ORIGINAL ARTICLE

CARDIAC MANIFESTATIONS IN HIV/AIDS PATIENTS AND THEIR CORRELATION WITH CD4+T CELL COUNT

Mehul Marwadi[1], Nileshkumar Doctor[2], Gaurang Gheewala[1], Viral Barfiwala[1], Jayesh Rana[3], Neha Bavarva[3]

[1]Resident doctor, Department of Medicine; [2]Associate Proff, Department of Medicine; [3]Resident Doctor, Department of Community Medicine, SMIMER, Surat
Correspondence: Dr. Mehul Marwadi, Email: dr.jayeshrana@gmail.com

ABSTRACT

Introduction: The cardiovascular diseases in HIV/AIDS are increasing in the developing world. Despite this, cardiac involvement is overlooked in HIV-positive patients. The relation of CD4 + T cell count is also important as it correlate with severity of cardiac involvement. The present study is to detect occurrence of cardiac involvement in HIV/AIDS cases and their correlation with CD4+Tcell count.

Objective: The present study is conducted to evaluate the cardiac manifestations, pattern of cardiac involvement and its correlation with CD4+T cell count in HIV/AIDS cases.

Methods: During the period of 1 year from July 2012 to July 2013, total 100 cases of HIV/AIDS were included. The occurrence of cardiac involvement in HIV/AIDS cases was determined based on cardiac enzymes, ECG findings & 2D Echocardiography findings. An attempt was made to correlate various cardiac findings with CD4 T cell count.

Results: Common clinical symptoms were fever (68%), cough (44%) & exertional breathlessness (33%). On 2D echocardiography, Left ventricular diastolic dysfunction was noticed in 28%, pericardial effusion in 14% & Restrictive cardiomyopathy in 7%cases. There was statistically significant relation between left ventricular diastolic dysfunction and pericardial effusion with low CD4+T count. However relation of restrictive cardiomyopathy with CD4+T count was not statistically significant.

Conclusions: Commonly observed cardiac abnormality in HIV/AIDS patients were LV diastolic dysfunction, pericardial effusion & restrictive cardiomyopathy. Asymptomatic cardiac manifestations in HIV/AIDS cases are common. The 2D echo is an important diagnostic tool for the evaluation of cardiac dysfunction. CD4+T cell count is significantly low in cases with cardiac manifestations.

Keywords: Cardiac Manifestation, HIV/AIDS, CD4+T Cell Count

INTRODUCTION

The infection with human immunodeficiency virus is a global pandemic, with cases reported from virtually every country. In Asia, an estimated 4.9 million people were living with HIV at the end of 2007. National prevalence of HIV/AIDS is highest in Southeast Asia, with wide variation in trends between different countries.[1]

The most important clinical application of HIV-related immunology is measurement and interpretation of the absolute CD4 cell count. It is currently recommended that patients have this test performed at the time of HIV diagnosis and then again approximately every 3 to 4 months, usually in conjunction with an HIV RNA (viral load) test. Recovery of the CD4+T cell count in response to anti retroviral treatment has been shown to be the most important predictor of clinical outcome, even more so than the virologic response. The wide range of cardiac abnormalities associated with HIV infection has been suggested by autopsy studies. The various abnormalities include pericardial effusion, lymphocytic interstitial myocarditis, dilated cardiomyopathy (frequently with myocarditis), infective endocarditis, and malignancy (myocardial Kaposi sarcoma and B-cell immunoblasic lymphoma).[2]

The cardiovascular diseases in HIV/AIDS are becoming increasingly recognized in the developing world. Despite this, cardiac involvement can be over looked in HIV-positive patients, because symptoms of breathlessness, fatigue, and poor exercise tolerance are frequently ascribed to other conditions associated with HIV patients is there fore extremely useful to identify cardiac-conditions common in HIV-positive patients. These conditions include pericardial effusion, left ventricular (LV) systolic dysfunction/ heart muscle disease, and intracardiac masses.[3] Heart muscle disease is the most

important cardiac manifestation of HIV infection and is likely to become evenmore prevalent as HIV infected-patients live longer. Myocardial involvement in HIV infection is multifactorial and may arise as a result of myocardial invasion with infection itself, opportunistic infection, autoimmune response to viral infection, drug-related cardiac toxicity, nutritional deficiencies and prolonged immune suppression.[4]

Early detection of cardiac involvement in HIV cases in pre-AIDS or AIDS phase of disease is therefore important to predict the outcome in such cases. The relation of CD4 + T cell count is also important as it correlate with severity of cardiac involvement.

The present study is therefore undertaken to detect occurrence of symptomatic or asymptomatic cardiac involvement in HIV/AIDS cases and their correlation with CD4+Tcell count.

OBJECTIVES

The present study is undertaking with the objectives to evaluate the cardiac manifestations in HIV/AIDS cases; to determine type of cardiac involvement in HIV/AIDS cases; and to correlate CD4+T cell count with pattern of cardiac involvement.

METHODS

The present study is prospective cross sectional study, which was carried out by the department of Medicine, SMIMER; Surat during the period of 1 year from July 2012 to July 2013.The patients admitted in general medicine ward, ICU and on OPD basis with the diagnosis of immunocompromised host were included. Only confirmed cases of HIV/AIDS were included in the study. All patients of human immune deficiency virus (HIV) infection who are asymptomatic or symptomatic for cardiac involvement were included in the study. Patients with established myocardial disease, valvular heart disease or congenital heart disease were excluded from the present study. Patients less than 18 years of age were excluded from the study.

Total 100 cases of HIV/AIDS were included irrespective of duration of illness and presence or absence of clinical symptoms of cardiac involvement. All cases were examined in details to find out any evidence of cardiac failure, infective endocarditis or any other complication of cardiac involvement. The detailed systemic examination was carried out for cardiovascular, respiratory and abdominal examination. The diagnosis of HIV/AIDS was established in all cases by carrying out blood test. It included COMBAIDS-RS screening test, NanoHIV1/2 Triline and Pareekshak spot test.[5]

All the cases included in the study were then subjected for the investigations. Hemoglobin estimation was done by Drab kin's method.[6] Total and differential leucocyte count was performed in all cases. The CD4 T cell count was carried out in all cases using flow cytometry by BD FACS count.[7]Various biochemical test included serum glutamate oxaloacetate transaminase (SGOT) estimation by optimized UV method[8] and Creatinine kinase MB (CKMB) estimation by immunoinhibitation method[9] and lactate dehydrogenase (LDH) estimation by UV method.[10]

All the cases were then subjected for investigation to suggest cardiac involvement. These included 12 lead ECG recording using Philips Paper writer 100, X-ray chest PA view and 2 Dimensional echocardiography. Left ventricular hypertrophy was diagnosed on ECG when it showed the changes as per the criteria given by Romhilt-Estes point score system (points). Increased QRS magnitude = 3 points (Any limb lead R wave or S wave ≥2.0mV) or SV1 or SV2≥3.0mV) or (RV5 to RV6≥3.0mV)

Two dimensional and M mode echocardiography were carried out in all cases using a Philips EnVisor C.1.5 2D-Echocardiography Machine. Left ventricular diastolic dysfunction was said to be present on 2D echocardiography when it showed abnormal myocardial relaxation. The mitral E (early diastolic mitral flow velocity) velocity & and A (late diastolic mitral flow velocity) velocity was also calculated.[11]The patient was said to have pericardial effusion if 2D echocardiographic showed echo-free space between the visceral and parietal pericardium persisted throughout the cardiac cycle. The diagnosis of restrictive cardiomyopathy was made on 2D echocardiography when it showed limited ventricular filling resulting from an idiopathic nonhypertrophied myocardial abnormality (fibrosis or decreased compliance or both) & typical ventricular diastolic pressure tracing in the dip-and-plateau, or square root configuration also the E/A ration to increase markedly (>2).[12]

The occurrence of cardiac involvement in HIV/AIDS cases was then determined based on cardiac enzymes, ECG findings & 2D Echocardiography findings. An attempt was made to correlate various cardiac finding with CD4 T cell count. The various grades of LV diastolic dysfunction & pericardial effusion were also correlated with CD4 T cell count.

The statistical analysis was done in all cases using chi-square test and results were summarized.

RESULTS

In the present study out of 100 cases studied, 75% cases were males and 25% cases were females. Male to female ratio was 3:1. Mean age of patient was 32.2 year. The results are depicted in the Table 1.

Table 1: Age and sex distribution

Age group(years)	Male (%)	Female (%)	Total (%)
20-30	22	8	30
31-40	30	8	38

41-50	23	9	32
Total	75	25	100

Common clinical symptoms were fever (68%), cough (44%) & exertional breathlessness (33%). Other symptoms observed were weight loss (22%), malaise (21%), loose motion (20%), headache (18%), vomiting (18%) & palpitation (11%). On general examination common findings were pallor (44%), lymphadenopathy (38%), tachycardia (36%) & raised Jugular venous pressure in 6%cases. Further oedema feet was seen in 4% and icterus was found in 4%cases.

Examination of cardiovascular system revealed no abnormality in any case. On respiratory system examination 11% patients had findings suggestive of pleural effusion, 8% patients had finding suggestive of fibroactive disease. On abdominal examination hepatosplenomegaly was seen in 19%patients.

Out of 100 cases 33%were having CD4+Tcell count more than 200cells/mm3 while in 9% cases CD4+T cell count less was than 50cells/mm3 CD4 count. The CD4+ T cell count was between151-200cells/mm3 in 26% cases, 51-100 in 13%patients and 101-150 cells/mm3 in 19%cases.In this study 24% patients had raised CKMB levels, 32% cases had raised LDH levels and 30% cases had raised SGOT levels. Clinically evident cardiac involvement was not observed in any of these cases.

In the present study, out of 100 cases studied 62% of the patients had normal X-ray chest. Cardiomegaly was present in 8%patients.Pleural effusion was seen in 6%cases and fibrocaseous lesion was seen in 7%patients.In 12% cases X ray chest was showing bilateral reticulonodular shadows & cavitary lesions were noticed in 5% cases. In the present study, out of 100 cases studied 62%patients had normal ECG. Commonest abnormalities were sinus tachycardia observed in 24% cases. Further ECG was suggestive of left ventricular hypertrophy in 8% cases & it showed low voltage complexes in 6% cases only.

Table 2: Correlation of 2D-echocardiographic findings with CD4+Tcell count:

Diagnosis		CD4 Count (N=100)		P value*
		≤200	>200	
LV diastolic dysfunction	Yes	27	1	<0.001
	No	40	32	
Pericardial effusion	Yes	14	0	0.002
	No	53	33	
Restrictive Cardiomyopathy	Yes	6	1	0.2601
	No	61	32	

*Chi-square test is applied

It was observed that 2D echocardiography was normal in 51%cases.Left ventricular diastolic dysfunction was the commonest findings being noticed in 28%.Pericardial effusion of various grades was observed in 14% cases& restrictive cardiomyopathy was noted in 7%cases.It was noticed further that all the 8%cases who showed evidence of LVH on ECG showed LV diastolic dysfunction and all 6% cases who had low voltage complexes in ECG had pericardial effusion on 2D echocardiography. Thus it can be concluded that based on ECG & 2D echocardiography, cardiac manifestation in HIV/AIDS cases was noticed in 49% cases.

An attempt was made in the present work to correlate various findings on 2D echocardiography with CD4+ T cell count as depicted in table 2.

It was noticed amongst 28% cases with left ventricular diastolic dysfunction; CD4+T cell count was less than 200cells/mm3 in 27% cases, while in 1% case it was more than 200cells/mm3. This is statistically significant.

Amongst 14% cases with pericardial effusion, all cases had CD4+ T cell count was less than 200cells/mm3. This is statistically significant.

Furthermore amongst 7% cases with restrictive cardiomyopathy, CD4+ T cell count was less than 200cells/mm3 in all 6% cases. This was however statistically not significant.

Two dimensional echocardiography was within normal limits in 51% cases.

Table 3: Correlation of CD4+Tcell count with severity of pericardial effusion:

Grades of pericardial effusion	Cases	CD4+Tcell count	
		≤200	>200
Mild	8	8	0
Moderate	5	5	0
Severe	1	1	0

Further among 14% cases with pericardial effusion, 8% cases had mild pericardial effusion, 5%cases had moderate pericardial effusion and 1%case had severe pericardial effusion. In all 14% cases with pericardial effusion CD4+T cell count was <200 cells/mm3. The 6% cases with moderate and severe pericardial effusion were subjected for pericardial paracentesis.

DISCUSSION

In the present work maximum cases were in the age group of 31-40 years of age and male to female ratio was 3:1. In a study carried by Shrinivas et al (2006) most of the patients belonged to young age between 26 to 40 years and male to female ration was 4:1.

The common symptoms noticed in the present study were fever in 68% cases, cough in 34% cases, breathlessness in 33% cases & weight loss in 22% cases. Basvaraj et al (2001)[13] noticed commonest symptoms in their study as fever (82.5%), cough (67.5%) and breathlessness (45%). Andrew et al(2009)[14] noticed fever in 81% of the patients, cough in 55% and weight loss in 51% in their study. The general physical examination in

the study population showed pallor in 44% cases, lymphadenopathy in 38% cases, and tachycardia in 36% cases. Andrew et al (2001) noticed clinical signs which included lymphadenopathy in 51% cases, pallor in 40% cases and hepatospleenomegaly in 20% cases.

In the present study, out of 100 cases 33% were having CD4+Tcell count more than 200cells/mm3 while in 9%cases CD4+Tcell count was less than 50cells/mm3. Shrinivas et al(2006)[25] noticed that out of 50 patients studied, 16 patients (32%) had CD4+T cell counts more than 200 cells/mm3, 6 patients (12%) had CD4+T cell count less than 50 cells/mm3.

In the present study, out of 100 cases studied 62% patients had normal X-ray chest. Cardiomegaly was present in 8% patients. Pleural effusion was seen in 6% cases and fibrocaseous lesion was seen in 7% patients. In 12% cases X ray chest was showing bilateral reticulonodular shadows.Shrinivas et al (2006)[15] noticed that out of 50 cases, 33 patients (66%) had normal chest x-ray. Commonest abnormality noted in chest x-ray in HIV individuals were cardiomegaly in 14% cases, pleural effusion in 12% cases.

In the present study, out of 100 cases studied, 62% patients had normal ECG. Commonest abnormalities were sinus tachycardia in 24% cases, left ventricular hypertrophy in 8% cases & low voltage complexes in 6% cases only. Hamide et al (2002)[16] noticed sinus tachycardia in 40% cases, low voltage complex in 10% cases, ischemic heart disease in 3% cases & left ventricular hypertrophy in 4% cases. The sinus tachycardia might suggest and early evidence of cardiac failure or left ventricular diastolic dysfunction.

It was observed that 2D echocardiography was normal in 51% cases, while various abnormalities were observed in 49% cases. Left ventricular diastolic dysfunction was the commonest findings being noticed in 28%. Other abnormal findings were pericardial effusion in 14% cases and restrictive cardiomyopathy in 7% cases. The finding of left ventricular diastolic dysfunction was much higher in the present work compared to previous workers. Basavraj et al (2002)[13] noticed it in 10% cases, Hamide et al[16] in 7% cases. A very high prevalence of 64% was noticed by Schuster et al (2008).[17] The left ventricular diastolic dysfunction is one of the earliest evidence of myocardial involvement and may be an asymptomatic in early stages. The clinical symptoms appear with higher grades of left ventricular diastolic dysfunction. In the present work high incidences of left ventricular diastolic dysfunction therefore might suggest higher symptomatic cardiac manifestations in case of HIV/AIDS.

Further among 14 cases with pericardial effusion, 8 (57.14%) had mild pericardial effusions, 5 (35.71%) cases had moderate effusion and 1(7.14%) case had severe pericardial effusion.

Shrinivas et al (2006)[15] noticed CD4 abnormalities in 28% cases of the pericardial effusion. Out of these 28% most of them were mild in 22% cases, moderate in 4% cases, large in 2% cases. Severity of pericardial effusion increases with lowering of CD4 counts.

Restrictive cardiomyopathy was observed in 7% cases in the present study. All these cases has CD4 +T cell count less than 200/mm3.Giuseppe et al (1999)[18] noted ecocardiograhphic diagnosis of restrictive cardiomyopathy in 8% cases. The incidence of restrictive cardiomyopathy was higher in the patients of CD4+ TCELL count less than 200/mm3.

In the Present work it was observed that in 28% cases with left ventricular diastolic dysfunction CD4 +T cell count was less than 200 cells/mm3 in 17 cases (60.71%) while it was more than 200cells/mm3 in 11(39.28%) cases. The correlation of CD4+ T cell count was correlated with severity of pericardial effusion. Shrinivas et al (2006)[15] correlated pericardial effusion with CD4+ T cell count and observed that presence of pericardial effusion is positively related to the less CD4 counts.

CONCLUSION& RECOMMENDATION

It is concluded from the present work that commonly observed cardiac abnormality in HIV/AIDS patients were LV diastolic dysfunction, Pericardial effusion & restrictive cardiomyopathy.

All the cases with cardiac manifestations in HIV/AIDS cases are not symptomatic. Asymtomatic cardiac manifestations in HIV/AIDS cases are common.

The 2D echo is an important diagnostic tool for the evaluation of cardiac dysfunction in all patients.

The CD4 T cell count is significantly low in cases with cardiac manifestations. There is statistically significant correlation with severity of pericardial effusion & left ventricular diastolic dysfunction.

It is therefore recommended that cardiac evaluation based on cardiac enzymes, ECG, & 2D Echocardiography should be undertaken at periodic interval to detect early involvement of cardiac system in HIV/AIDS cases.

REFERENCES

1. Anthony S,Facci,H.Clifford Lane,Harrison`s internal medicine 18th edition, volume 1, chapter 189, page no 1506,human immunodeficiency virus disease:AIDS and related disorders,Mc Graw Hill.
2. Paul E.sax Bruce D.Walker, Goldman: cecil Medicine,23rd ed.chapter 408,CLINICAL IMPLICATIONS OF HIV-RELATED IMMUNOLOGY, Saunders,An imprint of Elsvier.
3. Currie PF,Jacob AJ,Foreman AR, et al. Heart muscle disease related to HIV infection :prognostic implications.Br Med J 1994;309:1605-1607.[PMID:7819934]
4. Ntsekhe M,Hakim J. Impact of HIV infection on cardiovascular disease in A.CoralloS,MultinelliMR,Moroni M, et al. Echocardiography detects myocardial damage in PMID:18322768[Pubmed –indexed for MEDLINE]
5. Gallo RC ,Salahuddin SZ,Ppopovic,M et al science 224:500-503,1984.

6. Dacie and Lewis 10thediction practical hematology .[estimation of hemoglobin]
7. Rumke CHRL-Impression of ratio derived differential lymphocyte count.Blood cell 1985.11311-314.
8. IFCC CLIN CHIM 70/2 F19 [1976]
9. Wong ss 1996 Ana clin 26/4 301.
10. Recommendation for measurement of LDH in human serum at 30 degree Ann Biol,Chem (1982)
11. Libby:Braunwald's Heart Disease:A textbook of cardiovascular medicine,8thedElsvier.Chapter 14, Saunders,An Imprint of elsvier.
12. Heidi M.Connolly jae K. OH Joshua M.Hare , Libby:Braunwald`s Heart Disease
13. Basvaraj Anita et al,Cardiac dysfunction associated with HIV infection.JAPI Vol.51.DEC 2003:1182.
14. Andrew, Deepak, Rajiv, Jayprakash B, Rau NR Clinical profile of newly detected HIV patients:A prospective study in a tertiary hospital kasturba medical college,Manipal,Karnataka.
15. Shrinivas et al, A CLINICAL STUDY OF CARDIAC DYSFUNCTION WITH HIV INFECTION/AIDS;Rajiv Gandhi University of Health Sciences.textbook of cardiovascular medicine,8th ed page no.282.
16. Hamide et al,JIPMER, Pondicherry.
17. Schuster I,Thoni GJ,Ederhy S,Walther G,Nottin S,Vinet A,Boccara F,Khireddine M,Girad PM,Mauboussin JM,Rouanet I,Dauzat M,Cohen A,Messner –Pellenc P,Obert,Subclinical Cardiac abnormalities in HIV infected men receiving ART.
18. Giuseppe Barbaro , M.D., Gabriella Di Lorenzo, M.D., BenvenutoGrisorio,M.D., Giorgio Barbarini, M.D. for the GruppoItaliano Per lo studiocardiologicodeiPazientiAffetti da AIDS.Incidence of dilated cardiomyopathy and detection of HIV in myocardial cells of HIV positive Patients.