



Cardiovascular manifestations of People Newly Diagnosed HIV/AIDS and their Correlation with CD4 Count: Report from Northern India

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Authors' contributions

This work was carried out in collaboration among all authors. Authors MB and RA wrote the first draft and authors AK, MB and RA and SS critically reviewed and edited drafts. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: About 21.17 lakhs people in India and about 0.49 lakh people in Punjab are living with HIV according to National AIDS Control Organization Annual Report (2015-16). Cardiovascular complications of HIV infection tend to occur late in the disease and are therefore becoming more prevalent in our society as therapy and longevity improve.

Aims of this Study:

1. To study incidence of cardiovascular morbidity in newly diagnosed HIV/AIDS patients and their correlation with CD4 count.
2. To study the types of cardiovascular morbidities in newly diagnosed HIV/AIDS patients and their correlation with CD4 count.

Methods: 100 HIV patients newly diagnosed by ELISA technique were selected for the study. All patients were subjected to cardiovascular investigations like ECG, ECHO using Philips iE33 Ultrasound Machine with X-MATRIX Technology with X5-1, supports 3D,2D colour flow, M-mode, Pulsed Wave/Continuous Wave (PW/CW) Doppler, Tissue Doppler imaging and chest x-ray.

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Results: Majority of the patients were asymptomatic (84%). Commonest being Chest pain(1%). 7% patients had ECG abnormalities. Commonest being sinus tachycardia (4), one patient had atrial fibrillation and 2 had LVH.Two patients had Cardiomegaly on X ray examination while remaining 98 patients had normal cardiac size. Out of the 100 patients studied, 27% patients had cardiac involvement on Echocardiography / Colour Doppler study. Out of these 27 patients, 22(80.65%) had CD4 count less than 200, 4(12.90%) had CD4 count between 201-350 and 1(6.45%) had CD4 count>350.Diastolic Dysfunction was most common abnormality followed by tricuspid regurgitation and systolic dysfunction and pericardial effusion on echocardiography / colour Doppler study. 20 patients had Diastolic Dysfunction, out of which 19 had Grade 1 diastolic dysfunction and 1 had Grade 2 diastolic dysfunction. Grade 3 and Grade 4 diastolic dysfunction was not seen in any patient. All patients with Diastolic Dysfunction had CD4 counts less than 200.Six patients had Mild Systolic Dysfunction, out of them 4 were males and 2 were females, all the males had an EF=50%, while females had EF of 50% and 52% respectively. 4 patients had CD4 count less than 200, 1 had CD4 count between 201-350 and remaining 1 CD4 count more than 350.Two patients had Pericardial Effusion and their CD4 count was less than 200.

Conclusion: The commonest cardiac abnormality being detected diastolic dysfunction and least common being pericardial effusion. Diastolic dysfunction is directly related to CD4 count.

Keywords: Echocardiography; diastolic dysfunction; pericardial effusion; CD4 (cluster of differentiation 4).

ABBREVIATION

AIDS	:Acquired immunodeficiency disease syndrome
AR	: Aortic regurgitation
ART	: Anti-retroviral therapy
ASE	:American Society of Echocardiography
BP	: Blood Pressure
CAD	: Coronary artery disease
CD4	: Cluster of differentiation
CVD	: Cardiovascular disease
DCMP	: Dilated Cardiomyopathy
ECG	: Echocardiogram
ECHO	: Echocardiography
EF	: Ejection fraction
ELISA	:Enzyme linked immunosorbent assay
HAART	: Highly active antiretroviral therapy
HIV	: Human immunodeficiency
LVDD	: Left ventricular diastolic dysfunction
LVEDd	: Left ventricle end-diastolic diameter
LVEDS	: Left ventricle end-systolic diameter
LVEF	: Left ventricular ejection fraction
LVSD	: Left ventricular systolic dysfunction
MR	: Mitral Regurgitation
NT Pro BNP	:N-Terminal Pro Brain Natriuretic Peptide
PE	: Pericardial effusion
PLWHA	: People living with HIV and AIDS

Program on HIV and AIDS (UNAIDS) epidemic update 2010 revealed an estimate of 2.6 newly diagnosed HIV infections with 1.8 million estimated deaths secondary to Acquired Immunodeficiency Syndrome (AIDS) related illnesses world wide [1]. About 21.17 lakhs people in India and about 0.49 lakh people in Punjab are living with HIV according to National AIDS Control Organization Annual Report (2015-16) [2]. Cardiovascular complications of HIV infection tend to occur late in the disease and are therefore becoming more prevalent in our society as therapy and longevity improve [3].

There is paucity of data regarding cardiovascular manifestation's of HIV in north India particularly in Malwa belt of Punjab therefore we conducted this study at tertiary care hospital attached to medical college in Patiala district Punjab.

The following are Aims of this study

1. To study prevalence of cardiovascular morbidity in newly diagnosed HIV/AIDS patients and their correlation with CD4 count.
2. To study the types of cardiovascular morbidities in newly diagnosed HIV /AIDS patients and their correlation with CD4 count.

1. INTRODUCTION

Human Immunodeficiency Virus (HIV) infection is a global pandemic with cases reported from virtually every country. The United Nations

2. MATERIALS METHODS

This was an observational, prospective study conducted at Department of Internal medicine of

Government Medical college and Rajinder hospital Patiala, between January 2019 to January 2020. The Independent ethics committee of institute approved it. The study was conducted in 100 patients enrolled from the outpatient and inpatient department of the General Medicine and other departments of Rajindra Hospital, Patiala and also patients visiting ART Centre Rajindra Hospital, Patiala. Patients were selected with the following inclusion/exclusion criteria.

2.1 Sample Size: 100

Sample size was estimated based on expected number of Patients presenting to ART centre and Rajindera hospital with newly diagnosed HIV infection , which is around 300 subjects. Sample size required is 89 subjects which was calculated at 95 percent confidence level. Margin of error was taken as 7.5%, for possible dropouts it was decided to include 100 subjects

$$\text{Sample size} = \frac{z^2 \times p(1-p)}{e^2} \div 1 + \left(\frac{z^2 \times p(1-p)}{e^2 N} \right)$$

Where: N0 is the sample size, Z is the value for the selected alpha level, e.g. 1.96 for (0.05) i.e. at 95 percent confidence level. P is the estimated proportion of an attribute that is present in the population Here estimated (we have taken 5.0%)

N = total population 300

We will take 0.5. q is 1-p. D is the acceptable margin of error for proportion being

2.2 Inclusion Criteria

- The patients aged > 15years
- Patients newly diagnosed to have HIV infection/AIDS

2.3 Exclusion Criteria

- Patients <15 years of age.
- Patients with congenital heart disease.
- Patients with preexisting valvular heart disease.
- Patients with preexisting hypertension.
- Patients with preexisting diabetes mellitus
- Patients previously diagnosed with HIV/AIDS and on ART
- Patients with preexisting hypothyroidism

100 HIV patients newly diagnosed by ELISA technique were selected for the study. A detailed clinical profile including detailed history, general physical examination and systemic examination was done for each patient with special emphasis on cardiovascular system. Routine line of investigations was obtained for all the patients. All patients were subjected to cardiovascular investigations like ECG, ECHO using Philips iE33 Ultrasound Machine with X-MATRIX Technology with X5-1, supports 3D,2D color flow, M-mode,Pulsed Wave/Continuous Wave (PW/CW) Doppler, Tissue Doppler imaging and chest x-ray.

Complete echocardiographic study was done as per protocol of the American Society of Echocardiography (ASE) and all Doppler studies including Pulse wave, Continuous wave Doppler and other studies needed as per case. All M-mode measure was done according to ASE. ECG synchronized minimum 3 beat loop for two dimensional or colour Doppler image and minimum 3 Doppler spectral beats for the still images in case of PW and CW Doppler. For patients in Atrial fibrillation or any other ongoing arrhythmia minimum 5 beats were used. All relevant findings of echocardiography like of Left Ventricular End Dimension in systole [LVEDs], Left Ventricular End Dimension in diastole [LVEDd], interventricular septal thickness in systole and diastole and EF were studied. Doppler evaluation was used for analysis of early mitral flow, late mitral flow and their ratio, IVRT and deceleration time (DT) and systolic and diastolic function [4].

2.4 Statistical Analysis

The statistical analyses was performed with the help of SPSS statistical software, version 20.0, IBM SPSS, version 20 (SPSS, Inc., Chicago II, USA), P<0.05 as significant.

3. RESULTS

In this study 85% patients were less than 50 years of age and remaining 15% were above 50 years of age. This is statistically significant with a p<0.001.

This study comprised of 75% males and 25% females. It was found to be statistically significant with p<0.001. Of all the patients considered for this study, 45% had CD4 count less than 200, 28% had CD4 count between 201-350 and remaining 27% had CD4 count more than 350. It

was found to be statistically significant. Out of the 100 patients considered for study, only 16% had cardiac symptoms at presentation which was found to be statistically significant.

Out of the 16 patients with cardiac symptoms, 13 had dyspnea on exertion (NYHA1), 1 had chest pain while 2 had palpitations. On ECG examination of 100 patients 93 had ECG within normal limits while 4 patients had tachycardia, 2 had features of left ventricular hypertrophy and 1 had atrial fibrillation.

X-Ray examination of the patients revealed that 2 patients had cardiomegaly while remaining 98 had normal chest x ray. It was found to be statistically significant. Out of the 100 patients studied, 27 had cardiac involvement on ECHO while 73 had no cardiac involvement on ECHO which was statistically significant. In our study, out of the 100 patients 27 patients had abnormal ECHO. 66.67% of them were males and 33.33% were females. In this study, 27 patients had abnormal ECHO findings, 22 had CD4 counts less than 200, 4 had CD4 count between 201-350 and 1 had CD4 count more than 350 which is statistically significant.

Echocardiography examination of the patients demonstrated that 6 patients had mild systolic dysfunction, 20 patients had diastolic dysfunction

(Grade 1 and Grade 2), 7 had mitral regurgitation and 2 had pericardial effusion, 4 had aortic regurgitation, 17 had tricuspid regurgitation and 2 had pulmonary regurgitation. It was found to be statistically significant. Out of the 100 patients subjected to ECHO, 6 patients had systolic dysfunction and had CD4 count less than 200. In this study, twenty patients had diastolic dysfunction and all of them had CD4 count < 200. Out of the 20 patients who had diastolic dysfunction, 19 had Grade 1 diastolic dysfunction and only one had Grade 2 diastolic dysfunction. None of the patients had Grade 3 or Grade 4 diastolic dysfunction. In this study of 100 patients, 4 patients had pulmonary tuberculosis, of which 3 had diastolic dysfunction and 1 had both systolic and diastolic dysfunction. Two patients had Esophageal candidiasis (1 had Mitral Regurgitation and 1 had Pericardial Effusion). In this study 95 patients had Ejection Fraction more than 50% while remaining had $EF \leq 50\%$. This was found to be statistically significant. Out of the five patients who had $EF \leq 50\%$, 3 had CD4 count less than 200. Out of the 95 patients who had $EF > 50\%$, 42 had CD4 count less than 200, 27 had CD4 count between 201-350 and 26 had CD4 count more than 350. In this study 4 patients had Pulmonary tuberculosis, 6 had Esophageal Candidiasis, and one had Chronic Diarrhea and majority of them had CD4 count less than 200.

Table 1. Abnormal ECHOs in relation to CD4 count

CD4 Count	Number	Number of Abnormal ECHOs	%age of Abnormal ECHOs according to CD4 count	Chi Square	P value
1-200	45	22	80.65	28.667	<0.001
201-350	28	4	12.90		
>350	27	1	6.45		
Total	100	27	100.0		

Table 2. Various Cardiac Manifestations on ECHO

Cardiac disorder	Number	Percentage	Chi square	P value
Systolic dysfunction	6	6.0	38.310	<0.001
Diastolic dysfunction	20	20.0		
Mitral regurgitation	7	7.0		
Pericardial effusion	2	2.0		
Aortic regurgitation	4	4.0		
Tricuspid regurgitation	17	17.0		
Pulmonary regurgitation	2	2.0		

4. DISCUSSION

In the present study, newly diagnosed HIV/AIDS patients attending OPD/IPD/ART Centre of Medicine department of Rajindra Hospital, Patiala were considered. They were evaluated along with other relevant investigations including ECG and ECHO. To the best of knowledge, there are few studies related to this subject especially newly diagnosed HIV/AIDS patients. Main finding in this study was Diastolic Dysfunction.

In the present study, male to female ratio is 3:1 which is comparable to studies conducted by Sharma et al [5], Singh A [6], Chaudhary [7], Jain [8] and Marwadi [9]. In our study, out of 100 patients 75 were males and 25 were females (M:F= 3:1). Even in our ART Centre at Rajindra Hospital Patiala out of the 1722 patients registered, 1160 are males and 523 are females. In the present study Mean age was found to be 36.55 ± 11.81 which was comparable to studies conducted by Jain et al [8], Marwadi et al [9] and Chaudhary et al [7]. In our study 85% patients were less than 50 yrs of age and rest were more than 50 yrs of age. The mean age (male) was 34.99 ± 11.18 and mean age (female) was 41.24 ± 12.63 . the mean age came out to be 36.55 ± 11.81 . In the present study 16% patients had cardiac symptoms which is comparable to the study conducted by Jain et al [8]. In the present study 27% patients had abnormal echocardiographic studies which is comparable to study conducted by Mirri [10]. Study conducted by Aggarwal P et al [11] demonstrated 42.3% abnormal echocardiographic results. Studies conducted by Chaudhary et al [8] and Marwadi et al [9] had 52.1% and 49% abnormal ECHOs. The difference in the results of our study and previous studies may be attributed to the study being conducted in newly diagnosed HIV/AIDS patients who are mostly asymptomatic and may have only subtle cardiac involvement while other studies are mainly on patients who are already on treatment where other factors like effects of ART drugs also matters. In the present study Diastolic Dysfunction was found in 20% patients which is comparable to studies conducted by Aggarwal P et al [11], Chaudhary et al and Marwadi et al [9]. In the present study, 19% patients had Grade1 diastolic dysfunction and only 1% had Grade 2 diastolic dysfunction while In a study by Jain et al [8] 30.6% had Grade1 diastolic dysfunction and 10.2% patients had Grade2 diastolic dysfunction. In the present study, 5% patients had Ejection Fraction less than 50% which is comparable to study

conducted by Jain et al [8]. In our study, 95% patients had ejection fraction (EF) > 50% and remaining had EF \leq 50%. The results of our study match with the previous studies conducted on HIV/AIDS patients for evaluating cardiac dysfunction. The commonest cardiac abnormality being diastolic dysfunction and least common being pericardial effusion. So in order to detect cardiac involvement in newly diagnosed HIV/AIDS patients high index of suspicion will help in early diagnosis which in turn will decrease the morbidity and mortality.

5. CONCLUSION

It is concluded from our present study that cardiac involvement detected by clinical examination, ECG, Chest X-Ray and Echocardiography /Doppler study is significant in newly diagnosed HIV/AIDS patients. The commonest cardiac abnormality being detected diastolic dysfunction and least common being pericardial effusion. The prevalence was significant. Most of the patients were asymptomatic. The CD4 T cell count is significantly low in cases with cardiac involvement and there is direct relationship with low CD4 Count. With growing evidence of cardiac involvement in HIV/AIDS patients perhaps it is time to consider comprehensive cardiac evaluation including Echocardiography as a part of baseline evaluation of patients at diagnosis. This will make early diagnosis and treatment of cardiovascular diseases possible and improve overall care of the HIV/AIDS patients.

CONSENT AND ETHICS APPROVAL

Ethics approval was given by independent institute ethics committee. Consent to participate in the study was taken by all patients.

AVAILABILITY OF DATA AND MATERIAL

It is available on genuine request send to me on my Email ID- bhatiamandip@gmail.com

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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