

CARDIOVASCULAR MANIFESTATIONS IN HIV POSITIVE PATIENTS IN A TERTIARY CARE HOSPITAL, CENTRAL INDIA

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Abstract

Background: Acquired immune deficiency syndrome (AIDS) is one of the major public health problem in India. HIV estimates report (2019)⁽¹⁾ of the Government, India is estimated to have around 23.49 lakh people living with HIV/AIDS (PLHIV) in 2019. In Chhattisgarh it is 42520 & HIV incidence per 1,000 uninfected population is 0.1. With the recent advancements in therapy early mortality in HIV cases are significantly reduced but cardiovascular abnormalities are frequently seen as the disease progresses and is associated with decreased quality of life.

Aims and objective: To know the pattern and prevalence of various cardiovascular manifestations in HIV positive patients and its association with CD4 count, WHO stage of disease and ART

Material and Methods: For the period of 1.3 years from JANUARY 2019 TO APRIL 2020 study is conducted in the Department of Medicine, Pt. JNM Medical College and Dr. BRAMH, Raipur. A total of 137 HIV positive patients of age >18 years, all are on ART are included. Patients included in the study underwent detailed history taking, clinical examination and investigations. Details of the history, clinical examination and investigations were noted in the proforma. The cardiovascular examination in the form of chest x-ray, ECG, 2D echocardiography and NT-ProBNP was done and their correlations with CD4 count and WHO disease stage is studied accordingly. Electrocardiogram, chest x-ray and 2D echocardiography was done immediately following blood investigation.

Result: Majority (45.25%) of the patients involved in this study were in age group of 31-45 year with the overall average mean age of 38.86 years. Male to female ratio was 3.1:1. On x-ray cardiomegaly found in 25.5% pts. Baseline ECG abnormalities seen in 47.4% pts. Echocardiographic abnormality seen in 56.2% pts. The commonest finding in our study is valvular abnormalities in 55 pts (40.1%) followed by diastolic dysfunction in 45 pts (32.8%). Other less common cardiac manifestations in decreasing order of frequency were reduced LVEF in 33 pts (24%), pericardial effusion in 15 pts (10.9%), left ventricular hypertrophy in 13 pts (9.4%), pulmonary arterial hypertension in 10 pts (7.2%) and regional wall motion abnormality in 9 pts (6.5%). We found a strong statistical correlation found between CD4 count and pericardial effusion in 2D-ECHO ($p=0.0410023$). Also strong statistical correlation ($p=0.016456$) is found between the WHO stage of disease and cardiomegaly, strong statistical correlation found between WHO staging of disease and QRS abnormalities ($p=0.02551$) and inverted T wave ($p=0.000528$), strong statistical correlation found between WHO stage of disease and pulmonary arterial hypertension in 2D-ECHO ($p=0.006832$). And statistical association found between WHO stage of disease and regional wall motion abnormality (RWMA) in 2D-ECHO ($p=0.002541$).

Conclusion: The results of the study indicate that cardiovascular abnormalities in HIV infected patients are common. Cardiac involvement and cardiovascular complications are commonly seen in HIV-infected patients and can present without any clinical manifestation. The common cardiovascular manifestation seen in our study patients is valvular leaks, regional wall motion abnormality, pericardial effusion, reduced EF etc. The incidence of cardiovascular manifestations increases as the disease progresses and CD4 count decreases.

Keywords: Prevalence, Cardiovascular, Abnormalities & HIV.

Study Designed: Cross Sectional Observational Study.

Introduction

Acquired immune deficiency syndrome (AIDS) is described by a procured, significant, irreversible immunosuppression that inclines the patient to various pioneering diseases, harmful neoplasms and a reformist brokenness of numerous organ frameworks⁽¹⁾. The heart and incredible vessels are not the locales most as often as possible influenced by crafty contaminations and neoplastic cycles in patients with AIDS. Nonetheless, cardiovascular

intricacies happen in countless such patients and are the prompt reason for death in a few.

The Joint United Nations Program on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) assessed that 5.7 million individuals in India were tainted with the human immunodeficiency infection (HIV)⁽²⁾. In non-industrial nations, where ART isn't broadly accessible, an expansion in the pervasiveness of cardiomyopathy and pericardial emission, with a connected high death rate for congestive cardiovascular breakdown occur⁽³⁾.

With regards to new clinical discoveries, it has been seen in evolved nations that some ART regimens, particularly those including protease inhibitors, may cause an iatrogenic metabolic condition (HIV-related lipodystrophy disorder) that is related with an expanded derangements for cardiovascular functions (myocardial localized necrosis and ischemia) due to a cycle of quickened atherosclerosis.

From the beginning of the AIDS epidemic, it was recognized, first at autopsy and later by noninvasive techniques, that HIV infection can cause cardiac abnormalities. The prevalence of cardiac disease in HIV-infected individuals is not clear; the reported frequency of cardiac involvement depends on the population studied and the definition of cardiac abnormality. Before the advent of antiretroviral therapy (ART), clinically significant cardiac disease was unusual in the HIV-infected population and was detected in most cases only at autopsy. However, cardiac involvement in AIDS patients appears to be more common than previously thought. In fact, when HIV-infected patients were examined by echocardiography in the late 1980s, cardiac abnormalities were detected more often than would be expected from clinical symptoms and physical examinations.

Material & Method

Our study is prospective cross sectional study. In our study, 205 patients of HIV diagnosed as per National AIDS control organization (NACO) guidelines⁽⁴⁾ who were came to medicine OPD or for ART or admitted in wards / MICU or ICCU in department of medicine are randomly chosen are included in the study underwent detailed history taking, and 68 are excluded because of exclusion criteria rest 137 pts are underwent clinical examination and investigations.

Details of the history, clinical examination and investigations were noted in the proforma. Electrocardiogram, chest x-ray and 2D echocardiography was done immediately following blood investigation.

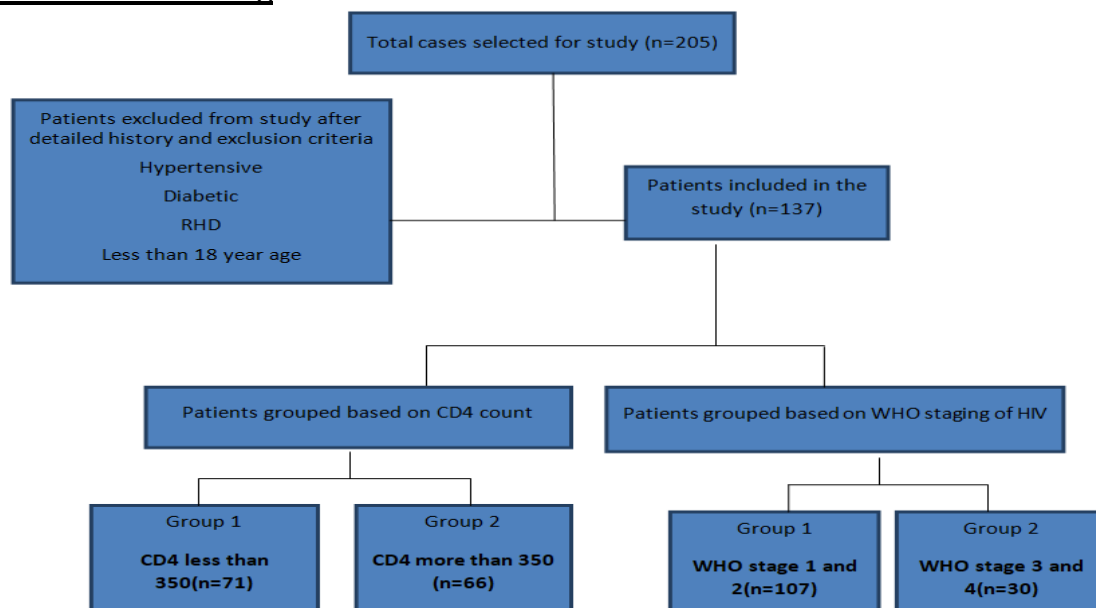
Blood sample of about 2-3 ml was collected for measurement of cardiac biomarker NT-proBNP after taking informed consent. Estimation is done using Roche Diagnostic cobas e 411 analyzer. When the NACB performance characteristics⁽⁵⁾ are compared to the values used in the ESC recommendations⁽⁶⁾, it can be seen that at 400pg/mL the negative predictive value is 99 %; thus at this cut-off it is very unlikely that the test will misclassify a sick person.

Echocardiography was performed using sononite S1-450 in the cardiology department. Pt. JNM medical college Raipur with a 3.5-MHZ transducer probe. Two-dimensional (2D), M- mode, pulse-wave, continuous-wave and colour Doppler echocardiography assessment was done with the subject in the left lateral decubitus position⁽⁷⁾. The two-dimensional images were obtained in the parasternal long and short-axis views, apical and subcostal views^(8,9).

CD4 count was done using kits supplied by the National AIDS control organization of India (NACO) to anti-retroviral therapy (ART) Centre; Pt. JNM medical college Raipur. CD4 count was done for all patients using flow cytometry using a BD FACS count system.

ECG is done on all the 137 patients using a Schiller Cardiovit AT-10 ECG machine operating at a speed of 25 mm/s and sensitivity of 10 mm/mV. This is performed in accordance with the American Heart Association specifications.⁽¹⁰⁾

Flow chart of case screening



Statistical analysis:

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

INCLUSION Criteria-

All HIV patients above the age of 18 years of either gender. Attending a medical outpatient department (OPD) or HIV clinic and admitted in medical wards of DR. BRAM hospital Raipur.

EXCLUSION Criteria-

- 1- Subjects below 18 years
- 2- H/O ischemic, rheumatic, congenital heart disease
- 3- Chronic respiratory illness based on history prior to diagnosis of HIV infection
- 4- Those who are not willing to give consent
- 5- Diabetes mellitus
- 6- Hypertension

Results-

Study included 137 patients and are on ART treatment .who are above 18 years of age and gave written consent, Male to female ratio was 3.1:1, Mean age of males 39.05 ± 10.65 & Mean age of females 38.24 ± 11.03 . Overall average age in this study – 38.86 years. Majority (45.25%) of the patients involved in this study were in age group of 31-45 year.

In this study chest x-ray revealed cardiomegaly in 35 (25.5%) patients .Out of 35, 18 patients having CD4 count less than 350 , whereas 17 have CD4 more than 350, we didn't find statistical significance of cardiomegaly with CD4 count.19 patients having cardiomegaly belongs to WHO stage 1 & 2 and rest 16 patients belong to WHO stage 3 and 4. There is a strong statistical correlation ($p=0.016456$) found between cardiomegaly and WHO stage. Various echocardiographic findings found in these 35 patients are Diastolic dysfunction seen in 21, Valvular leak in 22 , RA/RV dilatation in 3 , LVH seen in 4, Pericardial effusion in 9 patients .

We found ECG abnormalities in 65 patients (47.4%), The most common abnormality in our study is sinus tachycardia found in 26 patients (18.97%) followed by inverted T waves and QRS abnormalities. QRS abnormalities includes – conduction abnormalities – LBBB in 1, RBBB+LAFB in 1, Abnormal axis – Left axis deviation in 8, Right axis deviation in 2, Extreme axis in 1, Low voltage complex in

1 patient in 2D echo that patient revealed pericardial effusion, Left ventricular hypertrophy in 7, T wave inversion found in 23 patients, and on 2D echo revealed abnormality, RWMA is found in 7 patients. We found a strong statistical correlation between WHO staging and QRS abnormalities ($p= 0.02551$) and inverted T wave ($p= 0.000528$). No patient found with ectopics and 2 patients found with U waves. In our study, there was no significant correlation between the ECG findings and CD4 count (Table 3). There was no statistically significant association between the ECG abnormality and WHO class.

NT-proBNP test is done in 137 PLHIV patients as a cardiac biomarker , no statistical significant association was found between CD4 count, WHO staging and NT-proBNP in this study. Echocardiographic abnormalities were found in 56.2% of the PLHIV. The commonest finding in our study is valvular abnormalities in 55 pts (40.1%) followed by diastolic dysfunction in 45 pts (32.8%). Other less common cardiac manifestations in decreasing order of frequency were reduced LVEF in 33 pts (24%), pericardial effusion in 15 pts (10.9%), left ventricular hypertrophy in 13 pts (9.4%), pulmonary arterial hypertension in 10 pts (7.2%) and regional wall motion abnormality in 9 pts (6.5%). Diastolic dysfunction is characterized by elevated left ventricular end diastolic pressure despite normal or subnormal diastolic volume. we found 55 HIV pts (40.1%) with Valvular leak, abnormalities seen were mitral regurgitation, tricuspid regurgitation, aortic regurgitation and other multivalvular involvement. No statistical correlation is found in our study between valvular abnormalities and CD4 count, WHO stage of disease. in our study 45 pts (32.8%) diagnosed with left ventricular diastolic dysfunction. In this study we didn't find any statistical correlation between diastolic dysfunction and CD4 count, WHO staging . but out of 30 pts (who were WHO stage 3&4) 16 having diastolic dysfunction. in our study pericardial effusion is diagnosed in 10.9% HIV pts ,12 out of 15 pericardial effusions were reported in CD4 count <350 . And we found a statistical correlation with CD4 count ($p=0.0410023$) However, we didn't find a statistical significant correlation with the WHO Stages. we found reduced LVEF in 33 pts (24%), We have found a strong statistical correlation between WHO stage and reduced ejection fraction ($p=0.037929$). we found pulmonary hypertension in 10 pts (7.2%), in our study 6 out of 10 cases were having WHO stage 3&4 suggestive of advanced disease. we found regional wall motion abnormality in 9 Pts (6.5%) We have found a strong statistical correlation between WHO stage and RWMA ($p=0.002514$).

Table 1: Age Distribution

S. No.	Age Group	Total No.	Male	Female	Percentage
1	18-30	35	27	8	25.54
2	31-45	62	43	19	45.25
3	46-60	38	33	5	27.76
4	61-75	02	9	1	01.45

Table 2: relation of the cardiac abnormalities with the duration of ART.

Duration of antiretroviral therapy	X-ray abnormality	ECG abnormality	2D ECHO abnormality	Raised NT-pro BNP	Chi-square	P Value
Less than 6 month (TOTAL patient. N=18)	3 (16.6%)	4(22.2%)	8 (44.4%)	2 (11.1%)	1.9198	0.926923
6 to 12 months (TOTAL patient. N=15)	2 (13.3%)	4 (26.6%)	6 (40%)	0		
More than 12 months (TOTAL patient. N=104)	34 (32.6%)	57 (54.8%)	63 (60.5%)	27 (25.9%)		

Table 3: Distribution of cardiovascular abnormalities on the basis of CD4 count and its statistical significance using chi-square and p value

Diagnostic Procedures	Findings	CD4 less than 350(n=71)	CD4 more than 350 (n=66)	Statistical significance	
				Chi square	p value
X-RAY chest	Cardiomegaly (n=39)	20 (28.1%)	19 (28.7%)	0.0036	0.952279
ECG	Sinus tachecardia (n=26)	12 (16.9%)	14 (21.2%)	0.2812	0.59591
	Irregular rhythm(n=1)	0	1 (1.5%)		
	St elevation(n=0)	0	0		
	QRS abnormality(n=20)	13 (18.3%)	7 (10.6%)	1.2178	0.269801
	Inverted T wave (n=23)	13 (18.3%)	10 (15.1%)	0.1742	0.676387
	U wave (n=2)	2 (2.8%)	0		
NT-proBNP	Raised (n=29)	15 (21.1%)	14 (21.2%)	0.0001	0.992135
2D-echo	Valvular leak(n=55)				
	MR (n=53)	31 (43.6%)	22 (33.3%)	1.1153	0.773384
	TR (n=35)	23 (32.3%)	12 (18.1%)		
	AR (n=4)	3 (4.2%)	1 (1.5%)		
	Multiple (n=31)	21 (29.5%)	10 (15.1%)		
	Pericardial effusion(n=15)				
	Mild (n=12)	10 (14.0%)	2 (3.0%)	0.6787	0.0410023
	Moderate (n=3)	3(4.2%)	0		
	Pulmonary arterial hypertension (n=10)	7 (9.8%)	3 (4.5%)	1.2361	0.266225.
	Diastolic dysfunction (n=45)				
	Grade - 1	21 (29.5%)	18 (27.2%)	0.3462	0.556298.
	Grade - 2	4 (5.6%)	2 (3.0%)		
	RWMA(n=9)	6 (8.4%)	3 (4.5%)	0.7464	0.387629.
	Hypertrophy (n=13)	6 (8.4%)	7 (10.6%)	0.1528	0.69583.
	Reduced EF (n=33)	20 (28.1%)	13 (19.6%)	0.8244	0.363903

Table 4: Distribution of cardiovascular abnormalities on the basis of WHO staging and its statistical significance using chi-square and p value

Diagnostic procedures	Findings	WHO stage 1 and 2(n=107)	WHO stage 3 and 4(n=30)	Statistical significance	
				Chi square	p value
X-RAY chest	Cardiomegaly	23 (21.4%)	16 (53.3%)	5.7534	0.016456
ECG	Sinus tachecardia	17 (15.8%)	9 (30%)	1.9418	0.163474
	Irregular rhythm	1(0.9%)	0		
	St elevation	0	0		
	QRS abnormality	11 (10.2%)	9 (30%)	4.989	0.02551
	Inverted T wave	10 (9.3%)	13 (43.3%)	12.0134	0.000528
	U wave	1 (0.9%)	1 (3.3%)	0.8984	0.343216
NT-proBNP	Raised	18 (16.8%)	11 (36.6%)	3.3081	0.06894
2D-echo	Valvular leak(n=55)				
	MR	34 (31.7%)	19 (63.3%)	0.0693	0.96595
	TR	22 (20.5%)	13 (43.3%)		
	AR	0	4 (13.3%)		
	Multiple	19 (17.7%)	12 (40%)		
	Pericardial effusion(n=15)				
	Mild	9 (8.4%)	3 (10%)	0.0852	0.730335
	Moderate	2 (1.8%)	1 (3.3%)		

	Pulmonary arterial hypertension (n=10)	4 (3.7%)	6 (20%)	7.3167	0.006832
	Diastolic dysfunction (n=45)				
	Grade - 1	26 (24.2%)	13 (43.3%)	0.6304	0.427213
	Grade - 2	3 (2.8%)	3 (10%)		
	RWMA(n=9)	3 (2.8%)	6 (20%)	9.1111	0.002541
	Hypertrophy (n=13)	8 (7.4%)	5 (16.6%)	1.821	0.177197
	Reduced EF (n=33)	20 (18.6%)	13 (43.3%)	4.3082	0.037929

Table 5: Distribution of cardiac abnormalities in HIV patients

<u>abnormalities</u>	<u>No of cases</u>	<u>Statistical significance</u> <u>Chi square and p value</u>
<u>X ray abnormalities</u>	<u>35</u>	< .00001.
<u>Ecg abnormalities</u>	<u>65</u>	
<u>2d echo abnormalities</u>	<u>77</u>	
<u>Raised nt-pro bnp</u>	<u>29</u>	

The chi-square statistic is 26.2188. The p-value is < .00001. The result is significant at p < .05

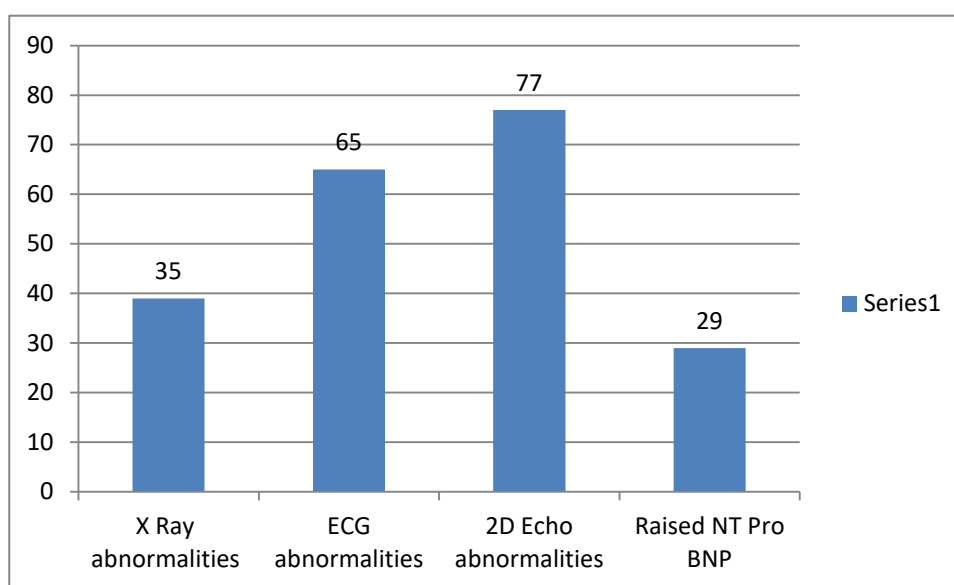


Figure 1: Distribution of Cardiovascular abnormalities in HIV Patients (N=137)

Discussion

The study included 137 patients diagnosed as per NACO criteria and are on ART treatment for the same.who are above 18 years of age and gave written consentMean age of males39.05±10.65 & Mean age of females 38.24±11.03. Overall average age in this study – 38.86 years. Majority (45.25%) of the patients involved in this study were in age group of 31-45 year, Our study shows similar characteristics to India HIV estimation 2019 technical report⁽¹⁾ stating that majority of PLHIV are in the 15-49 year age group and adult HIV prevalence is higher in males as compared to females .The india HIV estimation 2019 technical report⁽¹⁾ shown that most PLHA in india were young adults (15-49 yr age group) . the gender differentiation was also at par with technical report , where 42% of total HIV pts are in india were females and 58% males

in our study chest x-ray revealed cardiomegaly in 35 (25.5%) patients. Different other studies shows variations in the findings like Saritabajaj et al⁽¹¹⁾ showed cardiomegaly in 40.78% , akinbami et al⁽¹²⁾-6.86% , shyam Chaudhry et al⁽¹³⁾-11% , Trinathkumarmishra et al⁽¹⁴⁾- 8%, Raman kumarsharma et al⁽¹⁵⁾-12%, Out of 35, 18 patients having CD4 count less than 350 , whereas 17 have CD4 more than 350, we didn't find statistical significance of cardiomegaly with CD4 count.19 patients having cardiomegaly belongs to WHO stage 1 & 2 and rest 16 patients belong to WHO stage 3 and 4.There is a strong statistical correlation (p=0.016456) found between cardiomegaly and WHO stage.Various echocardiographic findings found in these 35 patients areDiastolic dysfunction seen in 21 ,Valvular leak in 22 , RA/RV dilatation in 3 , LVH seen in 4, Pericardial effusion in 9 patients . Our study found ECG abnormalities in 65 patients (47.4%)Study done by fisher el al⁽¹⁶⁾ suggested up to 57% of asymptomatic HIV infected patients with baseline ECG

abnormality which included supraventricular and ventricular ectopic beats. The most common abnormality in our study is sinus tachycardia found in 26 patients (18.97%) followed by inverted T waves and QRS abnormalities. QRS abnormalities includes – conduction abnormalities – LBBB in 1, RBBB+LAFB in 1, Abnormal axis – Left axis deviation in 8, Right axis deviation in 2, Extreme axis in 1, Low voltage complex in 1 patient in 2D echo that patient revealed pericardial effusion, Left ventricular hypertrophy in 7, T wave inversion found in 23 patients, and on 2D echo revealed RWMA in 7 patients (out of 23). We found a strong statistical correlation between WHO staging and QRS abnormalities ($p=0.02551$) and inverted T wave ($p=0.000528$). No patient found with ectopics and 2 patients found with U waves. In our study, there was no significant correlation between the ECG findings and CD4 count (Table 3). This is consistent with the recent results obtained by Ramankumar Sharma *et al.*⁽¹⁵⁾ and Kumar *et al.*⁽¹⁷⁾, Shyam Chaudhary *et al.*⁽¹³⁾ have also made similar conclusion when comparing the two groups of patients using a CD4 count cutoff of 350/mL. Importantly Soliman *et al.*⁽¹⁸⁾ demonstrated that the presence of ECG abnormalities is an independent predictor of CVD incidences. In addition, Sakthidavel *et al.*⁽¹⁹⁾ have found a strong relation between the CD4 count and ECG abnormalities ($p=0.000$). There was no statistically significant association found between the ECG abnormality and WHO class in our study (Table 4). This is consistent with the findings of Shyam Chaudhary *et al.*⁽¹³⁾ but not to the findings of Sundararajan *et al.*⁽²⁰⁾ which reports a significant increase in ECG abnormalities with the advancement of WHO class.

In our study NT-proBNP test is done in 137 PLHIV patients as a cardiac biomarker. A study done by Hervas *et al.*⁽²¹⁾ showed NT-proBNP having a positive correlation with ventricular diameter and pulmonary artery systolic pressure and therefore a role in the identification of patients with pulmonary hypertension. Tschope *et al.*⁽²²⁾ showed that NT-proBNP can reliably detect the presence of isolated diastolic dysfunction in symptomatic patients to rule out patients with reduced exercise tolerance of non-cardiac origin. Koc *et al.*⁽²³⁾ conducted a study to determine a cut off of NT-proBNP and found that 940pg/ml has a high sensitivity and specificity of predicting highest risk for future CVD. This study showed that NT-proBNP was raised in 29 out of 137 patients which included 15 patients with CD4 count <350 and 14 patients with CD4 >350 . 18 patients are in WHO stage 1 and 2, 11 pts are in WHO stage 3 and 4. Mansoor *et al.*⁽²⁴⁾ showed natriuretic peptide levels as a global marker of co-morbidity in the setting of HIV infection. He documented that HIV infected women have higher NT-proBNP levels than HIV uninfected women, no statistical significant association was found between CD4 count, WHO staging and NT-proBNP in this study.

In the present study, echocardiographic abnormalities were found in 56.2% of the PLHIV. The commonest finding in

our study is valvular abnormalities in 55 pts (40.1%) followed by diastolic dysfunction in 45 pts (32.8%). Other less common cardiac manifestations in decreasing order of frequency were reduced LVEF in 33 pts (24%), pericardial effusion in 15 pts (10.9%), left ventricular hypertrophy in 13 pts (9.4%), pulmonary arterial hypertension in 10 pts (7.2%) and regional wall motion abnormality in 9 pts (6.5%). Diastolic dysfunction is characterized by elevated left ventricular end diastolic pressure despite normal or subnormal diastolic volume. We found 55 HIV pts (40.1%) with Valvular leak, abnormalities seen were mitral regurgitation, tricuspid regurgitation, aortic regurgitation and other multivalvular involvement. No statistical correlation is found in our study between valvular abnormalities and CD4 count, WHO stage of disease. In our study 45 pts (32.8%) diagnosed with left ventricular diastolic dysfunction. In a study by Chang *et al.*⁽²⁵⁾ revealed that LV systolic and Diastolic dysfunctions were positively correlated with decreased CD4 count. The marked absence of endocardial involvement in this study may be related to the low prevalence of intravenous drug abusers⁽²⁶⁾. Interestingly, a study by Nayak *et al.*⁽²⁷⁾ have also reported a high prevalence (37%) of LVDD in a cohort of young (median age: 38 years) asymptomatic PLHA without any other risk factor for CVD. Though the prevalence was low in our study, a similarity in age group was found (mean age of our study was 38.8 year). A high percentage of young patients in our study group may be responsible for the similar findings. Erquo *et al.*⁽²⁸⁾ have reported that the pooled prevalence of grade I to grade III diastolic dysfunction is 29.3% and grade II to III diastolic dysfunction is 11.7%. In this study we didn't find any statistical correlation between diastolic dysfunction and CD4 count, WHO staging. But out of 30 pts (who were WHO stage 3&4) 16 having diastolic dysfunction. In our study pericardial effusion is diagnosed in 10.9% HIV pts. The effusion may be related to the opportunistic infections or malignancy, although a clear etiology could not be established in majority of the cases. The pericardial effusion detected was often small in amount and without any hemodynamic significance. Pericardial effusion in HIV patients may be marker of end stage HIV infection because it is associated with low CD4 count. 12 out of 15 pericardial effusions were reported in CD4 count <350 . And we found a statistical correlation with CD4 count ($p=0.0410023$). However, we didn't find a statistical significant correlation with the WHO Stages. A study done by Heidenreich *et al.*⁽²⁹⁾ showed an increasing trend of pericardial effusion with progression of HIV infection (Asymptomatic HIV positive patients showed an incidence of 0% whereas patients with AIDS had an incidence of 11% per year). We found reduced LVEF in 33 pts (24%). Reduction in ejection fraction without global hypokinesia or chamber enlargement but without any symptom probably represented a mild form of cardiac disease that will progress to a clinically evident form of dilated cardiomyopathy⁽³⁰⁾. We have found a strong

statistical correlation between WHO stage and reduced ejection fraction ($p=0.037929$). we found pulmonary hypertension in 10 pts (7.2%) which was higher than normal population and comparable to studies done by Pellicelli *et al*⁽³¹⁾ and Mehta *et al*⁽³²⁾ who also found higher incidence of pulmonary artery hypertension in HIV patients than normal population. However, in our study 6 out of 10 cases were having WHO stage 3&4 suggestive of advanced disease. In contrast to primary pulmonary hypertension (PPH), in which there is a female predominance, males are more affected by pulmonary arterial hypertension (PAH) associated with HIV infection (HIV-PAH). In our study, 80% (8 out of 10) patients with PAH were males. The pathogenesis of PAH is multifactorial and not known. Patients with HIV-PAH have worse survival than do HIV infected patients without PAH and often die from conditions related to the pulmonary hypertension, not the HIV infection *per se*. we found regional wall motion abnormality in 9 Pts (6.5%) and found a strong statistical correlation between WHO stage and RWMA ($p=0.002514$). We further analyzed the various cardiac abnormalities (chest X-ray, ECG and echocardiographic and NT-proBNP level) with respect to WHO stage and found that there were higher number of cardiovascular abnormalities in WHO Stage III and IV as compared to stages I, II with respect to chest X-ray, echo and ECG. However, valvular abnormalities were almost similar in both the groups. There is widespread agreement that the most important factor for the development of cardiac abnormalities is the level of immune suppression⁽³³⁾. Pericardial effusion has often been considered a marker of end-stage disease because it is associated with a low CD4 count as evident in our study. Our study also shows difference between the prevalence of cardiovascular abnormalities on the basis of CD4 count. The group with lower CD4 count <350 showed higher prevalence as compared to CD4 >350 . However, this difference was not statistically significant. Except pericardial effusion having strong statistical correlation with CD4 count ($p=0.0410023$).

The advanced disease stage also significantly correlated with the echocardiographic findings. Khunnawat *et al.* and Zareba and Lipshultz have reiterated that cardiac manifestations occur at the later stages of disease^(33,34). Sundarrajan *et al.* have also revealed a strong association between the disease stages and echocardiographic manifestations ($p=0.00$), indicating that cardiac abnormalities are directly proportional to the disease stage⁽²⁰⁾.

Our study also shows the relation of the cardiac abnormalities with the duration of ART (Table 2). Most of the patients on ART were more than a year of therapy. Considering these facts, we divided the study population in three groups on the basis of duration of ART. We found that, in the group of ART duration more than 1 year, the cardiovascular abnormalities were more as compared to group with duration of treatment less than 6 months or

between 6 months to 1 year. However, this was not statistically significant.

This finding is similar to several studies which suggested excess risk of cardiovascular events in PLHIV on ART in the form of dyslipidemia, myocardial infarction, and ischemic heart disease^(36,37,38).

Conclusion

1. Cardiac involvement and cardiovascular complications are commonly seen in HIV-infected patients and can present without any clinical manifestation.
2. Even asymptomatic patients had ECG and 2D-ECHO abnormal findings.
3. Heterosexual contact is the most common route for HIV transmission in India as compared to other modes of transmission in western population.
4. As the epidemic progresses and new treatments help increase the long-term survival of affected individuals, cardiovascular complications will become more common.
5. The common cardiovascular manifestation seen in HIV patients is valvular leaks, regional wall motion abnormality, pericardial effusion, reduced EF etc.
6. The incidence of cardiovascular manifestations increases as the disease progresses.
7. Strategies to prevent cardiovascular disease in HIV-infected patients should focus on reducing traditional risk factors, as well as HIV and ART-specific risk factors.
8. ECG and 2D-ECHO to be done as a baseline investigation. And in a regular time interval basis, specially in patients having CD4 count less than 200 and in higher stages (stage 3&4) of the disease.
9. Early recognition and prompt treatment are important to prevent significant morbidity from cardiac involvement. Whether this approach will prolong survival in AIDS patients remains to be seen.
10. Although in our study NT-proBNP was taken as a cardiac biomarker, but it will be better to use Troponin T and Troponin I as cardiac biomarkers specially in patients with ischemia and regional wall motion abnormalities.
11. Further investigational prospective study with greater number of HIV patients and follow-up investigations are required for better understanding of clinical picture and mechanism involved in the development of cardiovascular abnormalities.
12. It's important to stratify CVD risk in HIV-infected patients. Clinicians can use existing general risk stratification algorithms, such as the Framingham Risk Score, to measure HIV patients' risk for heart disease.
13. In essence, it means practicing good preventive medicine with all patients, including those who have HIV.

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