximately 25 percent of patients with AIDS. Many of these lesions are mild, and HIV-related heart disease probably causes symptoms in less than 10 percent and death in less than 2 percent of all patients with HIV infection. [4].

CARDIAC ABNORMALITIES:

In our study, among 150 patients25 patients (16.7%) had cardiac abnormalities either in the form of ECG or Echocardiography abnormality or combination of both. In Group I, sixteen patients out of 51 patients (31.4%) and in Group II, nine patients out of 99 (9.09%) had cardiac abnormalities.ECG abnormalities were low voltage complex, poor progression of R wave, right bundle branch block, ST- T changes, atrial and ventricular ectopy and sinus tachycardia. Echo abnormalities were pericardial effusion, dilated cardiomyopathy, septal hypokinesia and infective endocarditis.

WHO STAGING:

In our study, 50% of patients were in stage 1, 28% were in stage 2, 20% in stage 3 and 2% in stage 4. In Group I, out of 16 patients with cardiac abnormalities, 3 patients were each in stage 1,2,4 and 7 patients were in stage 3.P value was 0.024, statistically significant. In Group II, 9 patients with cardiac abnormalities were distributed as 4,2,3 in stage 1,2,3 respectively. P value was 0.169, statistically insignificant. Nirdesh *et al.;* study conducted in lucknow had 52 patients in stage 4 and 48 patients in stage 1,2,3. There was no correlation between who staging and cardiac involvement[5]. In Niakara *et al.;* study 36 (90%) patients were in CDC stage C AIDS, 3 (7.5%) in stage B and one (2.5%) in stage A[6]. In EL Hattaoui M *et al* study, significant correlation was found between HIV staging and cardiomyopathy[7]. SP Raffanti *et al.;* study showed no correlation between LV dysfunction and CDC classification [8]. Caggese L study found no correlation between CDC staging and cardiac abnormality[9]. Ayaskanasingh *et al.;* study conducted in India, in which patients were distributed in clinical stage 4 (40%) followed by Clinical stage 3 (35.7%), Clinical stage 2 (14.3%) and only 10% of cases in Stage 1. Maximum number of echocardiographic abnormalities was seen in WHO clinical stage IV [10].

Duration of HIV infection:

In this study, 66% (99/150) of patients had duration of illness between 1 -3 years. 12.7% (19/150) had less than a year and 21.3% (32/150) had duration of more than 3 years. The duration of illness ranged from 3 months to 9.5 years. Mean duration of illness in study population (150 patients) was 3.18 years. Mean duration of illness in Group I and Group II were 2.95 years and 3.3 years respectively. In Group I, among 16 patients with cardiac abnormalities, 9 patients had a duration of > 3 years, 4 patients had a duration of 1 -3 years and 3 patients had duration of less than a year. P value was 0.00015, statistically significant. In Group II, among 9 patients with cardiac abnormalities 7 patients had a duration of > 3 years, 1 patient had a duration of 1 -3 years and 1 patient had a duration of less than a year. P value was 0.000, statistically significant. There was a significant correlation between duration of HIV infection and cardiac abnormalities.In a study by P Kannan et *al.;*, the duration of illness ranged from 6 months to 7 years.[11].

Opportunistic infections:

Depletion in CD4 cells renders the body susceptible to opportunistic infections. The predominant opportunist infections seen in HIV disease are intracellular parasites (e.g., Mycobacterium tuberculosis) or pathogens susceptible to cell-mediated rather than antibody-mediated immune responses. Autopsy has confirmed a variety of opportunistic

infections of the myocardium in patients with AIDS. Infectious agents included Toxoplasma gondii in the hearts of adults and children, Cryptococcus species, Cytomegalovirus, Candida species, Pneumocystis carinii, Microsporidium, Histoplasma capsulatum, atypical mycobacteria, and Aspergillus organisms involving the myocardium. Despite this, a clear etiologic link between opportunistic infection and myocarditis in AIDS has yet to be established.

In our study 23 patients (15.4%) had opportunistic infections. Oral candidiasis was the most common (8.7%) followed by tuberculosis (4%) and herpes zoster (2.7%). Candidal infection indicates fairly advanced immunologic decline and occur in patients with CD4+ T cell counts of <300/L. Tuberculosis is the primary cause of death for 10–15% of HIV patients. Herpes zoster (shingles) is seen in 10–20% of patients with HIV infection. Varicella-zoster virus reactivation indicates a modest decline in immune function and may be the first indication of clinical immunodeficiency. In Group I, out of 16 patients with cardiac abnormalities, 8 patients had opportunistic infections. P value was 0.029, statistically significant. In Group II, out of 9 patients with cardiac abnormalities, 2 patients had opportunistic infections. P value was 0.103, statistically insignificant. So fall in CD4 count proportionally increases the predisposition to both opportunistic infections and cardiac abnormalities [11]. In Nirdesh *et al.;* study 25% had opportunistic infections and tuberculosis was the most common opportunistic infection. There was no relation between opportunistic infections and cardiac involvement [5]. In a study by De castro *et al.;* 72 patients (63%) had opportunistic infections or secondary malignancies. 45.6% had cardiac involvement presumably due to opportunistic infections and secondary malignancy [12]. Jose Silva Cardosa *et al.;* study showed significant correlation between opportunistic infections and congestive heart failure [13]. In Caggese L *et al.;* study, no correlation was found between opportunistic infections and cardiac abnormalities [9]. B longo *et al.;* study found out that onset cardiac involvement was protective against opportunistic infections [14]. In Mirri *et al.;* study, end diastolic left ventricular dimension was significantly higher in patients without opportunistic infections [15].

CONCLUSION:

In this study we found out that cardiac abnormalities and opportunistic infection increases in proportion with duration of HIV infection and WHO staging. Cardiac involvement impacts on the natural history and prognosis of the HIV disease and vice versa. This demands an awareness of cardiovascular manifestations by clinicians for a complete and rational diagnosis and management.

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