Original Research Article

A study on cardiac abnormalities in HIV patients and its relation with CD4 count and risk factors

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Abstract

Background: From the beginning of the AIDS epidemic, it was recognized first at autopsy and later by non-invasive techniques that HIV infection can cause cardiac abnormalities.
Aim of the study: To assess the cardiac abnormalities in HIV patients and its relation with CD4 count and risk factors.
Materials and methods: A total of 150 patients were divided into two groups depending on the CD4 count. Group I included 51 (34%) patients with CD4 count ≤ 350 cells / mm3 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. All patients were subjected to a questionnaire to assess the risks of acquiring HIV, risk factors for cardiac disease. A thorough clinical examination was done. BMI was calculated as per WHO criteria for Asian population.CD4 count, ECG, Echocardiogram were done for all patients. Cardiologic data were correlated with age, sex, BMI, alcohol, smoking and CD4 count.
Results: Our study populations mean age was 30.87± 6 years and mean BMI was 20.40 ±3.89 kg/m^2. Mean CD4 count was 473.34 ± 223.20 cell/mm^3 (Group I - 261.08 ± 83.75 cells/mm^3; Group II - 582.69 ± 191.24 cells/mm^3). Smokers and alcoholics constituted 7.3% (11 patients) and 8% (12 patients) respectively.Heterosexual was the most common (95.3%) route of infection. Prevalence of cardiac abnormality was 16.7%. Pericardial effusion was the most common abnormality.
Conclusion: Cardiac abnormalities were specifically correlated with CD4 count. There was no correlation between age, sex, BMI, smoking and alcohol with cardiac abnormalities.

Key words

HIV infection, Cardiac abnormality, ECG, Echocardiogram.

Introduction

Total PLHIV in India is estimated at 20.88 lakh (17.20 lakh-25.30 lakh) in 2011, of whom children < 15 years account for 7% (1.45 lakh) of all infections and 39% (8.16 lakh) are among women. India is estimated to have around 1.16 lakh (0.72–1.99 lakh) annual new HIV infections among adults (15 years and above) around 14,500 (10,974–19,346) new HIV infections among children. In Tamil Nadu, PLHIV estimated at 1.6 lakhs in 2011. Prevalence of HIV infection in adults is 0.34% (male -0.39%, females -0.18%) [1].

HIV/AIDS is a multi-systemic disease, affecting virtually every organ and system of the body, and causing progressive dysfunction [2]. It is an established fact that the heart is not spared in the exploits of this rampaging entity. Human immunodeficiency virus (HIV) possesses an intrinsic cardiopathogenic action that may be detected in even the early stages of HIV disease. Incidence of AIDS-related heart disease found in post-mortem studies is significantly higher than the incidence of abnormalities diagnosed clinically ante mortem [3]. Therefore it is possible that many AIDS patients have cardiac abnormalities that are not recognized during the course of their illness.

Materials and methods

The study was conducted in the Department of Medicine, along with ART Centre and Department of Cardiology at Kilpauk Medical College and Hospital Chennai, Tamil Nadu; from January 2008 to June 2008. A total of 150 patients were chosen after excluding 50 patients. Patients who have been diagnosed as HIV positive by ELISA method were included in the study after getting informed consent. Those who are having age less than 18 years and more than 55 years, treatment with anti-retroviral drugs or any cardio toxic drugs, diabetes, hypertension, previous congenital or acquired heart disease, neoplastic diseases, family history of cardiovascular diseases and lipid profile abnormalities were excluded from the study. Among them 62 were males and 88 were females. They were divided into two groups depending on the CD4 count. Group I included 51 patients with CD4 count $\leq$ 350 cells/mm^3. Group II included 99 patients with CD4 count > 350 cells/mm^3. Majority of South Indian HIV patients with CD4 counts of 200 - 350 cells/mm^3 have high viral road than North Indian and Western counter parts [4].

Clinical examination

All patients were meticulously examined for the presence of anemia, cyanosis, clubbing, pedal edema, dyspnea, jaundice, 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. BMI was calculated as per WHO criteria for Asian population. A thorough clinical examination of the cardiovascular system, respiratory system, abdomen and central nervous system was done.

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" value less than 0.05 was considered as significant.

Results

Study population analysis was as per **Table – 1**. Prevalence of cardiac abnormalities increased with decline in CD4 count (P <0.05) as per **Table - 2**. There was no statistically significant difference noted between age and cardiac abnormalities in both the groups (P > 0.05) as per **Table – 3.** There was no statistically significant difference noted between sex and cardiac abnormalities in both the groups (P > 0.05) as per **Table - 4**. There was statistically no significant difference noted between BMI and cardiac abnormalities in both the Groups (P > 0.05) as per **Table - 5**. There was no significant relation between smoking and cardiac abnormalities in both the groups (P > 0.05) as per **Table - 6**. Statistically significant difference not noted between alcohol and cardiac abnormalities in both the groups (P > 0.05) as per **Table - 7**.

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
Mean BMI (kg/m^2)	19.85 ± 4.01	20.68 ± 3.82	20.40 ± 3.89
Smoker/Alcoholic (No of patients)	4/7	7/5	11/12
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
Septalhypokinesia	1	-	1
Infective endocarditis	1	-	1

Table – 2: Cardiac abnormalities in relation to CD4 count.

Cardiac abnormality	**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%)

P value was 0.001 (statistically significant).

Discussion

Cardiovascular abnormalities are common in HIV-infected patients, although they are often clinically quiescent and frequently attributed to dysfunction in other organ systems [5]. In an autopsy study carried out in 1998, cardiac abnormalities were noted in two-thirds of the

patients with AIDS [6]. These abnormalities, which were attributed directly or indirectly to the HIV virus and/or treatment side effects, could largely have been detected early ante mortem using echocardiography, a non-invasive, radiation-free investigation. Echocardiographic assessment of HIV patients is extremely useful to identify those cardiac conditions: pericardial effusion, left ventricular (LV) systolic dysfunction/heart muscle disease and intra cardiac masses, appearance of the right ventricle, provide an indirect assessment of pulmonary pressures, and detect regional wall-motion abnormalities suggestive of coronary artery disease. ECG abnormalities and rhythm disturbances are not uncommon findings in HIV-positive patients with myocarditis or heart muscle disease, and ectopic beats, ventricular tachycardia, and sudden death have all been reported. These can be secondary to other cardiac pathology, or be a consequence of some forms of treatment. Conduction abnormalities and arrhythmias have been demonstrated in HIV-positive children with ECG abnormalities, possibly related to small vessel vasculitis, neural tissue fibrosis, or myocarditis [7].

Table – 3: Age distribution in relation to cardiac abnormalities and CD4 count.

AGE IN YEARS	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
20-25	3 (5.9%)	6 (11.8%)	9 (17.6%)	3 (3.1%)	14 (14.1%)	17 (17.2%)
26-30	4 (7.8%)	13 (25.5%)	17 (33.3%)	4 (4.1%)	38 (38.4%)	42 (42.4%)
31-35	6 (11.8%)	8 (15.7%)	14 (27.5%)	1 (1%)	21 (21.2%)	22 (22%)
36-40	1 (2%)	7 (13.7%)	8 (15.7%)	1 (1%)	13 (13.1%)	14 (14%)
≥ 41	2 (3.9%)	1 (2%)	3 (5.9%)	0 (0%)	4 (4%)	4 (4%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.352 P value for Group II was 0.639

Table – 4: Sex distribution in relation to cardiac abnormalities and CD4 count.

SEX	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
MALE	9 (17.6%)	21 (41.2%)	30 (58.8%)	5 (5.1%)	27 (27.3%)	32 (32.3%)
FEMALE	7 (13.7%)	14 (27.5%)	21 (41.2%)	4 (4%)	63 (63.6%)	67 (67.7%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.801 P value for Group II was 0.118

Table – 5: BMI in relation to cardiac abnormalities and CD4 count.

BMI	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
UNDER WEIGHT	7 (13.7%)	14 (27.5%)	21 (41.2%)	1 (1%)	28 (28.3%)	29 (29.3%)
NORMAL	7 (13.7%)	13 (25.5%)	20 (39.2%)	6 (6.1%)	42 (42.4%)	48 (48.5%)
OVER WEIGHT	2 (3.9%)	8 (15.7%)	10 (19.6%)	1 (1%)	18 (18.2%)	19 (19.2%)
OBESE	0 (0%)	0 (0%)	0 (0%)	1 (1%)	2 (2%)	3 (3%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.684 P value for Group II was 0.234

Table – 6: smoking in relation to cardiac abnormalities and CD4 count.

SMOKING	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
PRESENT	2 (3.9%)	2 (3.9%)	4 (7.8%)	0 (0%)	7 (7.1%)	7 (7.1%)
ABSENT	14 (27.5%)	33 (64.7%)	47 (92.2%)	9 (9.1%)	83 (83.8%)	92 (92.9%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.403 P value for Group II was 0.385

Table – 7: Alcohol in relation to cardiac abnormalities and CD4 count.

ALCOHOL	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
PRESENT	3 (5.9%)	4 (7.8%)	7 (13.7%)	0 (0%)	5 (5.1%)	5 (5.1%)
ABSENT	13 (25.5%)	31 (60.8%)	44 (86.3%)	9 (9.1%)	85 (85.9%)	94 (94.9%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.481 P value for Group II was 0.468

Age distribution

The mean age of our study group was 30.87 ± 6.11 years with the age group ranging from 22 to 50 years. Mean age of Group I and group II were 31.43 ±6.23 years and 30.58 ± 6.06 years respectively. In Joshi, et al. study at Mumbai, the age group ranged from 17 to 52 years with the mean age of 29.8 years [10]. Nirdesh, et al. study had 100 patients with mean age of 37.31±8.71 years [8]. In Group I, out of 16 patients with cardiac abnormalities 3 patients were in 20 - 25 years age group, 4 patients were 26 - 30 years age group, 6 patients were in 31 - 35 years age group, one patient was in 36 - 40 years age group and 2 patients were in more than 40 years of age group. In Group II, out of 9 patients with cardiac abnormalities 3 patients were in 20 - 25 years age group, 4 patients were in 26 - 30 years age group, one patient each in 31 - 35 years and 36 - 40 years of age group. P values for Group I and Group II were 0.352 and 0.639 respectively which was statistically insignificant. There was no correlation between age and cardiac abnormalities in this study similar to the study conducted by Caggese, et al. and Nirdesh, et al. [8, 9].

Gender distribution

The gender distribution was 58.7 % (88) of females compared to 41.3% (62) of males. In Joshi, et al. study, male and female ratio was 5.7:1 (63 males and 11 females) [10]. In P Kannan, et al. study males were 120 and females were 80 [11]. In El Hattoui, et al. study males and females were 88 and 70 respectively [12]. In Group I, 9 males and 7 females had cardiac abnormalities. In Group II, 5 males and 4 females had cardiac abnormalities. P values for Group I and Group II were 0.801 and 0.118 respectively which was statistically insignificant. Nirdesh, et al. had 78 male and 22 female patients and no correlation was found out between sex and cardiac abnormality like in our study [8].

Risk factors

In our study group, 7.3% were smokers. In Group I, among 16 patients with cardiac abnormalities two patients were smokers. In Group II, all patients with cardiac abnormalities were non smokers. P values for both the groups were 0.403 and 0.385 respectively, statistically insignificant. In this study 8% were alcoholic. In Group I, among 16 patients with cardiac abnormalities 3 were alcoholics. In Group II, all patients with cardiac abnormalities were non alcoholics. P values for both the groups were 0.481 and 0.468, statistically insignificant. In Nirdesh, et al. study 35 patients were smokers and 17 patients were alcoholic. There was no significant correlation between smoking and alcohol with cardiac abnormalities in our study similar to the study by Nirdesh, et al. and Caggese, et al. [8, 9].

BMI

The mean BMI of our study group was 20.40 ±3.89 kg/m^2. The mean BMI of Group I and Group II were 19.85 ± 4.01 kg/m^{2}and 20.68 ± 3.82 kg/m^2 respectively. In Group I, out of 16 patients with cardiac abnormalities, 7 were underweight, 2 patients were overweight and 7 patients had normal BMI. In Group II, out of 9 patients with cardiac abnormalities, 6 patients had normal BMI, one patient was underweight, one patient was overweight and one patient was obese. P values for Group I and Group II were 0.684 and 0.234 respectively, statistically insignificant. There was no significant correlation between BMI and cardiac abnormalities.

Cardiac abnormalities

The exact prevalence of cardiac involvement in HIV/AIDS is uncertain, and it varies from 28% to 73% depending on the screening methods selected, the population studied, and the definition of cardiac abnormality [13]. The cardiac diseases in HIV infections include pericardial effusion, left ventricular dysfunction myocarditis, dilated cardiomyopathy, endocarditis, pulmonary hypertension, malignant neoplasm, coronary artery disease and drug related cardiotoxicity [14].

In our study, among 150 patients, 25 patients (16.7%) had cardiac abnormalities either in the form of ECG or Echocardiography abnormality. It is observed that 16 patients out of 51 patients (31.4%) in Group I and 9 patients out of 99 (9.09%) patients in Group II had cardiac abnormalities.Thirteen patients had both ECG and Echo abnormalities. Nine patients had ECG abnormalities alone and three patients had echo abnormality alone. 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 present in 16 (10.7%) patients. pericardial effusion (n=9) was the commonest. Pericardial disease is an important feature of HIV associated heart disease. Symptomless effusions have been found in up to 22% of AIDS patients [15]. Dilated cardiomyopathy was found in five patients. Dilated cardiomyopathy has been associated with advanced immunosuppression and lower CD4 counts, and it is an independent risk factor for death [16]. Many studies have shown that HIV is an important cause of dilated cardiomyopathy. Other factors such as zidovudine cardiotoxicity and nutritional deficiencies are associated with dilated cardiomyopathy in HIV infected patients [17]. One patient had septal hypokinesia. Regional LV dysfunction may be the earliest stage of subsequent global LV dysfunction, the identification of this early stage is critical in the management of HIV-associated myocardial disease [18]. One of our patients who had infective endocarditis was iv drug abuser. Infective endocarditis in HIV seems to be related to intravenous drug use. It occurs in 6.3%–34% of HIV infected intravenous drug users [15].

Limitations

The mean duration of the disease in our patients was less. This could be responsible for low incidence of cardiac abnormalities in our patients. Follow up study was not done. So the incidence of cardiac abnormalities in patients with previous normal echocardiography as well as the natural history of those who had Cardiac abnormality could not be studied. Since the critically ill patients were not included in our study the entire spectrum of cardiac abnormalities could not be established. Viral load could not be estimated due to constraints. Histopathologic studies like pericardial biopsy, endomyocardial biopsy and cytological study of pericardial fluid to determine the etiology of pericardial effusion and cardiomyopathy were not done.

Conclusion

Cardiac abnormalities are very common in HIV patients, pericardial effusion being the commonest. There was significant correlation noted between cardiac abnormalities and CD4 count (P value was 0.001). Various studies agree that the most important factor in development of cardiac abnormalities is the level of immunosuppression and there is tight correlation between CD4 count and echocardiographic abnormalities, which is also demonstrated in the present study [9, 16, 19, 20]. In our study, no correlation was found between cardiac involvement with other traditional variables like age, gender, BMI, smoking and alcohol.

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