

Cardiac Dysfunction in HIV Infected Children : A Pilot Study

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Twenty six perinatally acquired HAART-naïve HIV positive children asymptomatic for cardiac disease in age group of 1-9 years were evaluated for cardiac abnormalities by echocardiography. All children were classified according to the revised CDC classification for HIV infection in children. 20 (76.9%) patients had evidence of cardiac abnormalities on echocardiography. 18 (69.2%) patients in category B had statistically significant abnormal echocardiographic finding ($p < 0.02$). The commonest echocardiographic abnormalities seen were left ventricular dilatation in 10 (38.5%) and left ventricular hypertrophy in 10 (38.5%) patients. Echocardiographic abnormalities are present even in HIV-infected children who are asymptomatic for cardiac dysfunction.

Keywords: *Acquired immunodeficiency syndrome, Human immunodeficiency virus, Echocardiography.*

THE incidence of cardiovascular disease reported amongst HIV infected children ranges from 72% to over 90% (1,2). Common cardiac abnormalities noted in HIV infected individuals include cardiomyopathy, myocarditis, pericardial effusion and pulmonary hypertension (3). Grenier, *et al.* (4) reported that cardiac disease was the primary cause of death in 25% of HIV positive patients. Studies carried out in Indian subcontinent have demonstrated the presence of diastolic dysfunction on echocardiography in HIV-infected adults (5). Considering the paucity of similar data regarding HIV-infected children in the Indian subcontinent, we conducted this study to determine the incidence and nature of sub-clinical cardiac abnormalities in HIV-infected children.

Subjects and Methods

Twenty six consecutive children in the age group from 1 year to 9 years with perinatally acquired human immunodeficiency virus

(HIV) infection were prospectively evaluated for sub-clinical cardiac abnormalities at a tertiary pediatric teaching hospital with Pediatric Cardiology and Pediatric & Perinatal HIV sub-specialties, Mumbai, India over a period of 6 months following verbal informed consent. In children aged 18 months and above referred to us with a positive HIV ELISA test, HIV was tested by two different HIV antibody-third generation ELISA tests using DETECT- HIV MC (v.2) and HIV CHEX kits after informed consent from the parents/guardians. Both pre test and post test counseling was done. HIV infection was established on the basis of positive results obtained with both the kits. The diagnosis of HIV infection in children aged less than 18 months was based on positive result by HIV DNA qualitative PCR test using SK38 and SK39 primers. Vertical transmission was established by doing the maternal HIV testing.

HIV positive patients were classified into

category N, A, B or C as per the revised (1994) Center for disease control (CDC) classification system for HIV infection in children(6). All subjects were assessed clinically for evidence of cardiac disease and underwent a 2-dimensional, M-mode echocardiography and Color Doppler analysis on Hewlett Packard Sonos 2000 machine to study the anatomy of the heart and its functional hemodynamics. The patients were evaluated for left ventricular systolic function in the form of fractional shortening and ejection fraction, left ventricular dimensions, left ventricular diastolic functions in form of mitral inflow velocities, valvular abnormalities and pericardial disease that were compared with the normal values(7).

Results

All the HIV infected children enrolled in the study ranged in the age group of 1 to 9 years. None of the enrolled subjects/their guardians reported the presence of cardiac symptoms such as cyanosis, breathlessness, fatigue, palpitations, chest pain, syncope or edema. On examination, no patient had evidence of tachycardia, arrhythmia, increased jugular venous pressure, clubbing, cardiomegaly, murmur or gallop. The commonest clinical manifestations seen were hepatosplenomegaly in 16 (61.5%), lymphadenopathy in 15 (57.7%), failure to thrive in 12 (46.2%), pulmonary and extra pulmonary tuberculosis in 10(38.5%), skin diseases in 6 (23.1%), pyrexia in 5(19.2%), oral candidiasis in 3 (11.5%), recurrent lower respiratory tract infections in 2 (7.7%), chronic parotitis in 1(3.8%), chronic otitis media in 1 (3.8%) and chronic diarrhea in 1 (3.8%) patient. When subjected to echocardiography, 20 patients (76.9%) demonstrated abnormal echocardiographic findings as illustrated in *Table I*.

Left ventricular dilatation and left ventricular hypertrophy were the most

frequent echocardiographic abnormalities (*Table II*). All 3 patients with pericardial effusion had suffered from pulmonary tuberculosis in the past and received anti-tuberculous therapy. None of the patients expired during the study.

Discussion

HIV-infected adults are known to have cardiac involvement in the form of diseases of the pericardium, epicardium, myocardium and the endocardium(8). Although pathogenesis of cardiac involvement in HIV infection is uncertain; autoimmunity, autoimmune dysfunction and abnormal ventricular growth have been proposed as the possible mechanisms(1,9).

Cardiac involvement in HIV infected children is sub-clinical and progressive. Clinical examination, chest radiographs and electrocardiography may pick up manifest cardiac disease. Sub-clinical manifestations such as left ventricular dilatation, hypertrophy and decreased systolic dysfunction can be detected only by echocardiography. Progressive left ventricular dilatation is common in HIV-1 positive children and may be a harbinger of congestive cardiac failure. In many HIV infected children, dilatation is associated with inadequate left ventricular hypertrophy, elevated afterload and reduced left ventricular (LV) function(10).

TABLE I—*HIV Infection in Children – Clinical Category and Echocardiographic Findings.*

Clinical category	Abnormal echocardiographic findings n(%)
N	2 (50.0)
A	2 (66.7)
B	16 (88.9)
C	0 (0)

TABLE II—Common Echocardiographic Abnormalities in HIV Positive Children.

Echocardiographic findings	CDC category				Total	Percentage
	N	A	B	C		
Normal	2	1	2	1	6	23.1%
Decreased left ventricular systolic function	–	1	4	–	5	19.2%
Left ventricular dilation	2	–	8	–	10	38.5%
Left ventricular hypertrophy	1	–	9	–	10	38.5%
Mild Tricuspid regurgitation	–	–	3	–	3	11.5%
Pericardial effusion	–	–	3	–	3	11.5%
Right ventricular enlargement	–	–	1	–	1	3.9%

In this study 20 patients (76.9%) had evidence of sub-clinical cardiac abnormality, which is similar to other reports that have ranged from 72% to over 90%(1,2). Left ventricular dilatation and left ventricular hypertrophy (38.5% each) were the commonest abnormal echocardiographic findings in our study as also seen in P²C² multi-centric study(10). Direct cytotoxic effect of HIV virus on cardiac cells has been proposed to be the cause of progressive dilatation of left ventricle in HIV infected children(11) and its incidence is found to range from 5-30%(12,13). Decreased left ventricular systolic function is seen when the ventricular hypertrophy fails to keep with progressive left ventricular dilatation. The incidence of decreased left ventricular systolic function of 19.2% in our study corresponds to those found in other studies(1,12). One patient had right ventricular enlargement and isolated right ventricular enlargement has been postulated to be secondary to repetitive pulmonary infection and not due to myocardial disease(1). Similarly, tricuspid regurgitation may be seen in patients with recurrent lung infections(14), which were present in 11.5% of our patients. The

relationship of cardiac abnormalities to the stage of HIV infections remains still obscure. We found that cardiac abnormalities were more frequently associated with category B (69.2%).

Annual echocardiography examination is recommended to evaluate the progression of cardiac disease and treat the same before it becomes irreversible in HIV infected children. Effects of ART may confound the effects on the heart and cardiac assessment may be required in patients on HAART. Immunomodulation with IVIG has been previously reported to normalize the LV dysfunction in HIV-1 infected children(15), but needs further evaluation.

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