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A Study of Cardiac Manifestations in HIV Patients.

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ABSTRACT

Background: The advances in diagnosis, treatment, monitoring of HIV infection and the availability of antiretroviral drugs have lead to improved survival of patients but this has resulted manifestations of late stage disease including cardiac manifestations. This study was intended to find out the cardiac manifestations in HIV patients and to correlate them with CD4 count. Aims: To study cardiac manifesations in HIV patients. **Methods:** This was a cross-sectional prospective study carried out in 148 patients with serologically positive HIV status, aged between 18 to 60 years, admitted at tertiary care hospital with or without opportunistic infections. History collection, clinical examination, electrocrdiogram, echocardiography, fasting lipid profile and other laboratory investigations were performed as a part of work up and all the patients were treated accordingly **Results**: Majority of the patients were males (73%) and the commonest age group was 31 to 40 years (38.5%). The CD4 count was between 50-199/cum in 33.8% and <50/cum was found in 27.7% of the patients. Cardiac manifestations were present in 56.1% of the patients. The prominent cardiac manifestations included pericardial effusion (17.6%) , dilated cardiomyopathy (13.5%), valvular heart disease (12.2%) , few patients has diastolic and systolic dysfunctions (8%) and pulmonary arterial hypertension (2.7%). Cardiac manifestations were significantly high in patients with CD4 count <50/cum (74.42%; p=0.002). **Conclusion:** Cardiac manifestations like pericardial effusion and dilated cardiomyopathy were more common and were compared with duration of HIV and significant correlation was found with duration greater than 5years. Hence, routine 2D echocardiography is recommended in those patients.

Keywords: Acquired Immunodeficiency Syndrome; Cardiac manifestations; Human immunodeficiency virus.

INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) caused by infection with human immunodeficiency virus (HIV) is characterized by an acquired, profound, irreversible, immune suppression that predisposes the patient to multiple opportunistic infections and progressive dysfunction of multiple organ systems.[1] HIV/AIDS is a global problem touching virtually every country and every family around the world. It continues to be a major global public health issue, having claimed more than 35 million lives so far. In 2016, 1.0 million people died from HIV-related causes globally. There were approximately 36.7 million people living with HIV at the end of 2016 with 1.8 million people becoming newly infected in 2016 globally.[2] 1 million people died from AIDS-related illnesses in 2016.

According to the UNAIDS 2016 estimations India had 80,000 (62,000 – 1,00,000) new HIV infections and 62,000 (43000 - 91000) AIDS-related deaths. There were 21,00,000 (17,00,000 – 26,00,000) people living with HIV in 2016, among whom 49% (40% - 61%) were accessing antiretroviral therapy.[3]

HIV cannot be cured but can be suppressed by combination ART which controls viral replication within a person's body and allows an individual's immune system to strengthen and regain the capacity to fight with infections. However, its prolonged usage can lead to metabolic abnormalities for which regular monitoring and evaluation is needed.[4]

Treatment with these potent ART's has increased the survival of patient and transformed HIV into chronic illness which was otherwise a rapidly progressive fatal disease. Under the 2016 World Health Organization (WHO) guidelines, in mid-2017, 20.9 million people living with HIV were receiving antiretroviral therapy (ART) globally.54% of adults and 43% of children living with HIV are currently receiving lifelong antiretroviral therapy (ART).[2]

With the availability of a large armamentarium of ART drugs and recent advances in the diagnosis, treatment and monitoring of persons living with HIV and AIDS (PLHA), options with better tolerability, higher efficacy, and lower rates of treatment discontinuation there has been visible improved survival of such patients. Between 2000 and 2016,

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new HIV infections fell by 39%, and HIV-related deaths fell by one third with 13.1 million lives saved due to ART in the same period.[2]

Due to the longer survival of PLHA, the manifestations of late stage HIV infection are now being met with more commonly than before, which among is the HIV related cardiac diseases.[5]

Although not fully recognized in the early days of HIV epidemic, cardiac involvement has been reported with increasing frequency in recent years.[5]

The prevalence of cardiac involvement in AIDS patients have been reported to range between 28% and 73%.5The 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.[6]

Patients with HIV/AIDS and symptoms suggestive of cardiac disease represent a diagnostic and therapeutic challenge in clinical practice; An algorithmic, anatomic approach to diagnosis, localizing disease to the endocardium, myocardium and pericardium can be useful. An intimate knowledge of opportunistic infections affecting the heart, effects of HAART therapy and therapy for opportunistic infections on the heart is needed to be able to formulate a differential diagnosis.[5]

Effects of HAART therapy, especially protease inhibitors on lipid and glucose metabolism, and their influence on progression to premature vascular disease require consideration.

Considering the above facts, the present study was planned to assess the various cardiac manifestations in patients with HIV infection and to correlate them with CD4 count.

MATERIALS AND METHODS

This cross sectional prospective study included outpatients and inpatients at tertiary care center, between September 2015 to March 2018, who were diagnosed as seropositive for HIV. All patients with HIV seropositive, aged more than 18years were included in the studied and patients with past history of ischemic heart disease hypertensive heart disease, rheumatic heart disease, congenital heart disease were excluded. A detailed history, general physical examination, systemic examination and investigations were performed on all patients having HIV.

The ECG was done on 12 lead surface ECG machine. All the patients were evaluated using M Mode and two-dimensional transthoracic echocardiography and color flow doppler examination. Each two-dimensional study consists of parasternal long and short axis, and apical two and four chamber views. The 2D Echocardiography findings were evaluated as for pericardial effusion, dilated cardiomyopathy, systolic/diastolic dysfunction, regional wall motion abnormalities, clot, vegetation and ejection fraction.

CD4 count was done for all patients using flowcytometry using a BD FACS Count system. The CD4 count was done using kits supplied by the National AIDS Control Organization of India (NACO) to Anti-Retroviral Therapy (ART) Centers.

Statistical Analysis

The patients were informed about study in all respects and informed consent was obtained. Statistical analysis of data was done using Mean ± SD, Diagrams, Correlation coefficient, Chi-square test.

RESULTS

In current study a total of 148 Patients with age ranged from 18 to 60 years were included. The mean age of the study population was 41 years as shown in the [Table 1]. 108 (73%) patients were males and 40 patients (27%) were females, accounting a ratio of male to female 2.7:1 as shown in [Table 2].

Table 1: Age Distribution

	Min	Max	Mean	SD
AGE (Years)	18	60	41.0	10.0

Table 2: Sex Distribution in Current Study

Sex	Number of Patients	Percentage
Male	108	73
Female	40	27
Total	148	100%

Table 3: Distribution of cases according to Echocardiography

2DECHO Cardiography	N	%
Normal Study	65	43.9%
Pericardial Effusion	26	17.6%
Dilated Cardiomyopathy	20	13.5%
Valvular Lesion	18	12.2%
Systolic Dysfunction	7	4.7%
Diastolic Dysfunction	5	3.4%
Pulmonary Artery Hypertension	4	2.7%
Rwma	5	3.4%

On Echocardiographic study, 65 patients(43.9%) had normal study, however 83 patients (56.1%) had various cardiac abnormalities – Dilated cardiomyopathy-20(13.5%), Pericardial effusion-26(17.6%), Valvular lesions in 18(12.2%), Regional wall motion abnormality-5 (3.4%), Systolic dysfunction 7(4.7%), Diastolic dysfunction-5(3.4%), Pulmonary arterial hypertension in 4(2.7%) as depicted in the [Table 3].

The duration of HIV infection varied from 1 month to 20 years. In 126 patients (85.1%) duration was either 5 or less than 5 years. In 22 patients (14.9%) it was more than 5 years. We observed 126 patients who had infection of 5 years or less, 68 had cardiac abnormalities, 58 patients had normal study, p value

was 0.21. Whereas 22 patients who had infection of >5 years, 15 patients showed cardiac abnormalities, 7 patients have normal 2d echo findings, p value was 0.015 as shown in [Table 4].

Table 4: Association of Cardiac manifestations and duration of HIV

Duration of disease (yrs)	Cardiac manifestations					
	N		%		N	p value
≤5	68	54.0	58	46.0	126	0.21
>5	15	68.2	7	31.8	22	0.015*
Total	83	56.1	65	43.9	148	

Table 5: Distribution of Cases Acccording To Lipid profile (Fasting)

Variable	Number of Patients	Percentage %
Total Cholesterol (mg/dl)		
<200	127	85.8
≥200	21	14.2
HDL (mg/dl)		
<40	119	80.4
≥40	29	19.6
LDL(mg/dl)		
<100	93	62.8
≥100	55	37.2
TRIGLYCERIDES(mg/dl)		
<150	91	61.5
≥150	57	38.5

In our study as depicted in Table 5, 127 patients (85.8%) had Total cholesterol of < 200 mg/dl and in 16 patients (14.2%) was > 200 mg/dl. In 119 patients (80.4%) had HDL of < 40mg/dl, 29 patients (19.6%) had > 40 mg/dl. When LDL were estimated 93 patients (62.8%) had < 100 mg/dL and remaining 55 patients (37.2%) had >100 mg/dl. In our study 91 patients (61.5%) had Triglycerides < 150 mg/dl, 57 patients (48.5%) had >150 mg/dl.

Table 6: Association of Cardiac Manifestations and CD4 Count

Cd4 Count			Cardiac Manifestations				p value
	Total		Present		Absent		
	N	%	N	%	N	%	
<50	41	27.7	30	73.2	11	26.8	<0.001*
50-199	50	33.8	29	58.0	21	42.0	0.11
200-499	34	23	14	41.2	20	58.8	0.15
≥500	23	15.5	10	43.5	13	56.5	0.38
Total	148	100	83	56.1	65	43.9	

In this study when Cardiac manifestations were compared with CD4 counts. In patients with CD4 counts less than 50, abnormalities were found in 30 patients (p value 0.001) and in 11 patients no Echocardiographic abnormalities were seen. In patients with CD4 Counts between 50-199, 29 had manifestations and 21 did not and the p value was 0.11. In patients with Counts between 200-499, 14 had cardiac manifestations and 20 did not and p value was 0.15. In patients with CD4 counts > 500, 10 had cardiac manifestations and 13 did not, p value 0.38 as shown in [Table 6].

DISCUSSION

In the present study of 148 patients with HIV infection, different cardiac manifestations were observed and same was compared with various factor. In this study, maximum number of cases were in the age group of 31 to 40. HIV infection was found more common in younger age group, same was observed by NACO annual report 2016- 20177. Similar observations were made by Das S et al and Currie et al.[8,9]

Taking sex into consideration we observed males were more affected as compared to females in these studied patients. Same sex difference was observed by NACO annual report (2016-2017).[7] Same conclusion was drawn by Das et al8 and Aggarwal et al.[9]

The duration of HIV infection maximum number of patients were either five years or less than five years and correlation(p 0.015) was seen between longer duration of HIV (>5years) and cardiac manifestations which was similar to the study conducted by Lyons A et al,[10] they have found that rate of heart attack increased with duration of infection, from 0.43 per 1000 person-years in people infected for five years or less, to 0.86 per 1000 person-years in those infected for five to ten years, 1.06 per 1000 person-years in those infected for ten to fifteen years and 2.65 per 1000 person years of follow-up in those infected for more than 15 years.

Echocardiographic evaluation of study patient population showed normal study in 65 patients (43.9%.) In remaining 83 patients (56.1%) various cardiac abnormalities were observed which were Pericardial effusion, Dilated cardiomyopathy, Regional wall motion abnormality, Systolic dysfunction and diastolic dysfunction, Valvular lesions and Pulmonary artery hypertension similar to various studies done by Das et al,8 Aggarwal et al (India),[11] Hakim et al,[12] in Zimbabwe and Reinsch N et.al in U.S.[13]

The fasting lipid profile studies in these patients showed that 127 patients (85.8%) had total cholesterol < 200 mg/dl and in only 21 patients (14.2%) it was more than 200 mg/dl. HDL was less than 40 mg/dl in 119 patients (80.4%), equal or more than 40 mg/dl in 29 patients (19.6%). In 93 patients (62.8%) the LDL was less than 100 mg/dl and in remaining 55 patients (37.2%) it was equal to or more than 100 mg/dl. 91 patients (61.5%) had

Triglycerides below 150 mg/dl and 57 patients (38.5%) had equal to or more than 150 mg/dl. When compared to studies by Baker et al,[14] El- Sadr et al,[15] they found low CD4 count associated with lower LDL-C, HDL-C. Another study by Riddler et al,[16] in patients of HIV seroconversion was associated with decreased triglycerides, LDLC, HDL-C levels. In our study majority, i.e. 85.8 % had total cholesterol less than 200 this difference is little difficult to explain owing to our small sample size. No association was seen when the lipid levels were compared with the cardiac manifestations

When comparison was made between CD4 count and cardiac manifestation, significant association was seen in patients with CD4 count <50/cmm (p-value <0.001). Mean CD4 count was 191.4 had positive correlation with cardiac manifestation. (p=0.015; statistically significant) Similar observation was made by Aggarwal et al.[11] The comparison of CD4 count by various authors has shown cardiac abnormalities increase with the level of immunosuppression and low CD4 count which is also observed in our study. Low CD4 count in our study was probably due to advanced disease state as all our patients were admitted cases in hospital.

In our study when cardiac manifestations and duration of HIV were compared association was seen with duration of disease greater than 5 years either on treatment with ART or not.

It has become easier in the recent years to find various cardiac abnormalities in patients with HIV infection because of availability of sophisticated investigations routinely in most of hospitals/centers.

The various cardiac abnormalities observed in our small sample size of 148 patients is little difficult to explain, it could be direct HIV infection, may be opportunistic infection, progressive disease state or may be ART drug toxicity, needs to be addressed by detailed study and large sample size.

CONCLUSION

Cardiac manifestations like pericardial effusion and dilated cardiomyopathy were more common and were compared with duration of HIV and significant correlation was found with duration greater than 5years. Hence, routine 2D echocardiography is recommended in those patients.

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