

Study of Cardiovascular Manifestations in Patients with Hiv Infection And Their Correlation With Cd4 Count In Population Of Western Rajasthan

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Abstract: The WHO estimated that more than 40 million people had been infected by HIV at the end of 2005 and there are now 5 million new infection and 3 million deaths every year. In India, HIV prevalence among the general population was 2.39 million [NACO (National AIDS Control Organisation)]. Although HIV-related heart disease is common, it is frequently overlooked because it is either subclinical or produces nonspecific symptoms such as breathlessness and fatigue that are mistakenly attributed to other problems such as anemia. The prevalence of cardiac abnormalities in HIV-positive patients ranges from 25% to 75%. 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. Early recognition and prompt treatment are important to prevent significant morbidity from cardiac involvement. Echocardiography is the investigation tool. The results of this study indicated that cardiovascular abnormalities in HIV infected patients are common and can occur without any clinical manifestation. The most common cardiovascular finding was of asymptomatic Fractional Shortening (20.7%), followed by that of reduced ejection fraction (15.5%), Diastolic dysfunction (12.2%).

Keywords: NACO, Pericardial effusion, Echocardiography, Fractional Shortening and Diastolic dysfunction

I. Introduction

Acquired Immunodeficiency Syndrome (AIDS) caused by infection with human immunodeficiency virus (HIV) is characterized by profound immunosuppression that predisposes a patient to wide array of opportunistic infections, malignant neoplasm and multi-organ dysfunction¹.

The WHO estimated that more than 40 million people had been infected by HIV at the end of 2005 and, there are now 5 million new infection and, 3 million deaths every year². In India, HIV prevalence among the general population was 2.39 million [NACO (National AIDS Control Organisation)].

Although HIV-related heart disease is common, it is frequently overlooked because it is either subclinical or produces nonspecific symptoms such as breathlessness and fatigue that are mistakenly attributed to other problems such as anemia³.

With the availability of a large armamentarium of anti-retro-viral drugs and recent advances in the diagnosis, treat-ment and monitoring of persons living with HIV and AIDS (PLHA), there has been visible improved survival of such patients. Due to the longer survival of PLHA, the manifestations of late stage HIV infection are now being met with more commonly than before, which in-cludes HIV related cardiac diseases. The prevalence of cardiac abnormalities in HIV-positive patients ranges from 25% to 75%^{4,5}.

Cardiac abnormalities in HIV infection may involve any of structure of the heart including pericardium, myocardium, and endocardium⁶.

The cardiac diseases in HIV infections include pericardial effusion, left ventricular dysfunction, myocarditis, dilated cardio-myopathy, endocarditis, pulmonary hypertension, malignant neoplasm, coronary artery disease and drug re-lated cardiotoxicity⁷.

Echocardiography is very helpful in detecting cardiac dysfunction at an early stage, much before overt clinical manifestations develop. The most common sign of cardiac involvement is impairment of LV fractional shortening. This could be explained by reduction of cardiac contractility. Early recognition and prompt treatment are important to prevent significant morbidity from cardiac involvement⁸.

II. Materials And Methods

It is a cross-sectional study conducted in DR.S.N.MEDICAL COLLEGE JODHPUR and hospital attached to it, which is premier tertiary care centre in western Rajasthan. All patients diagnosed with HIV infection / AIDS after positive ELISA test were included in the study. Patient suffering from congenital heart

disease, Rheumatic heart disease, patient of hypertension and ischemic heart disease, diagnosed before HIV screening were excluded from study.

Data Collection:

As the subjects under study were either hospitalized patients or attended outpatient department of this tertiary care centre, consent was taken at the point from the patients for conducting the required investigation as detailed below.

All patients were assessed clinically by detailed medical history, health behavior questionnaire, assessment of medication use with complete physical examination. Individual were subjected to baseline investigation including complete hemogram, renal and hepatic function test, complete urine examination, blood sugar fasting and post –prandial , thyroid profile, ECG, chest X-ray PA view and, specific investigations were undertaken to establish diagnosis of HIV infection including ELISA test and screened for opportunistic infections. CD4 count was done for all patients using flow-cytometry using a BD FACS Count system. The CD4 count was done using kits supplied by the National AIDS Control Organisation of India (NACO) to anti Retroviral Therapy (ART) Centre, MDMH Jodhpur. Staging of the disease was done according to revised WHO clinical staging of the disease.

All patients were evaluated using M Mode and Two dimensional transthoracic echocardiography and colour flow doppler examination in left lateral supine position and examined in standard parasternal long and short axis and, apical two and four chamber views using echocardiographic machine at department of cardiology in MDMH Jodhpur. The measurements were made in accordance with recommendations of the American Society of Echocardiography. Normal chamber measurement values were defined according to current guidelines⁹, including the measurement of ejection fraction (EF) by quantitative biplane method of disk. Each patient underwent pulsed wave Doppler examination of mitral inflow before and during Valsalva maneuver and of pulmonary venous inflow and Doppler tissue imaging of the mitral annulus. Diastolic function was categorized according to the progression of diastolic dysfunction as follows: normal; mild, defined as impaired relaxation without evidence of increased filling pressures; moderate, defined as impaired relaxation associated with moderate elevation of filling pressures or pseudonormal filling, and severe, defined as advanced reduction in compliance or reversible or fixed restrictive filling. Participants were required to have two Doppler criteria consistent with mild, moderate or severe DD to be so classified . Additionally, pulsed Doppler pulmonary venous flow and TEI-Index were measured . Left ventricular mass was calculated by the equation of Devereux¹⁰.

III. Observations And Results

Table: 1 Incidence of Cardiovascular Manifestations in Hiv Patients

CARDIOVASCULAR MANIFESTATIONS	MALE (n=138)	FEMALE (n=75)	TOTAL
PATIENTS			213
DCM	12 (8.7%)	4(5.3%)	16(7.5%)
PE	12 (8.7%)	6(8%)	18 (8.5%)
VHD	3 (2.2%)	3(4%)	6(2.8%)
PAH	4(2.9%)	2(2.7%)	6(2.8%)
HF	2(1.4%)	1(1.3%)	3(1.4%)
IHD	5(3.6%)	0	5(2.3%)
INFECTIVE ENDOCARDITIS	0	1(1.3%)	1(0.4%)
FS (<30%)	32(23.2%)	12(16%)	44(20.7%)
DIASTOLIC DYSFUNCTION	16(11.6%)	10(13.3%)	26(12.2%)
REDUCED EF (<50%)	22(16%)	11(14.7%)	33(15.5%)
FS (<30%) WITH REDUCED EF (<50%)	4(3%)	4(5.3%)	7(3.3%)
REGIONAL LV HYPOKINESIS	4(3%)	1(1.3%)	5(2.4%)

Table no 1 depicts the incidence of cardiovascular manifestations in HIV infected males and females.

From the table it is observed that the most common cardiovascular manifestations are asymptomatic being present in 30% and symptomatic cardiovascular manifestations present in 20% out of 213 patients. Most common manifestation is reduced fractional shortening (20.7%), followed by reduced ejection fraction (15.5%), diastolic dysfunction (12.2%), pericardial effusion (8.5%) and dilated cardiomyopathy (7.5%).

Out of 138 male patients 12 (8.7%) had dilated cardiomyopathy, 12(8.7%) had pericardial effusion, 3(2.2%) had valvular heart disease, 4(2.9%) had pulmonary artery hypertension, 2(1.4%) had heart failure, 5(3.6%) had IHD, while 32(23.2%) patients had fractional shortening (<30%) in their echo finding, diastolic dysfunction was present in 16(11.6%) patients, reduced ejection fraction (<50%) was in 22(16%), FS (<30%) with reduced ejection fraction (<50%) in 4 (3%) and regional LV hypokinesia was present in 4 (3%) patients.

Out of 75 female patients 4(5.3%) had dilated cardiomyopathy, 6(8%) had pericardial effusion, 3(4%) had valvular heart disease, 2(2.7%) had pulmonary artery hypertension, 1(1.3%) had heart failure, 1(1.3%) had

Infective Endocarditis, while 12(16%) patients had fractional shortening (<30%) in their echo finding, diastolic dysfunction was present in 10(13.3%) patients, reduced ejection fraction (<50%) was in 11(14.7%), fractional shortening (<30%) with reduced ejection fraction (<50%) in 4(5.3%) and regional LV hypokinesia was present in 1(1.3%) patients.

TABLE: 2 CORRELATION BETWEEN CD-4 COUNTS AND CARDIOVASCULAR MANIFESTATIONS IN HIV PATIENTS

CD4 COUNTS PER micro L	SYMPTOMATIC CARDIOVASCULAAR MANIFESTATIONS (n=43)							ASYMPTOMATIC CARDIOVASCULAAR FINDINGS (n=63)							WITHOUT CARDIO VASCULAR MANIFESTATION (n=107)
	CHD (n=5)	NON CHD (n=38)													
		DCM	PE	VHD	PAH	HF	IE	FS (<30%)	DIASTOLIC DYSFUNCTION	REF (<50%)	FS (<30%) WITH REF (<50%)	ASYMPTOMATIC PAH	REGIONAL LV HYPOKINESIS	ASYMPTOMATIC PE	
< 50	0	4	3	1	0	0	1	2	3	3	2	0	0	0	3
50 - 100	0	12	4	5	5	3	0	13	8	7	4	1	2	8	13
101 - 200	0	0	0	0	0	0	0	2	1	1	1	0	1	2	15
> 200	5	0	0	0	0	0	0	0	1	0	0	0	0	1	76

Table no- 2: Depicts a correlation between CD-4 counts and cardiovascular manifestations in HIV patients. Out of 43 patients with symptomatic cardiovascular manifestations 38(88.4%) patients had CD-4 counts less than 100 per micro L, while 5(11.6%) patients who had CHD, had CD-4 counts more than 200 per micro L. 16(100%) patients of DCM had CD4 counts less than 100 PER micro L, out of which 4(25%) patients had less than 50 per micro L. While in pericardial effusion 3(43%) patients had CD4 count less than 50 per micro L and 4(57%) patients had CD4 counts in between 50 to 100 per micro L. While all patients of Valvular heart disease, PAH, Heart failure and Infective endocarditis had CD-4 counts of less than 100 per micro L.

Among 63 patients of asymptomatic cardiovascular findings, patients who had CD4 counts less than 50 per micro L, show Fractional shortening(<30%) in 3.2% and reduced Ejection fraction (<50%) in 4.7%, reduced ejection fraction with fractional shortening in 3.2%, and diastolic dysfunction in 4.7%. While patients who had CD4 counts in between 50-100 per micro L had fractional shortening in 20.6%, reduced ejection fraction in 14.28%, fractional shortening with reduced ejection fraction in 7.5%, regional LV hypokinesia in 3.2%, pericardial effusion in 12.7%, asymptomatic PAH in 1.5% and diastolic dysfunction in 12.7%. While 1.5% had diastolic dysfunction and 1.5% had pericardial effusion in Echo finding in patients who had CD4 more than 200. Out of 107 Patients without cardiovascular manifestations, 76(21%) patients had CD4 counts >200 , 15(14%) patients had CD4 counts between 101 to 200, 13(12.2%) patients had between 50 to 100, and 3(2.8%) patients had CD4 less than 50 per micro L.

TABLE: 3 CORRELATION BETWEEN WHO STAGING AND CARDIOVASCULAR MANIFESTATIONS IN PLHA

WHO CLINICAL STAGE	SYMPTOMATIC CARDIOVASCULAR MANIFESTATIONS (n=43)							ASYMPTOMATIC CARDIOVASCULAR FINDINGS (n=63)							WITHOUT CARDIOVASCULAR MANIFESTATION (n=107)
	CHD (n=5)	NON CHD(n=38)						FS (<30%)	DIASTOLIC DYSFUNCTION	REF (<50%)	FS (<30%) WITH REF (<50%)	ASYMPTOMATIC PAH	REGIONAL LV HYPOKINESIS	ASYMPTOMATIC PE	
	DCM	PE	VHD	PAH	HF	IE									
I	3	0	0	0	0	0	0	1	1	0	0	0	0	0	70
II	2	0	0	1	1	0	0	2	2	1	0	0	0	0	17
III	0	4	1	1	1	0	0	4	4	3	3	1	1	3	5
IV	0	12	6	4	3	3	1	10	6	7	4	0	2	8	15

Table no- 3: Depicts a correlation between WHO clinical staging and cardiovascular manifestations in HIV patients. Out of 43 patients with symptomatic cardiovascular manifestations, 3(6.9%) patients in stage I had CHD. Out of 4(9.3%) patients in stage II having symptomatic cardiovascular manifestations 2(50%) patients had CHD, 1(25%) had VHD and 1(25%) had PAH. While out of 7(16.3%) patients in stage III, 4(57%) patients had DCM, 1(14.2) had PE, 1(14.2) had VHD and 1(14.2) had PAH. Out of 29(67.4%) patients in stage IV, 12(41.3%) patients had DCM, 6(20.7%) had PE, 4(13.8%) had VHD, 3(10.3%) had HF, 3(10.3%) had PAH and 1(3.4%) had infective endocarditis.

Out of 63 patients with asymptomatic cardiovascular finding, Among 2(3.2%) patients in stage I, 1(50%) patient had Fractional shortening(<30%) and 1(50%) had Diastolic dysfunction. Out of 5(7.9%) patients in stage II, 2(40%) patients had Fractional shortening(<30%), 1(20%) had reduced Ejection fraction (<50%) and 2(40%) had Diastolic dysfunction. While out of 19 patients in stage III, 4(21%) had Fractional shortening(<30%), 3(15.8%) had reduced Ejection fraction (<50%), 3(15.8%) had reduced Ejection fraction with Fractional shortening, 4(21%) had Diastolic dysfunction, 1(5.3%) had Regional LV Hypokinesia, 3(15.8%) had asymptomatic PE and 1(5.3%) had increased Pulmonary artery pressure. Out of 37(58.7%) patients in stage IV, 10(27%) had Fractional shortening(<30%), 7(19%) had reduced Ejection fraction (<50%), 4(11%) had reduced Ejection fraction with Fractional shortening, 6(16%) Diastolic dysfunction, 2(5.4%) had Regional LV Hypokinesia and 8(21.6%) had asymptomatic PE.

Out of 107 Patients without cardiovascular manifestations, 70(65.4%) patients were in WHO stage I, 17(16%) patients were in WHO stage II, 5(4.7%) patients were in WHO stage III and 15(14%) patients were in WHO stage IV.

IV. DISCUSSION

Out of the 213 patients enrolled 81% were from rural and 19% were from urban background. Among them 65% were males and 35% were females. Patients enrolled to the study belonged to the age group 20 to 59 yrs, among them 68% were in age group 20 to 39 yrs and 32% were in the age groups 40 to 59 yrs.

In the present study out of 213 patients 20% had symptomatic cardiovascular disease, 30% had asymptomatic cardiovascular finding and 50% had no cardiovascular disease. The finding of present study similar to that by Lipshutz et al who found symptomatic cardiovascular disease in 10% and asymptomatic manifestations in 25%.

In present study, 150(70%) patients were in the younger age group of 20-39yrs as this group is at maximum risk of HIV related morbidity and mortality.

Out of 150 patients belonging to younger age group 20 to 39 yrs, 76(50.7%) had cardiovascular manifestations. Among them 67% male patients and 47% female patients had cardiovascular disease. It is in concordance with the annual NACO report of 2009-2010 which shows cardiovascular manifestations in 64.3% males and 35.7% females this shows that males are more affected than females in ratio of 2:1.

In present study the incidence of symptomatic cardiovascular manifestations was 20%. In present study the incidence of Dilated Cardiomyopathy was 7.5%, incidence of symptomatic Pericardial Effusion was 3.3%, incidence of valvular heart disease and pulmonary artery hypertension was similar and it was 2.8%. Incidence of Heart Failure was 1.4% and that of Infective Endocarditis is 0.4%. the incidence is similar for DCM as studies by Moreno et al. who found an incidence of 6%, Hakim et al. who found an incidence of 5% and Barbaro. G et al, Himelman et al and Anderson et al. who found an incidence of 8%. Incidence of pericardial effusion in present study on including both symptomatic and asymptomatic cases was 8.5% , which was similar to that in studies by Aggarwal et al. who found an incidence of 11.5%, Himelman et al. who found an incidence of 10%. Incidence of pulmonary hypertension was in concordance with the study by Himelman et al. who found an incidence of 0.5%. Studies by Pellicelli et al and Mehta et al found a higher incidence (11.4%), which was much

higher than the present study and that of Himelman et al. The incidence of valvular heart disease and Infective Endocarditis was similar to that seen in the general population.

In present study the incidence of asymptomatic cardiac findings is 30%. Out of this the most common is Fractional Shortening present in 8% which is similar to study by Lipshultz et al. who found an incidence of 8%, other study Corrallo et al found an incidence of 22% which was 3 times more than that of the present study. Incidence of diastolic dysfunction was 6.1% in the present study which was in concordance with study by Hakim et al. who found an incidence of 8.5%. Regional LV wall motion abnormality was present in 1.4%, which was similar to that seen in other studies.

In the present study the most common symptom of presentation of patients with symptomatic cardiac disease after excluding OI's was shortness of breath (55.8%), followed by cough and fatigue (41.9%). Followed by pedal edema(25.6%) and palpitations(18.6%) and chest pain(18.6%). Most of the cases of DCM presented with shortness of breath. Cough, palpitations and fatigue were commonly symptoms of PAH and DCM with Heart Failure.

The results were similar to study by Anita et al. shortness of breath (28.6%) and cough (30%).

In the present study it was found that among patients with symptomatic cardiovascular manifestations 20.9% had CD-4 <50 per micro L, 67.4% had CD-4 count between 50-100 per micro L, 11.6% have CD-4 count >200 per micro L. 11.6% patients with symptomatic cardiac disease were all cases of IHD and were on HAART. Among the asymptomatic group 68.3% had CD-4 count between 50-100 per micro L, 15.8% had <50 per micro L, 12.7% had CD-4 between 100-200 per micro L and 3.2% had CD-4 >200 per micro L. Whereas in group without cardiac findings, most of whom were on HAART, 21% had CD4 counts >200, 14% patients had CD4 counts between 101 to 200, 12.2% patients had between 50 to 100, and 2.8% patients had CD4 less than 50 per micro L. The results of the present study were similar to studies by S. Castro et al.; G. Barbaro et al and S. B. Devi et al all of whom found cardiovascular manifestations to increase in HIV patients with CD-4 counts <200 cells per micro L.

Present study revealed that 29(76.3%) patients with symptomatic cardiac diseases except ones with IHD, were in WHO stage IV, 7(18.4%) were in WHO stage III, 2(5.2%) were in WHO stage II and only (6.9%) cases all of which were cases of IHD on HAART, were in WHO stage I. Among asymptomatic cases 37(58.7%) and 19(30.2%) were in WHO stages IV and III respectively, and 7(11.11%) were in WHO stage I and II. In the group without cardiovascular manifestations 70(65.4%) were in WHO stage I, 17(15.9%) were in WHO stage II, 5(4.6%) were in WHO stage III and 15(14%) patients were in WHO stage IV. The results of the present study were similar to studies by Khunnawat et al. and Lipshultz et al both found that most of the Echocardiographic abnormalities are seen in WHO clinical stage IV.

V. Conclusion

The results of the study indicate that cardiovascular abnormalities in HIV infected patients are common and can occur without any clinical manifestation. The most common cardiovascular finding was of asymptomatic Fractional Shortening (20.7%), followed by that of reduced ejection fraction (15.5%), Diastolic dysfunction (12.2%). In western rajasthan ,where most of the population belongs to rural and desert areas and they are less litrate, awareness about the disease and its course plays important role. We tried to find out various cardiac outcomes in these patients.

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