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Original Research Article

Echocardiographic assessment of left ventricular function in asymptomatic HIV patients: A single arm blinded study from north India

Abhishek Agrawal *, Laxmikant Goyal, Kamlesh Sharma, C.L. Nawal, Pradeep Mital, Dileep Kumar

Department of Medicine, SMS Medical College & Hospital, Jaipur, India

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ABSTRACT

Aim: To assess left ventricular (LV) function in HIV patients by two-dimensional (2D) echocardiography to determine the pattern of myocardial dysfunction, and any correlation between cardiac dysfunction and severity of HIV infection.

Background: Human immunodeficiency virus (HIV) infection may cause various cardiac dysfunctions in humans even in the asymptomatic state and its timely detection may have prognostic value.

Materials and methods: One hundred treatment naïve, asymptomatic HIV cases were subjected to trans-thoracic echocardiographic (2D, M-mode, pulse-wave, continuous-wave and colour Doppler) assessment by a single blinded cardiologist.

Results: Twenty-nine (29%) of 100 patients (mean age: 36.8 years; male: 54%) had echocardiographic abnormalities. Grade 1 diastolic dysfunction was present in 20, reduced fractional shortening in 12, reduced ejection fraction (<50%) in two (2%), and dilated cardiomyopathy, pericardial effusion and regional wall motion abnormality in one patient each. Four had both systolic and diastolic dysfunction. In patients with diastolic dysfunction, 17 had CD4 count <200/μl ($P < 0.001$). Most cases with cardiac manifestation were in clinical stage III and IV.

Cases having diastolic dysfunction had significantly different CD4 counts, haemoglobin level and erythrocyte sedimentation rate (ESR) values than the cases without cardiac dysfunction.

CD4 counts were significantly negatively correlated with deceleration time ($r = -0.2622$, $P < 0.05$) and iso-volumetric relaxation time (IVRT) ($r = -0.3681$, $P < 0.05$) and significantly positively correlated with E/A ratio ($r = +0.3291$, $P < 0.05$).

Conclusions: Twenty-nine (29%) HIV cases in relatively advanced clinical stage had cardiac dysfunction on echocardiography without overt cardiac manifestations. The CD4 cell counts significantly correlated with the presence of diastolic dysfunction.

1. Introduction

Human Immune deficiency virus (HIV) infection is characterized by an acquired, profound, immune suppression that predisposes not only to the development of multiple opportunistic infections and neoplasms but also to a progressive dysfunction of multiple organ systems including the cardiovascular system [1].

In HIV infected persons, the cardiovascular dysfunction is common (28–73%), although often clinically quiescent [2–6]. The various forms of cardiovascular dysfunction seen in HIV infection are left ventricular dysfunction, myocarditis, dilated cardiomyopathy, endocarditis, pulmonary hypertension, malignant neoplasms, pericardial effusion, coronary artery disease and drug related cardiotoxicity [7].

It has been observed that HIV infected persons, even in the asymptomatic stage, develop left ventricular (LV) dysfunction, particularly of diastolic function, due to myocardial involvement which may have adverse effect on future outcomes [8].

Echocardiography, a non-invasive tool, may detect cardiac involvement in HIV patients at an early stage, even before development of clinical signs or symptoms [9].

This study aims to evaluate LV function in asymptomatic, treatment naïve HIV sero-positives by trans-thoracic 2D

* Corresponding author at: 959, Kissan Marg, Barkat Nagar, Tonk Road, Jaipur 302 015, India. Tel.: +91 9829298691.
E-mail address: drabhie@yahoo.com (A. Agrawal).

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echocardiography (2D echo) in north Indian patients attending a tertiary care hospital and to study the correlation of LV dysfunction with the disease severity (CD4 cell count).

2. Materials and methods

This observational study was done among 100 treatment naïve HIV sero-positive cases (above 18 years of age) at Anti Retroviral Treatment (ART) centre in a tertiary care hospital in north India during the period from May 2012 to December 2013 after permission of the institutional ethics committee. Informed consent was taken from all study participants. Cases having ischaemic, rheumatic, congenital or hypertensive heart disease prior to diagnosis of HIV infection, and those having chronic renal failure, chronic lung disease or thyroid dysfunction as detected from past history and drug history were excluded from the study. Subjects with history of smoking, ethanol intake and illicit drug use were also excluded from the study.

After taking a detailed history and clinical examination, staging of the HIV infection was done as per revised WHO clinical staging system (see Box 1) [10]. Venous blood samples, collected after overnight fasting, were sent for complete blood count (CBC), erythrocyte sedimentation rate (ESR), renal function tests, liver function tests, thyroid function tests, lipid profile and CD4 cell count. The CD4 cell count was done on BD FACS Calibur™ system by BD Bioscience, USA, at our institute. A standard 12 lead Electrocardiogram was obtained for all the patients, to rule out presence of ischaemic heart disease, heart blocks or arrhythmias. Trans-thoracic echocardiographic (two-dimensional (2D), M-mode, pulse-wave, continuous-wave and colour Doppler) assessment of every case was performed by a single cardiologist, who was blinded to the fact that the patients were a part of the study, on iE33 xMATRIX echocardiography system by Philips USA in the cardiology department of the institute.

The two-dimensional images were obtained in the parasternal long- and short-axis views, and apical and subcostal views along various levels with patient in semi-recumbent position with varying degree of left lateral rotation to obtain optimum images [11,12]. The conventions of American Society of Echocardiography were followed in obtaining left atrial dimensions, left ventricular end systolic volume (LVESV) and end diastolic volume (LVEDV) and various diameters (left ventricular end systolic diameters, LVESd; left ventricular end diastolic diameters, LVEDd). Three consecutive cardiac cycles were assessed and averaged for Doppler measurements. Left ventricular ejection fraction (EF) was calculated by using the formula:

$$EF = \frac{(LVEDV - LVESV) \times 100}{LVEDV}$$

Left ventricular fractional shortening (FS) was calculated by the formula:

$$FS = \frac{(LVEDd - LVESd) \times 100}{LVEDd}$$

Left ventricular systolic dysfunction was determined by a reduced ejection fraction and a reduction in left ventricular fractional shortening (LVFS) <28% and presence of regional wall motion abnormalities. Dilated cardiomyopathy (DCMP) was diagnosed using three criteria – LVEDd >55 mm, presence of global hypokinesia and EF <30% [12,15–19].

The left ventricular diastolic function parameters measured were: deceleration time (DT, interval from the peak of the E velocity to its extrapolation to the baseline), iso-volumetric relaxation time (IVRT, interval from aortic valve closure to mitral valve opening on M-mode echo) and E/A ratio [ratio of E wave velocity (peak mitral flow velocity of the early rapid filling) to A wave velocity (peak mitral velocity of late filling)] [12–19].

Box 1. Summary of revised WHO clinical staging of HIV/AIDS for adults and adolescents [10].

Clinical stage 1
- Asymptomatic
- Persistent generalized lymphadenopathy (PGL)

Clinical stage 2
- Unexplained weight loss (<10%)
- Recurrent respiratory tract infections
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulcerations
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections of fingers

Clinical stage 3
- Severe weight loss (>10%) and chronic diarrhoea (>1 month)
- Persistent fever (>1 month) and oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (TB)
- Severe bacterial infections
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia or neutropenia or thrombocytopenia (>1 month)

Clinical stage 4
- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent bacterial pneumonia
- Chronic herpes simplex (HSV) infection (>1 month)
- Oesophageal candidiasis or Candida of trachea, bronchi or lungs
- Extrapulmonary TB
- Kaposi's sarcoma
- Central nervous system Toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy (PML)
- Cryptosporidiosis and or Isosporiasis
- Visceral HSV infection
- Cytomegalovirus (CMV) infection
- Any disseminated mycosis
- Recurrent non-typhoidal salmonella septicaemia
- Lymphoma (cerebral or B cell non-Hodgkin)
- Invasive cervical carcinoma
- Visceral leishmaniasis

The left ventricular diastolic dysfunction (LVDD) was diagnosed when any of the following were present: Impaired relaxation with an E/A ratio <1, IVRT >100 ms and DT >240 ms as grade 1 LVDD; pseudonormalization resembling the normal trans-mitral configuration with regard to the mitral inflow but with normal or low DT as grade 2 LVDD and restrictive pattern with E/A ratio >2, IVRT <70 ms and DT <160 ms as grade 3 diastolic dysfunction [20].

The cases were also screened for presence of various echocardiographic abnormalities, e.g. pericardial effusion, thickening, separation, valvular lesions such as stenoses, and regurgitations and regional wall-motion abnormalities (RWMA).

3. Results

Mean age of the study participants was 36.8 ± 8.52 years (range 19–60 years) with male to female ratio of 1:0.85. The 66% patients were in WHO stage 1 or 2. Overall, twenty-nine (29%) cases were detected to have some degree of LV dysfunction.

Broadly, of the 29 patients with asymptomatic cardiac dysfunction on 2D echo, eight had systolic dysfunction (FS <28%) and sixteen had diastolic dysfunction, four patients had