Association of CD4 Counts with Cardiovascular Dysfunction among HIV/AIDS Patients - A Hospital Based Study in North Karnataka

Nandini Devru[1], Swetha Rajshekhar Lakshetty[2], Anand Katageri[3]

[1, 2] Department of Internal Medicine, ESI Medical College, Kalaburagi, Gulbarga, Karnataka, India. [3]Department of Internal Medicine, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Kalaburagi, Gulbarga, Karnataka, India.

ABSTRACT

BACKGROUND

Globally the number of people living with human immunodeficiency virus/ acquired immunodeficiency syndrome (HIV/AIDS) has been rising steadily since 2011 nearing more than 33 million whereas in developing countries like India it is 2.4 million with a prevalence of 0.3%. The purpose of this study was to assess the association of CD4 counts with cardiovascular dysfunction among HIV/AIDS patients.

METHODS

This was a hospital-based study conducted at the Vijayanagara Institute of Medical Sciences, Bellary. Convenience sampling was used and patients admitted to the wards of the internal medicine as well as those attending anti-retroviral therapy (ART) centre out-patient department (OPD) were included in the study. A total of 200 cases of seropositivity of HIV patient diagnosed by Elisa technique were assessed after obtaining informed consent. Clinical profile and laboratory investigations were carried out on the patients such as CD4 counts and analyzed with various cardiac dysfunction.

RESULTS

Commonest affected with HIV infection were young male (26 – 40 years) 77.5 % followed by young female 60 % Commonest symptoms were fever, cough 82 % each and breathlessness 44 %. Commonest clinical findings were pallor 80 %, pedal oedema 68 %, and lymphadenopathy 32 %. 26 % of patients had electrocardiography (ECG) abnormalities with commonest being sinus tachycardia 18 %, low voltage complex 4 %, IHD (ischemic heart disease) 2 %, LVH (left ventricular failure) 2 %. 34 % had chest x-ray abnormalities such as cardiomegaly 14 %, pleural effusion 12 % and PTB (pulmonary tuberculosis) 2 %. Abnormal CD4 counts were noted in 94 % of patients, with 12 % having very low CD4 counts that is less than 50. Statistically significant pericardial effusion was noted with low CD4 counts on 2D ECHO cardiography.

CONCLUSIONS

The study concludes that decrease in CD4 count is statistically associated with increased pericardial effusion among HIV/AIDS patients.

KEYWORDS

CD4 Counts, HIV/AIDS Patients, Cardiovascular Dysfunction, Pericardial Effusion

Corresponding Author:
Dr. Swetha Rajshekhar Lakshetty,
Senior Resident,
ESI Medical College,
Kalaburagi, Karnataka, India.
E-mail: intellects19@yahoo.com

DOI: 10.18410/jebmh/2021/477

How to Cite This Article:
Devru N, Lakshetty SR, Katageri A. Association of CD4 counts with cardiovascular dysfunction among HIV/AIDS patients - a hospital-based study in north Karnataka. J Evid Based Med Healthc 2021;8(29):2584-2588. DOI: 10.18410/jebmh/2021/477

Submission 03-02-2021,
Peer Review 14-02-2021,
Acceptance 29-05-2021,
Published 19-07-2021.

BACKGROUND

The prevalence of cardiac involvement in AIDS patients has been reported to range between 28 % and 73 %.[1] From a meagre 5 cases reported in homosexual men in 1981 the disease has grown into a global pandemic. In 2008, the number of cases reached an estimated 33.4 million [31.1 million – 35.8 million]. People living with HIV in India in 2008 were 22.7 lakh with an estimated adult HIV prevalence of 0.29 %. While prevalence in Tamil Nadu during 2007 was 0.44.[2] Females constituted around 39 % of the burden (0.9 million) and children below 15 years constituted 3.5 % of the burden. AIDS is the result of severe HIV infection and the infected individual's immune system gets severely compromised.

Cardiovascular abnormalities especially coronary heart diseases (CHD), pericardial effusion, myocarditis, cardiomyopathy, endocarditis as well as drug induced cardiotoxicity are more commonly seen among HIV patients due to long survival of these patients. Various studies have shown rapid fatality among AIDS patients and demonstrated that cardiomyopathy is 10 % higher among them as compared to other individuals. Pericardial effusion in HIV patients may be a marker of end-stage HIV infection because it is associated with low CD4 cell count and is often caused by opportunistic infections and malignant neoplasms seen in the advanced stage of AIDS.[3-5]

Acute HIV syndrome occurs within 3 - 6 weeks after infection in 50 – 70 % of infected individuals and can vary in severity from individual to individual. It presents as an acute mononucleosis like illness. CD8 + CD38 + T lymphocytes are cytotoxic and increased percentage of CD38 + CD8 + T lymphocytes in peripheral blood reflects a higher viral load and disease progression.[4,5] The currently available techniques for CD4 + T cell counting can be classified into automated and manual methods. Automated methods include flow cytometry and dedicated cytometers. Flow cytometry is the gold standard technology for CD4 + T cell counting.

Human immunodeficiency virus has an extraordinary ability of mutation on V3 region of gp120 and hence escape neutralizing antibodies. The CD8 + T lymphocytes require lymphocytes produces induction as well as maintenance of CD4 + T cell responses. CD8 +T cell are reduced with the depletion of CD8 + T cells function. There are also deletion and loss of CD8 + T lymphocytes due to increased exposure to viral antigen. Antibody demonstration using enzyme linked immune sorbent assay (ELISA) is the standard screening test for HIV infection with the sensitivity of > 99.5 %. Whereas western blot test is the confirmatory test to detect antibodies to HIV proteins other investigations include deoxyribonucleic acid (DNA), polymerase chain reaction (PCR)< ribonucleic acid- polymerase chain reaction (RNA-PCR), P 24 antigen and b DNA. AIDS manifestations vary widely among different individuals and hence difficult to predict but certain traits help in staging of disease and also predicts the opportunistic infection. Anti P24 core antibodies decline correlates with poor prognosis among patients with HIV. While absence of anti gp 120 antibodies associated with clinical AIDS manifestation.[5,6]

The CD4 + T cell counts reveal the degree of immune deficiency as well as predict the risk of opportunistic infections. While HIV RNA helps to predicts the response of immune system. RT-PCR (Reverse transcription-polymerase chain reaction), nucleic acid sequence-based amplification (NASBA) and branched DNA (b-DNA) are used to measure plasma RNA. These tests can detect viral level as low as 20 - 50 molecule of HIV RNA per ml of plasma. The plasma viral load can be used to assess the disease progression as well as prediction to start anti-retroviral therapy. Plasma viral load of more than 30,000 and bDNA assay >55000 is an indication to put the patients on antiretroviral therapy. The effectiveness of treatment is assessed by low viral load which is assessed once in every 3 to 4 months after initiating the anti-retroviral therapy.

Research also reveals that one in every five HIV patients have pericardial effusion, which shows highest cardiovascular involvement among these patients. They also manifest various asymptomatic cardiovascular presentations like cardiac tamponade and constructive pericarditis. Clinical manifestations of pericarditis are similar between patients with and without HIV infection. Hence with this background present study was undertaken to assess the correlations of CD4 count, ECHO, chest X-ray and ECG on cardiac abnormalities among HIV/AIDS patients in North Karnataka.

Objectives

To assess the clinical profile of cardiac abnormalities in HIV/AIDS patients and its correlations CD4 count, Echo, chest X-ray and ECG.

METHODS

This was a hospital based cross-sectional study conducted at the Vijayanagara Institute of Medical Sciences, Bellary. Patients admitted to the wards of the internal medicine and patients attending ART centre out-patient department were subjects of the study. This study was carried out from February 2011 to June 2012. A total of 200 cases of seropositivity of HIV patient diagnosed by ELISA technique were selected for the study based on hospital based convenience sampling technique. The patients were enrolled after obtaining a detailed socio demographic profile and history about illness. They underwent complete general physical and systemic examination including detailed cardiovascular examination. The cardiovascular investigations included CD4 counts, ECG, ECHO, chest x-ray and analyzed for different cardiac dysfunction. The findings of LV internal dimension in systole and diastole (LVIDs and LVIDd), inter ventricular septal thickness in systole as well as diastole, fractional shortening (FS) and ejection fraction (EF) were studied in ECG. The patients were further evaluated for CD$ counts for different cardiac dysfunction. The study was started after obtaining ethical clearance from institutional ethical committee and informed consent from the participants. Investigations required were routine investigations of blood HIV 1 and 2 (ELISA), CD4 count**.**

Inclusion / Exclusion Criteria

The patients aged >15 years attending OPD, ART centre and in patients, those diagnosed to have HIV infection/AIDS after S.D Bioline, Triline and Tri-spot tests being positive were included in the study. While those with congenital heart diseases, pre-existing valvular heart disease, hypertension, diabetes mellitus were excluded from the study.

Statistical Methods

Chi-square and Fisher exact test were used to test the significance of proportion of pericardial effusion in relation to counts and Odds Ratio has been used to find the relationship of cardiac dysfunction with CD4 counts. Microsoft excel were used to calculate percentage, mean, standard deviation and to generate tables.

RESULTS

200 ELISA positive HIV infected individuals who fit into inclusion criteria during the study period were taken up for this present study. Following are the results and observations of the study. 80 % of the patients were males and 20 % were females. Most of our patients belong to young age between 26 to 40 years. Male were more 77.5 % as compared to females 60 %. 28 patients (56 %) had CD4 counts between 50 - 200 while 13 patients (26 %) had CD4 counts 200 to 350. Six patients (12 %) had CD4 counts less than 50 while only 3 patients (6 %) had good CD4 counts that are more than 350.

CD4 counts were analyzed against different cardiac dysfunction in all patients. The results showed that 56 patients (28 %) had pericardial effusion on 2D ECHO, while 144 patients were without pericardial effusion. Most of them were mild pericardial effusion (22 %) while moderate were 4 % and large 2 %. Patients presented with pericardial effusion are 9.9 times significantly more to have CD4 counts less than < 200 and the results were statistically significant. Presence of pericardial effusion is positively related to the less CD4 counts (CD4 < 200). (Table No.1)

Present study shows that risk of developing pericardial effusion, systolic dysfunction and pulmonary hypertension increases when CD4 counts decreases less than 200 per micro litre. It is statistically significant with P less than 0.05. Pericardial effusion was seen among 38 % of patients with CD4 count ≤ 200 while only 6 % pericardial effusion was seen with CD4 counts > 200.

While dilated cardiomyopathy, diastolic dysfunction mitral regurgitation and pericardial effusion were not significantly associated with CD4 counts with 3 % dilated cardiomyopathy seen with ≤ 200. 9 % of the patients with ≤ 200 showed systolic dysfunction while no systolic dysfunction was seen among patients with > 200 CD4 counts. The CD4 counts when cardiac dysfunction is absent is 224.45 ± 160.51 ranging from 33 to 700 and when the cardiac dysfunction is present the CD4 count decreased to 107.48 ± 57.68 ranging from 8 to 226 with P value 0.030. Diastolic dysfunction, Mitral regurgitation and pericardial effusion were seen in 15 %, 3 % and 29 % of patients with CD4 counts ≤ 200 respectively but the association was not statistically significant. 21 % of patients with pulmonary hypertension had CD4 counts ≤ 200 and the results were statistically significant with P value < 0.05.

Significant cardiac dysfunction noted in HIV infected individuals. 2D ECHO cardiography is an important diagnostic tool for the evaluation of cardiac dysfunction in these patients. Significant cardiac dysfunctions were noted with low CD4 counts. Pericardial effusion, Pulmonary hypertension, asymptomatic diastolic dysfunction were commonly encountered.

	Variables	CD4 Count (cells/µL) ≤ 200 n (%) = 136	CD4 Count (cells/µL) ➢ 200 n (%) = 64	χ^2-Value / Fisher's Exact test (P - Value)
Pericardial effusion	Yes	52 (38)	4 (6)	< 0.001*
	No	84 (62)	60 (94)	
Dilated cardio myopathy	Yes	4 (3)	0 (0.0)	0.308
	No	132 (97)	64 (100)	
Systolic dysfunction	Yes	12 (9)	0 (0.0)	0.01*
	No	124 (91)	64 (100)	
Diastolic dysfunction	Yes	20 (15)	4 (6)	0.104
	No	116 (85)	60 (94)	
Mitral regurgitation	Yes	4 (3)	0 (0.0)	0.308
	No	132 (97)	64 (100)	
Pulmonary hypertension	Yes	28 (21)	0 (0.0)	< 0.05*
	No	108 (79)	64 (100)	
Pericardial effusion	Mild	40 (29)	4 (6)	0.567
	Moderate and large	12 (71)	0 (0.0)	

Table 1. Association of CD4 Counts with Cardiac Dysfunction in HIV/AIDS

***indicates statistically significant associations**

	Present Study	Heidenreich et al[9]
CD4 count <200	26%	12%
CD4 count >200	2%	4%

Table 2. Comparison of CD4 Counts among Different Studies

DISCUSSION

HIV infection has become pandemic and its incidence and prevalence is fast increasing. The trend is no different in India. Cardiac involvement in HIV infected individuals occurs frequently and occurs quite early in disease process. Cardiac dysfunction is clinically quiescent in the early stages and later it may become direct cause of death. The technique for CD4+ T cell counting is basically of two types which are automated and manual. Automated technique includes flow and dedicated cytometry. Flow cytometry is the standard technology for CD4 + T cell counting.

Cardiac dysfunction was noticed 42 % in present study, compared to 55 % involvement in Basvaraj Anita et al.[5] CD4 abnormalities noted in 28 % of the pericardial effusion in present study. Most of them were mild 22 %, moderate 4 % and severe 2 %. Severity of pericardial effusion increases with lowering of CD4 counts. Same was observed in international study, confirming pericardial effusion is seen in advance stage of HIV infection.[6,7] The CD4 + lymphocyte count is less than 200/micro litre in HIV/AIDS patients. The opportunistic infections, neoplasms and neurological disorders seen at this stage constitute the AIDS defining conditions.[8] (Table No.2)

Routine assessment of vital signs like blood pressure and blood sugar are essential among HIV infected patients since

they are at increased risk of developing cardiac abnormalities even at younger age group as compared to general population. Predisposing factors include vasculitis, acquired resistance to glucocorticoids, acute as well as chronic renal failure, interaction with drugs like indinavir with stavudine, phenyl propanolamine as well as atherosclerosis. Echo cardiography serves as a useful tool in assessing increased left ventricular mass and right ventricular pressure in patients with pulmonary hypertension.

Presence of p24 antigenemia with low CD4 + T cell count is a very strong predictor of disease progression Sabin et al. (2001).[9] A positive P 24 antigen result, in chronic HIV infected individual is associated with declining CD4 cell counts – Hughes et al.[10] P24 antigen detection is hindered by P24 antigen–antibody complex. In advanced HIV disease, diminished delayed hypersensitivity response to recall antigens (mumps, candida, tetanus and trichophyton) is seen. Anergy was earlier used as a criterium in Walter reed staging system.[10] CD4 + lymphocytes play a central role in both humoral and cell mediated immune defense. Progressive depletion of CD4 + lymphocytes is the hallmark of HIV disease.

CD4 + lymphocytes are progressively lost during the course of HIV disease and lower levels of CD4 + lymphocyte count are indicative of more serious immunodeficiency and more advanced disease.[11,12] Echocardiographic findings, include 4–chamber enlargement, diffuse left ventricular hypokinesis, and decreased fractional shortening. Coudray and colleagues.[13]

Various researches have shown that left ventricular diastolic impairment is more common during initial stage of HIV infection. Dilated cardiomyopathy occurs late in the course of HIV infection and is usually associated with a significant reduced CD4 cell count.[14,15] However, there was no association between the progression of left ventricular dysfunction and the rate of CD4 cell count decline.[16]

Several studies[17,18] have supported the direct role for HIV-1-mediated cardiac injury, but the mechanism remains unclear. While the findings showed myocardial inflammation was induced due to the alteration of T-helper cell function and uncontrolled hyper gammaglobulinemia. The HIV gene may provoke cell surface cardiac muscle protein, resulting in the induction of circulated cardiac autoantibodies, which can trigger a progressively destructive autoimmune reaction.[19]

In the present study, sinus tachycardia was commonest observation followed by low voltage complexes and IHD changes. They are on par with most of the national and international studies.[5,8] Commonest ECHO cardiograph abnormality noticed was pericardial effusion is 28 % in present study. Other abnormalities noted in present study are pulmonary hypertension 14 %, diastolic dysfunction 12 %, systolic dysfunction 6 % which are on par with other studies.[5,8]

Moreno et al. reviewed echocardiographic studies in 141 HIV-infected patients, and 55 (39.0% of them had pericardial effusion. The study was mainly used to compare the clinical presentation of patients of pericarditis with mild, moderate and severe pericardial effusion. The study revealed that abnormalities such as pericardial friction rub and electrocardiographic repolarisation which are persistent among pericarditis patients were also common among patients with moderate and severe pericardial effusion. The results are quite unclear, as cause for pericardial effusion among HIV patients is not possible.[20]

In a study carried out by Flum et al. among 29 AIDS patients with pericardial effusion to assess the cause for pericardial effusion. These patients underwent pericardial fluid culture and pericardial biopsies to assess the cause for pericardial effusion. The results revealed that major cause for pericardial effusion among AIDS patients were lymphoma followed by *Staphylococcus aureus* and *Mycobacterium tuberculosis*. The also showed that *Staphylococcus aureus* pericarditis is a fetal condition while cardiac tamponade develops rapidly.[21,22]

In a study carried out by Karve et al. revealed that HIV patients with pneumococcal pericarditis showed high prevalence of cardiac tamponade. Another study revealed that AIDS patients with *Mycobacterium tuberculosis* had easily developed extrapulmonary tuberculosis. They also showed that 5 % of the patients with extra pulmonary tuberculosis developed tuberculosis pericarditis. Research also showed that AIDS patients with cryptococcal infection had pericarditis. The other causes for pericardial effusion and cardiac tamponade among AIDS patients were Kaposi sarcoma and multiple unusual organisms.[23,24,25]

Heidenreich et al. carried out research to assess the incidence of pericardial effusion and its association with mortality among people leaving with AIDS. This was a cohort study carried out among AIDS patients for a duration of five years. The results showed that majority of the patients developed small pericardial effusion followed by moderate and large pericardial effusion. Very few patients developed cardiac tamponade that required drainage. The results also showed that AIDS patients with pericardial effusion had higher incidence of cardiac tamponade, while size of pericardial effusion was not significantly associated with survival.[8]

CONCLUSIONS

26 % of patients had ECG abnormalities with commonest being sinus tachycardia 18 %, low voltage complex 4 %, IHD 2 %, LVH (left ventricular hypertension) 2 %. Abnormal CD4 count was noted in 94 % of patients, with 12 % having very low CD4 count less than 50. Statistically significant pericardial effusion was noted in low CD4 count on 2D ECHO cardiography, pericardial effusion noted in 28 % of the individual, followed by pulmonary hypertension 14 %, followed by diastolic dysfunction 12 %. Hence, we suggest all HIV infected patients to undergo cardiac evaluation by 2D ECHO cardiography, at diagnosis and at periodic intervals.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Aggarwal P, Sharma A, Bhardwaj R, et al. Myocardial dysfunction in human immunodeficieny virus infection: an echocardiographic study. J Assoc Physicians India 2009;57:745-746.

[2] HIV Sentinel Surveillance and HIV Estimation 2007: A Technical Brief. National Aids Control Organisation, Ministry of Health and Family Welfare, Government of India, Oct 2008.

[3] Cohen O, Weissmann D, Fauci AS. The immune pathogenesis of HIV infection. Chap - 44. In: Paul E, edr. Fundamental Immunology. 4th edn. Philadelphia: Lippincott-Raven Publishers 1999: p. 1455-1510.

[4] Kelly M. Natural history of HIV infection. Chap – 3. In: Hoy J, Lewin S, eds. HIV management in Australasiaa guide for clinical care. Australian Society for HIV Medicine Inc., 2003: p. 41-49.

[5] Basvaraj A. Cardiac dysfunction associated with HIV infection. J Assoc Pjysicians India 2003;51:1182.

[6] Lafeuillade A, Tamalet C, Pellegrino P, et al. Correlation between surrogate markers, viral load and disease progression in HIV-1 infection. J Acquir Immune Defic Syndr 1994;7(10):1028-1033.

[7] Tsoukas CM, Bernard NF. Markers predicting progression of human immunodeficiency virus related disease. Clinical Microbiology Reviews 1994;7(1):14-28.

[8] Heidenreich PA, Eisenberg MJ, Kee LL, et al. Pericardial effusions in AIDS: incidence and survival. Circulation 1995;92(11):3229-3234.

[9] Sabin CA, Lepri AC, Devereux H, et al. Relationship among the detection of p24 antigen. Human Immunodeficiency Virus (HIV) RNA level. CD4 cell count and disease progression in HIV- infected individuals with haemophilia. J infect Dis 2001;184(4):511-514.

[10] Hughes MD, Stein DS, Gundacker HM, et al. Within subject variation in CD4 lymphocyte count in asymptomatic human immunodeficiency virus infection: implications for patient monitoring. J Infect Dis 1994;169(1):28-36.

[11] Portella MC, Simpson KN. Markers cofactors and staging systems in study of HIV disease progression – a review. Mem Inst Oswaldo Cruz 1997;92(4):437-457.

[12] Phillips AN, Lee AC, Elford J, et al. Serial CD4 lymphocyte counts and development of AIDS. Lancet 1991;337(8738):389-392.

[13] Coudray N, de Zuttere D, Force D, et al. Left ventricular diastolic function in asymptomatic and symptomatic human immunodeficiency virus carriers: an echocardiographic study. Eur Heart J 1995;16(1):61-67.

[14] Currie PF, Jacob AJ, Foreman AR, et al. Heart muscle disease related to HIV infection: prognostic implications. BMJ 1994;309(6969):1605-1607.

[15] Jacob AJ, Sutherland GR, Bird AG, et al. Myocardial dysfunction in patients Infected with HIV: prevalence and risk factors. Br Heart J 1992;68(6):549-553.

[16] Acierno LJ. Cardiac complications in acquired immune deficiency syndrome (AIDS): a review. J Am Coll Cardiol 1989;13(5):1144-1154.

[17] Nathan PE, Arsura EL, Zappi M. Pericarditis with tamponade due to cytomegalovirus in the acquired immune deficiency syndrome. Chest 1991;99(3):765-766.

[18] Ho DD, Pomerantz RJ, Kaplan JC. Pathogenesis of infection with human immunodeficiency virus. N Engl J Med 1987;317(5):278-286.

[19] Herskowitz A, Neumann DA, Ansari AA. Concepts of autoimmunity applied to idiopathic dilated cardiomyopathy. J Am Coll Cardiol 1993;22(5):1385-1388.

[20] Moreno R, Villacastin JP, Bueno H, et al. Clinical and echocardiographic findings in HIV patients with pericardial effusion. Cardiology 1997;88(5):397-400.

[21] Flum DR, McGinn JT, Tyras DH. The role of the 'pericardial window' in AIDS. Chest 1995;107(6):1522-1525.

[22] Decker CF, Tuazon CU. Staphylococcus aureus pericarditis in HIV- infected patients. Chest 1994;105(2):615-616.

[23] Karve MM, Murali MR, Shah HM, et al. Rapid evolution of cardiac tamponade due to bacterial pericarditis in two patients with HIV-1 Infection. Chest 1992;101(5):1461-1463.

[24] Sunderam G, McDonald RJ, Maniatis T, et al. Tuberculosis as a manifestation of the acquired immunodeficiency dyndrome (AIDS). JAMA 1986;256(3):362-366.

[25] Zuger A, Louie E, Holzman RS, et al. Cryptococcal disease in patients with the acquired immunodeficiency syndrome: diagnostic Features and outcome of treatment. Ann Intern Med 1986;104(2):234-240.