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Cardiac Abnormalities in HIV Infected Children Presenting to a Tertiary Level Teaching Hospital at New Delhi

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Authors' contributions

All authors designed the study, wrote the protocol, performed statistical analysis and drafted the manuscript. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims: The aim of our study was to study the prevalence of various cardiac abnormalities in HIV positive children.
Study Design: Cross sectional observational study.
Place of Study: Antiretroviral treatment clinic of Maulana Azad Medical College and associated Lok Nayak Hospital and Department of Cardiology at G.B.Pant Hospital ,New Delhi .
Duration of study : March 2009 to Mar 2010.
Methodology: Sixty perinatally acquired, HIV-positive children asymptomatic for cardiac disease in age group of 0-12 years were evaluated for cardiac abnormalities by echocardiography. All children were classified according to the WHO clinical staging for HIV-positive children and also divided into immunologic category as per the age-specific CD4-T lymphocyte count.
Results: Sixteen (26.6%) children had evidence of cardiac abnormalities on echocardiography. Twelve (20%) patients in WHO stage III and IV had significant abnormal echocardiographic findings. The major echocardiographic findings seen were left ventricular dilatation in 4 (6.7%) and left ventricular diastolic dysfunction in 3 (5%)

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children.
Conclusions: A baseline echocardiographic study should be done in all patients with symptomatic HIV infection at first contact. Serial echocardiographies should be done to determine the evolution of cardiac disease in HIV infected children. Echocardiographic abnormalities are present even in HIV- infected children who are asymptomatic for cardiac dysfunction.

Keywords: HIV; Children; asymptomatic cardiac abnormalities.

1. INTRODUCTION

The incidence of cardiovascular disease reported amongst HIV-infected children ranges from 70% to over 90% [1,2]. Common cardiac abnormalities noted in HIV-infected individuals include cardiomyopathy, myocarditis, pericardial effusion and pulmonary hypertension. Grenier, et al. [3] reported that cardiac disease was the primary cause of death in 25% of HIV positive patients. Higher prevalence rates of heart disease, ranging from 14% to 45%, may be attributable to selective recruitment and detection bias [3,4]. In most clinical situations, asymptomatic HIV seropositive children are not evaluated by echocardiography on routine basis. We conducted an observational cross-sectional study to determine the structural and functional abnormalities of the heart in HIV-infected children attending ART center of a tertiary care hospital of North India.

2. MATERIAL AND METHODS

Sixty children below 12 years of age attending the ART center at Lok Nayak Hospital, New Delhi, India from March 2009 to March 2010 with confirmed HIV positive status were enrolled in the study and evaluated for cardiac abnormalities. Informed consent was taken from parents/ caretaker of the children who participated in the study and the study was cleared by the Ethics Committee of the Maulana Azad Medical College, New Delhi, India. Demographic details were recorded and information retrieved with regard to the diagnosis of HIV infection, duration of illness and CD-4 count from the clinic records. All details were recorded in a predesigned proforma. They were classified into clinical stage I, II, III or IV as per WHO classification given for infants and children with confirmed HIV infection. They were also divided into immunologic category as per the age-specific CD4-T lymphocyte counts. Children were evaluated clinically with particular emphasis on signs and symptoms suggestive of cardiac involvement. These children were investigated by means of chest skiagram (postero-anterior view; cardiothoracic ratio of more than 50% was taken as cardiomegaly), electrocardiography (ECG) without sedation (as per the guidelines set by Committee on Electrocardiography of the American Heart Association, and analyzed using the normal ECG standards for infants and children by Davington et al. [5] as reference). Echocardiography was performed by a blinded cardiologist in all patients in a standardized way at the cardiology laboratory. Subxiphoid, apical and parasternal views were used to define intra-cardiac anatomy and to obtain cardiac measurements and indices of cardiac function:

1. Left ventricular function was assessed by modified Simpson's method.
2. Right ventricular function was assessed by eye balling.
3. Diastolic function was assessed by parameters like E/A ratio and deceleration time.

4. Tissue Doppler was done at mitral annulus and basal ventricular and interventricular septum to detect any subclinical left ventricular dysfunction.
5. Associated findings like valvular lesions and pericardial effusions were recorded.

3. RESULTS AND DISCUSSION

Sixty HIV positive children were enrolled in the study. All had acquired the HIV infection perinatally. Forty nine (81.6%) cases were between 6-12 years of age, with none less than one year of age. Eleven (18.4%) children were below 5 years of age and seventy percent children were males. Majority of these were in WHO clinical stage I (30%) and II (28.4%), with 39 (65%) having no evidence of immunosuppression, 15 (25%) having moderate and 6 (10%) having severe immunosuppression- Table 1. Coexisting Tuberculosis was present in 25 out of 60 children. Forty eight children (80%) were on antiretroviral treatment.

Table 1. Immunological characteristics of the children

Age in years	No immune suppression	Moderate immune suppression	Severe immune suppression
1-5 years	5	4	2
6-12 years	34	11	4
	39(65%)	15(25%)	6(10%)

Forty eight (80%) children were on ART, with 66.7% of these being on stavudine, lamividine and nevirapine and rest (13.3%) on zidovudine, lamivudine and nevirapine. No child had HCV co infection. One child had a past history of *Pneumocystis carinii* pneumonia. Besides HIV, no other systemic illness was identified in these 60 children. Most of the children (81.7%) were asymptomatic with respect to the cardiovascular system. In the rest of the children, most common symptom was breathlessness (15%) followed by easy fatigability (3.3%). On examination, except for tachycardia which was found in 10% of the children, none of the enrolled subjects had evidence of arrhythmias, increased jugular venous pressure, clubbing, cardiomegaly, murmur or gallop. However most of the signs and symptoms were non-specific, as many had concomitant chest infection or nutritional deficiencies. When subjected to echocardiography, sixteen children (26.6%) demonstrated abnormal echocardiographic findings as illustrated in Table 2. In this study left ventricular dilatation was the most common major echocardiographic abnormality found in 4 children (6.7%). Among these 2 children had an ejection fraction <50% with depressed fractional shortening and the other 2 children had LV dilatation with normal ejection fraction with fractional shortening <25%.

Table 2. Results of echocardiography in 60 HIV positive children

Echo findings	WHO Stage 1	WHO Stage 2	WHO Stage 3	WHO Stage 4	Total
LV diastolic dysfunction	_	_	1	2	3(5%)
LV dilatation	_	_	1	3	4(6.7%)
Mitral regurgitation	_	_	_	1	1(1.7%)
Tricuspid regurgitation	1	3	3	1	8(13.3%)
Total	1(6.2%)	3(18.7%)	5(31.3%)	7(43.8%)	16(26.6%)

The other major echo finding was left ventricular diastolic dysfunction which was seen in 5% cases. (Table 3) Mild tricuspid regurgitation was seen in 8 (13.3%) cases. Trivial mitral regurgitation was found in only one child who had associated LV dilatation with depressed ejection fraction. Only 3 (5%) children had left ventricular fractional shortening < 25% and all these children were in WHO clinical stage 4.Two children died during the study. Both were in WHO clinical stage IV and were severely immunosuppressed. One died due to disseminated tuberculosis and other due to hepatic encephalopathy.

Table 3. Summary of echocardiographic abnormalities

Systolic dysfunction	Number (Total 60)	Percentage
LVEF <50 %	3	5%
FS < 25%	3	5%
FS < 28%	12	20%
Diastolic dysfunction		
E/A <1	3	5%
LV dilatation	4	6.7%
Tricuspid regurgitation	8	13.3%

4. Discussion

HIV-infected adults are known to have cardiac involvement in the form of diseases of the pericardium, epicardium, myocardium and the endocardium [6]. 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 function can be detected only by echocardiography. Majority of studies have reported cardiac abnormalities in HIV infected children who were terminally ill, had advanced AIDS or AIDS related complex, or had symptomatic HIV disease with severe immunosuppression [7,8,9]. In our study, majority of children were in WHO clinical stage I and II and 65% of them did not have any clinical evidence of immunosuppression. Most (81.7%) of our patients were clinically asymptomatic at presentation. This corroborates with the study by S Lubega et al[9] on 230 HIV positive children, where only 5 children had abnormal clinical findings, and by I Shah et al. [10], where there were no cardiac symptoms and no evidence of cardiac disease or congestive heart failure on examination out of 26 HIV positive children and still, twenty (76.9%) of these patients had evidence of cardiac abnormalities on echocardiography. As noted in other studies[9, 10], prevalence of cardiac abnormalities in our study was more in WHO clinical stage III and IV and those who were moderate to severely immunosuppressed. Similarly, only one child in our study had cardiomegaly on chest skiagram, who was in WHO clinical stage IV and had severe immunosuppression. The prevalence of cardiac abnormalities on echocardiography in our study was 26.6%, which is similar to other reports that have ranged from 18% to 78% [1,7,8,9]. Major cardiac findings like left ventricular dilatation with or without decreased ejection fraction, left ventricular diastolic dysfunction are more prevalent in children who were moderate to severely immunosuppressed and in WHO clinical stage III and IV while minor abnormalities like mild tricuspid regurgitation and trivial mitral regurgitation were equally prevalent in all immunological categories. Left ventricular dilatation (6.7%) was the most common major echocardiographic abnormality found in our study, prevalence of which is ranging from 5% to 65% in various studies [9,10,11]. The prevalence of LV diastolic dysfunction detected in various adult studies ranges from 2% to 19.2% [12]. In our study, LV diastolic dysfunction was found in 5% children. Trivial mitral

regurgitation was found in only one child who had associated LV dilatation with depressed ejection fraction. Mild tricuspid regurgitation was found in 8 (13.3%) children in our study which has been postulated to be secondary to recurrent lung infections with isolated right ventricular enlargement and not due to myocardial disease [13]. Various other echocardiographic findings reported in literature were not found in our study population. This could be due to majority of our study patients being in WHO clinical stage I or II with no evidence of immunosuppression, and of the 26 children who had opportunistic infections; majority had already recovered from it or were in recovery phase. With prolonged survival of HIV infected persons with effective treatment, HIV infection seems destined to become an important cause of cardiac complications worldwide. Echocardiography is a cheaper and effective modality in identifying early cardiac involvement in asymptomatic HIV infected patients. A longer follow-up time of children is necessary to evaluate the impact of combination anti-retroviral therapy on the onset of cardiac manifestations. There is no Indian study on echocardiographic findings in normal children. However in a study by Steinberger J et al in a cohort of 357 children echocardiography identified 13 (3.6%) children with previously unknown cardiac abnormalities [14].

In a study by Zormpala A et al impaired distensibility of ascending aorta was seen in HIV infected adults patients. It was seen that HIV infection is independently associated with decreased distensibility of the ascending aorta, a marker of subclinical atherosclerosis. Increasing age and duration of exposure to HAART are factors further contributing to decreased aortic distensibility [15].

An accelerated biological aging is of particular concern and recently debated in HIV infected people [16].

HIV infection has been associated with increased cardiovascular risk. Individuals with HIV infection and borderline or definite hypertension have higher symmetric ambulatory arterial stiffness index (AASI) and 24 hour systolic and pulse pressure than HIV uninfected controls. Higher ambulatory BP may play a role in the HIV related increase in cardiovascular risk [17].

An attenuation of the physiological day-night blood pressure (BP) reduction is an important predictor of cardiovascular events and death. In this study by De Socio GV et al, HIV infection per se negatively affects circadian BP rhythm. These findings obtained in subjects without major CV risk factors and antiretroviral naïve suggest that day night BP changes may play a role in the HIV related increase in CV risk [18].

There is some controversy regarding the association of HAART and cardiovascular disease in children with HIV infection. Prior to HAART the 2-5 year incidence of symptomatic heart failure ranged from 4-28% in HIV infected patients. In children aged 10 or younger 25% died from cardiac disease prior to availability of HAART and up to 28% experienced serious cardiac events after an AIDS defining illness [19,20]. The institution of HAART is beneficial in reducing the clinically important HIV associated cardiac disease. Recent findings suggest that long term HAART exposure may be cardioprotective for a finite period early in life but its benefit decreases as this population ages into adulthood [21]. Cardiac toxicity of antiretroviral drugs has also been documented. Zidovudine has been implicated in skeletal muscle myopathies and NRTIs may lead to increase in lipid abnormalities. Protease inhibitors especially ritonavir are known to cause dyslipidemia and accelerated atherosclerosis [22,23].

4. CONCLUSION

Cardiac abnormalities are common in perinatally acquired HIV infection. Most of these children are asymptomatic. Regular echocardiographic screening will help clinicians pick up many subtle cardiac abnormalities in symptomatic HIV infected children.

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CONSENT

All the patients have given their informed consent for the case report to be published.

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

The authors have obtained all necessary ethical approval from suitable Institutional ethical. This confirms either that this study is not against the public interest, or that the release of information is allowed by legislation.

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Lipshultz SE, Chanock S, Sanders SP, Colan SD, McIntocsh K. Cardiovascular manifestations of human immunodeficiency virus infection in infants and children. Am J Cardiol. 1989;63:1489-1497.
2. Luginbuhl LM, Orav EJ, McIntosh K, Lipshultz SE. Cardiac morbidity and related mortality in children with HIV infection. JAMA. 1993;269:2869-2875.
3. Grenier MA, Karr SS, Rakusan JA, Martin GR. Cardiac disease in children with HIV: relationship of cardiac diasese to HIV symptomatology. Pediatric Aids. 1994;5:174-79.
4. Domanski MJ, Sloas MM, Follman DA. Effect of zidovudine and didanosine treatment on heart function in children infected with human immunodeficiency virus. J Pediatr. 1995;127:137-146.
5. Davignon A, Rautaharju P, Boisselle E. Normal ECG standards for infants and children. Pediatr Cardiol. 1979;1:123-131.
6. Francis CK. Cardiac involvement in AIDS. Curr Prob Cardiol. 1990;15:571-589.
7. Bannerman C, Chitsike I. Cor pulmonale in children with HIV infection. Ann Trop Paediatr. 1995;15:129-134.
8. Sherron P, Pickoff AS, Ferrer PL. Echocardiographic evaluation of myocardial function in pediatric AIDS patients. Am Heart J. 1985;110:710.

9. Lubega S, Zirembuzi GW, Lwabi P. Heart disease among children with HIV/AIDS attending the pediatric infectious disease clinic at Mulago Hospital. Afr Health Science. 2005;5(3):219-22.
10. Shah I, Prabhu S.S, Sumitra V, Shashikiran HS. Cardiac dysfunction in HIV infected children. Ind Pediatr. 2005;42:146-9.
11. Cunha M. AIDS in childhood: Cardiac involvement with or without triple combination anti-retroviral therapy. Arq Bras Cardiol 2008;90(1):11-17.
12. Aggarwal P, Sharma A, Bhardwaj R. Myocardial dysfunction in human immunodeficiency infection: An echocardiographic study. J of Asso of Physicians of Ind. 2009;57:144-49.
13. Coudray N, Force G, Pourny JC, Antony I. Left ventricular diastolic function in asymptomatic and symptomatic human immunodeficiency virus carriers: an echocardiographic study. Eur Heart J. 1995;16:61-67.
14. Steinberger J, Moller JH, Berry JM, Sinaiko AR. Echocardiographic diagnosis of heart disease in apparently healthy adolescents. Pediatrics. 2000;105(4);815-818.
15. Zormpala A, Sipsas NV, Moyssakis I, Georgiadou SP, Gamaletsou MN, Kontos AN et al. Impaired distensibility of ascending aorta in patients with HIV infection.BMC infectious diseases. 2012;12:167.
16. De Socio GV, Ricci E, Parruti G, Maggi P, Madeddu G,Quirino T et al.Chronological and biological age in HIV infection .J Infect. 2010;61(5):428-30.
17. Schillaci G , Maggi P, Maddedu G, Pucci G,Mazzotta E,Penco G et al. Symmetric ambulatory arterial stiffness index and 24 hour pulse pressure in HIV infection: results of a nationwide cross-sectional study .J Hypertens. 2013;31(3):560-7.
18. De Socio GV, Bonfanti P, Martinelli C, Ricci G, Marinoni M. J Acquir Immune Defic Syndr. 2010;55(3):356-60.
19. Lipshultz SE, Easley KA, Orav EJ, Kaplan S, Starc TJ, Bricker JT, et al. Cardiac dysfunction and mortality in HIV-infected children: the prospective P^2C^2 HIV multicenter study. Pediatric pulmonary and cardiac complications of vertically transmitted HIV infection (P^2C^2 HIV) study group. Circulation. 2000;102:1542–8.
20. Morse CG, Kovacs JA. Metabolic and skeletal complications of HIV infection: the price of success. JAMA. 2006;296:844–54.
21. Lipshultz SE, Miller TL, Wilkinson JD, Scott GB, Somarriba G, Cochran TR and Fisher SD. Cardiac effects in perinatally HIV-infected and HIV-exposed but uninfected children and adolescents: a view from the United States of America. J Int AIDS Soc. 2013; 16(1): 18597.
22. Dapena M, Jiménez B, Noguera-Julian A, Soler-Palacín P, Fortuny C, Lahoz R, et al. Metabolic disorders in vertically HIV-infected children: future adults at risk for cardiovascular disease. J Pediatr Endocrinol Metab. 2012;25(5–6):529–35.
23. Piloya T, Bakeera-Kitaka S, Kekitiinwa A, Kamya MR. Lipodystrophy among HIV-infected children and adolescents on highly active antiretroviral therapy in Uganda: a cross sectional study. J Int AIDS Soc. 2012;15(2):17427.

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