# CARDIAC MANIFESTATIONS IN CHILDREN WITH ACQUIRED IMMUNODEFICIENCY SYNDROME AT KENYATTA NATIONAL HOSPITAL.

A dissertation in part fulfilment for the degree of Master of Medicine in Paediatrics in the University of Nairobi.

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## DECLARATION

This dissertation is my own original work and has not, to my knowledge, been published or presented for any degree in any other University.

_____ Date June 3, 2004.

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## DEDICATION

To my wife Lydiah, for her constant encouragement and support during the preparation of this manuscript.

To my daughter Hilda, for her concern.

## ACKNOWLEDGEMENTS

I would like to express my sincere appreciation to:-

1.   My supervisors, Dr. C.A Jowi and Dr. D.A Mbori-Ngacha; both of the department of Paediatrics, University of Nairobi for their encouragement, guidance, patience and support throughout the preparation of this thesis.

2.   Mr. Fred Oyugi of the department of Microbiology, University of Nairobi for the data processing.

3.   My professional colleagues who offered useful suggestions.

4.   All the children who participated in the study and their parents/guardians.

# CONTENTS

## LIST OF ABBREVIATIONS.

| | | |
|---|---|---|
| AIDS | - | Acquired immunodeficiency syndrome |
| AO | - | Aorta |
| CD | - | Cluster of differentiation classification |
| CD4+ T Lymphocytes | - | T helper lymphocytes |
| CD8+ T Lymphocytes | - | T suppressor lymphocytes |
| CI | - | confidence interval |
| CNS | - | Central nervous system |
| CO | - | Cardiac output |
| CXR | - | Chest X-ray |
| DNA | - | Deoxyribonucleic acid |
| ECG | - | Electrocardiography |
| EF | - | Ejection fraction |
| ELISA | - | Enzyme linked immunosorbent assay |
| FS | - | Fractional shortening |
| GIT | - | gastrointestinal tract |
| Hb | - | Haemoglobin level |
| HIV - 1 | - | Human immunodeficiency virus type one |
| HIV - 2 | - | Human immunodeficiency virus type two |
| KNH | - | Kenyatta National Hospital |
| IVS | - | Interventricular septum |
| LA | - | Left atrium |
| LV | - | Left ventricle |
| LVDD | - | Left ventricular end diastolic dimension |
| LVPWD | - | Left ventricular posterior wall dimension |
| LVSD | - | Left ventricular end systolic dimension |
| OR | - | odds ratio |
| PCR | - | Polymerase chain reaction |
| RNA | - | Ribonucleic acid |
| RVD | - | Right ventricular dimension |
| SV | - | Stroke volume |
| WHO | - | World Health Organisation |

## LIST OF FIGURES

## LIST OF TABLES

# ABSTRACT

**Introduction**: AIDS and its associated opportunistic infections and neoplasms affect virtually every organ. The heart of the patient with AIDS is also affected in a number of mechanisms that result in its dysfunction. No study has been done locally to show the prevalence of cardiac disease in children with AIDS.

**Objective:** To determine the cardiac profiles of children with AIDS at the Kenyatta National Hospital.

**Design:** Cross-sectional study.

**Setting:** The Kenyatta National Hospital general paediatric wards.

**Subjects:** Sick children aged below 12years, who met the WHO clinical diagnostic criteria for paediatric AIDS and had a positive HIV ELISA test.

**Procedures:** The subjects had a full haemogram, a plain chest x-ray, surface electrocardiography and echocardiography done.

**Study duration:** December 2002 - May 2003.

**Results:** A total of 99 subjects were recruited to the study. Fifty five (56%) were males and 44 (44%) were females. The age range was 3months to 144months, with a median age of 36months and mean age of 4years 1month. Cardiac involvement was revealed in 64 (65%) subjects. Of these, left ventricular dysfunction was found in 35 (35%) subjects, pericarditis and or pericardial effusion in 27 (27%) subjects, myocarditis in 21 (21%) subjects, and pulmonary hypertension in 15 (15%) subjects. Left ventricular dysfunction was significantly correlated with anaemia, p-value 0.014, odds ratio 4.06 and 95% confidence interval 1.16 – 15.56. Dyspnoea was significantly related to right ventricular dysfunction, p-value 0.009, odds ratio 10; 95% confidence interval 1.27 – 213.1. From the logistic regression model, pneumonia was of statistical significance as a correlate to cardiac disease. It seemed to confer protection, p-value of 0.014 odds ratio 0.155 and a 95% confidence interval of 0.035 – 0.681.

**Conclusion:** The study revealed a high prevalence of cardiac disease in children with AIDS (65%), the commonest problem being left ventricular dysfunction on (35%). Right ventricular dysfunction was significantly related to dyspnoea. Left ventricular dysfunction was significantly related to anaemia.

**Recommendation:** Cardiac evaluation by echocardiography should be done on all patients with AIDS since clinical characteristics are not reliable predictors for cardiac complications.

## INTRODUCTION AND LITERATURE REVIEW

## INTRODUCTION

The acquired immunodeficiency syndrome (AIDS) was first recognised in the United States in 1981 and in 1983, human immunodeficiency virus (HIV) was isolated. The cardiac complications of HIV infection and AIDS have been recognized from the time of the onset of the pandemic in 1981 [1]. The spectrum of cardiac disease in HIV infected individuals is emerging increasingly as a significant cause of morbidity and to a lesser degree, mortality. Accurate assessment of the prevalence and nature of heart disease is hampered by the fact that the cardiac effects may be asymptomatic or may present with features which are incorrectly ascribed to other organ systems. This is particularly true of breathlessness which may be mistakenly attributed to respiratory infection. Cardiac involvement has been reported as a common post mortem finding in HIV/AIDS than it is found clinically. Post mortem findings report cardiac involvement in 2.7 to 92 percent of adults who died of AIDS in two studies, one in Italy and the other in India [2, 3]. Cardiac involvement has been reported to occur clinically and detected by CXR, ECG and echocardiography in 6.5 to 63 percent of adults in two Italian studies [4, 5]. The types of cardiac abnormalities which may occur include: heart muscle disease, pericarditis, ventricular dysfunction, valvular abnormalities and conduction defects.

The reported prevalence of dilated cardiomyopathy in association with HIV infection or more appropriately HIV heart muscle disease varies between 7.9 percent of adults in an

Italian study [6] and 32 percent of children in a Brazilian study [7]. Dilated cardiomyopathy has been shown to be the commonest cardiac manifestation of HIV infection in children in two studies, one in Brazil and another in New Jersey, USA [7, 8]. Pericarditis with or without effusion is common in HIV infected patients with a reported prevalence ranging from 14.8 to 30 percent in several studies [4, 5, 7, 9, 10]. The prevalence of myocarditis in HIV infection has been reported to range from about 6 percent in adults clinically and on endomyocardial biopsy in two studies done in Italy [6, 10] to a high of 56 percent from autopsies in an Indian study [3]. In two Brazilian studies, ventricular arrhythmias were reported in 32 to 35 percent of HIV infected children [7, 11].

Isolated right ventricular dysfunction affects HIV infected individuals with a reported prevalence ranging from 4 percent of adults in a study in Edinburgh to 48 percent of children in a Zimbabwean study, being commoner in children and those with late stage HIV disease [4,12,13]. Left ventricular dysfunction has been reported to occur with a prevalence ranging from 6.4 percent of these patients in the Edinburgh study [12] to 60 percent in an Indian study [14]. The prevalence of valvular lesions in HIV infected patients has been reported from echocardiographic series to range from 4.1 percent of adults in an Italian study [10] to 10.6 percent in an Indian study [14]. The prevalence of vegetations, indicating endocarditis with or without valvular involvement, has been reported to range from 1.2 percent of these patients in a study in Kinshasa [9] to 13 percent in adults in another study in Italy [4]. Endocarditis is commoner in those HIV infected patients who are intravenous drug abusers.

# CLINICO-PATHOPHYSIOLOGICAL FEATURES AND DIAGNOSIS

Virtually every organ or system in the body is vulnerable to disease either as a direct effect of HIV infection or secondary to opportunistic infections and neoplasms in these individuals. These lead to abnormality or dysfunction of the affected organ [15].

The heart muscle of an HIV infected individual may be affected in a number of suggested ways. Direct infection by the HIV virus itself has been demonstrated by viral culture from the myocardium, or its parts identified by DNA or RNA polymerase chain reaction (PCR). The virus can cause myocardial cell damage by induction of apoptosis or cytopathicity. It is a specific phenomenon related to HIV infection per se and not merely a manifestation of chronic illness or intercurrent opportunistic infections [5]. Myocardial damage may also be caused by cytokines like tumour necrosis factor $\propto$ (TNF$\propto$), interleukin-1, interleukin-6, transforming growth factor ß (TGFß) and interferon gamma (INFγ) released from HIV-infected monocytes or lymphocytes. Cardiolipin in myocytes share a degree of homology with HIV membrane glycoprotein gp120 and gp41. This similarity may lead to generation of autoantibodies to cardiolipin, the cross-reaction resulting in myocardial damage. HIV cardiomyopathy or more appropriately HIV heart muscle disease has been strongly associated with low CD4+ T lymphocyte counts below 100 per microlitre in adults [12]. HIV cardiomyopathy has also been associated with low immunoglobulin levels [16]. The myocardial damage results in depression of myocardial function [15, 17].

HIV heart muscle disease occurs in both children [7, 8, 16, 18, 19] and adults [2, 4, 5, 6, 12, 14], being more frequent in late stage disease than in the early asymptomatic stage of the disease [5]. HIV heart muscle disease may be asymptomatic or present with features of congestive heart failure including irritability, anorexia, cough, dyspnoea, palpitations and leg swelling. The signs of HIV heart muscle disease include cold pale skin, small volume pulses, low pulse pressure, tachycardia, elevated jugular venous pressure, hepatomegaly and dependent oedema. Cardiac apex may be displaced downward and outward. There may be a pansystolic murmur of mitral regurgitation or tricuspid regurgitation or a gallop rhythm. Chest x-ray may reveal enlarged cardiac silhouette, pulmonary congestion or a pleural effusion. The ECG may show arrhythmias, non-specific ST-T wave changes and varying degrees of left and right ventricular hypertrophy. The echocardiograph may show poor left ventricular function with reduced stroke volume, reduced ejection fraction and increased end diastolic volume and end systolic volume. There may be poor contractions, enlargement of the left atrium and displacement of the mitral valve. A study in Edinburgh showed that survival is significantly reduced in adults with HIV-related dilated cardiomyopathy as compared to those with HIV infection and normal hearts [12].

Myocarditis may be caused by one of the many opportunistic organisms or HIV itself. The organisms noted to cause myocarditis in these patients include toxoplasma gondii, cryptococcus neoformans, histoplasma capsulatum, aspergillus fumigatus, or other viruses including cytomegalovirus, Epstein-Barr virus and coxsackie virus [6, 15]. HIV may enter the cardiac myocyte and cause damage directly or indirectly, cell damage being analogous

to that on the CD4+ T lymphocytes. The opportunistic organisms may cause damage to the cardiac myocytes by similar mechanisms or being synergistic to HIV. They may cause a fulminant inflammatory process characterized by cellular infiltration by macrophages, plasma cells, lymphocytes and eosinophils. There is cell degeneration, necrosis and subsequently fibrosis. Chronic inflammation may be perpetuated by host immune response with cytotoxic T lymphocytes. The opportunistic infections may also alter major histocompatibility complex (MHC) expression with exposure of neoantigens and resultant autoimmune damage to the myocardium. A granulomatous reaction can occur with formation of multinucleated giant cells derived from damaged myocytes.

Symptoms of myocarditis include chest pain, dyspnoea and fatigue; while signs may include fever, tachycardia, weak pulses, distant heart sounds, gallop rhythm, and murmur of mitral regurgitation and there may be pericardial friction rub if the pericardium is involved. Chest x-ray may show cardiac enlargement or pulmonary oedema. The ECG may show sinus tachycardia, arrhythmias, decreased QRS voltages and ST-T wave abnormalities. Echocardiographic changes are not specific and may show dyskinesia, dilatation or reduced wall thickness. Pericardial effusion may be found in some cases.

The most common neoplasms involving the heart in HIV infected patients are Kaposi's sarcoma and non-Hodgkin lymphomas derived mainly from B cell series, both being uncommon in the paediatric age group. Myocardial involvement may cause conduction defects or space occupying lesions impairing myocardial contractility. Opportunistic neoplasms involving the heart may be asymptomatic or present with features of

pericardial effusion, conduction defects or cardiac failure. The opportunistic neoplasms may be detected at echocardiography or seen at autopsy [20, 21, 22]. An autopsy report from Florida of an HIV infected child with thrombotic thrombocytopenic purpura showed microthrombi in multiple organs including the cardiac conducting system [23]. Conduction through damaged myocardium is delayed compared to that through normal myocardium, resulting in reentry mechanism with the occurrence of ventricular arrhythmias [11].

Drugs used in the treatment of these patients, like doxorubicin, ifosfamide, zidovudine or didanosine may cause inflammatory myocardial injury and dysfunction. Nutritional deficiencies like selenium, zinc, folate and group B vitamin deficiency may also cause myocardial damage [15]. The injury and damage may lead to left ventricular or biventricular dysfunction.

Left ventricular dysfunction may be asymptomatic or present with features of congestive cardiac failure [5, 7, 9, 10, 12, 14, 19, 24]. The left ventricular dysfunction worsens on follow up of most of these HIV infected patients [7, 12, 19], and may progress even on appropriate anti-failure treatment and respond only to addition of combined antiretroviral drugs [12]. The chest x-rays of affected patients may show features of left ventricular enlargement or biventricular enlargement. Electrocardiography may show features of left axis deviation and left ventricular hypertrophy. Echocardiography may show left ventricular dilatation, decreased left ventricular fractional shortening and decreased wall motion.

The aetiological agents of pericarditis with or without effusion may be the opportunistic infections and neoplasms or due to HIV itself [5]. Reported causes include mycobacterium tuberculosis [25], aspergillosis [26], Kaposi's sarcoma [21] and non-Hodgkin lymphomas [20, 22]. The other causes of pericarditis and/or effusion in the non-HIV infected patient may also cause them in HIV infected ones. These agents cause an inflammatory process with hyperaemia, oedema and cellular infiltration. An exudate, which may be turbid, straw coloured, purulent or bloodstained, may accumulate in the pericardial space. Fibrin may be deposited on the surfaces of the pericardium. This process heals by fibrosis with adhesions and pericardial thickening. Rapid or large accumulation of the fluid interferes with atrial filling. Tuberculous pericarditis often becomes chronic and calcification of the pericardium may occur, leading to constriction. Pericardial Kaposi's sarcoma may cause haemorrhage into the pericardial space.

Pericarditis and pericardial effusions may be asymptomatic or present with symptoms of fever, chest pain, cough and dyspnoea. Common signs are tachypnoea, tachycardia, weak pulses, pulsus paradoxus, elevated jugular venous pressure, diffuse cardiac apex, enlarged percussible heart, distant heart sounds and there may be a friction rub. The chest x-ray is normal initially unless there is lung pathology. Later with increasing effusion, it shows features of cardiomegaly with a globular shaped heart shadow. With venous engorgement, the CXR shows enlargement of the superior vena cava. The ECG initially shows ST segment elevation in 2 or 3 standard limb leads and $V_2$ to $V_6$ with reciprocal depression in aVR and sometimes in $V_1$. These later return to normal and T waves may become

inverted then. With an effusion there is decreased QRS voltage and features of electrical alternans. Echocardiography may show thickening of the pericardium and demonstrate effusion if present - swinging motion of the heart within the fluid and whether it is localised or generalised. Indicators of cardiac tamponade include diastolic collapse of the right atrium and right ventricle with poor inspiratory collapse of the inferior vena cava.

Recurrent respiratory infections, which include bacterial pneumonia, mycobacterial infections, pneumocystis carinii pneumonia, fungal and cytomegalovirus pneumonia, common in HIV-infected patients, can cause pulmonary hypertension. These infections cause a state of hypoxemia with resultant pulmonary arterial spasm. Arterial wall changes occur characterised by endothethial swelling and medial hypertrophy, which contribute to increased vascular resistance with time. Some of these infections may cause destructive lung disease with loss of pulmonary vasculature, contributing to pulmonary hypertension. HIV may predispose to the development of pulmonary hypertension directly or through immunological mechanisms. Pulmonary hypertension predisposes to secondary right ventricular failure (cor pulmonale). The severity of the right ventricular enlargement is a function of the increased afterload [5, 13, 27].

Patients with isolated right ventricular failure present with features of oedema, congestive hepatomegaly and systemic venous congestion; orthopnoea and paroxysmal nocturnal dyspnoea being less common. CXR shows features of enlargement of the right ventricle. ECG shows features of the right axis deviation and right ventricular hypertrophy and the

echocardiograph may show dilated right ventricle and right atrium and features of pulmonary hypertension [4, 12, 13].

Valvular lesions may result from previous valvular endocarditis or the lesion may be secondarily infected. The aetiological agents are bacterial infections as in the non HIV infected individual as well as fungi like candida albicans and aspergillus fumigatus [4, 9]. Vegetations consisting of platelets, fibrin and the infecting organisms form on the affected valve and may extend to adjacent endocardium and myocardium. Extensive vegetations, especially those caused by fungal infections may occlude the valve orifice. Immunological valve destruction may occur. Healing occurs with scar formation resulting in valvular stenosis or regurgitation. Extension of infection to the myocardium and endocardium may lead to conduction defects; rupture of chordae or rupture of a papillary muscle. Embolisation of detached vegetations may lead to embolic phenomena.

The clinical features of valvular lesions and endocarditis may include fever, finger clubbing, petechiae, splenomegaly, cardiac murmurs, and secondary neurological manifestations. Other manifestations include anaemia, proteinuria, microscopic haematuria, elevated erythrocyte sedimentation rate and increased circulating immune complexes. Echocardiography may show vegetations in the endocardium or on the valves and with Doppler may show valvular dysfunction [4, 9].

# STUDY JUSTIFICATION AND UTILITY

HIV infection/AIDS in children is a common problem in our setup.

The appropriate treatment of opportunistic infections has made children with AIDS survive longer, with increased chances of organ-specific syndromes including cardiac complications.

It is probable that the features due to cardiac involvement are incorrectly ascribed to other organ systems or are masked by features of involvement of these systems, this causing their not being properly addressed during treatment. No study has been done locally to show the profile of cardiac disease in children with AIDS.

The results of this study may demonstrate the existence of cardiac complications in HIV infection and their magnitude, so that those who take care of these patients can be advised to investigate for these complications and start appropriate treatment early.

The results of the study may be used as baseline data for other follow-up longitudinal studies in this area.

## STUDY OBJECTIVES

### MAIN OBJECTIVE

To determine the cardiac manifestations in children with AIDS at the Kenyatta National Hospital.

### SPECIFIC OBJECTIVES

- To determine the prevalence of cardiac disease in children with AIDS at the Kenyatta National Hospital.
- To describe clinical presentations of cardiac disease in children with AIDS at the Kenyatta National Hospital.
- To determine the clinical predictors of cardiac disease in children with AIDS at the Kenyatta National Hospital.

## MATERIALS AND METHODS.

## STUDY DESIGN

Cross sectional study.

## STUDY AREA

The study was carried out at the Kenyatta National Hospital (KNH) general paediatric wards. KNH is a teaching hospital for the University of Nairobi, and also a referral hospital in Nairobi, Kenya.

The patients seen in this hospital are mainly of low socio-economic status, from Nairobi and the nearby districts, and also referrals from other parts of the country. There are four general paediatric wards in the hospital, each admitting in turns every four days. The average number of patients admitted in a day is between 40 and 50. Usually on each admission day, there are about 3 or 4 patients who meet the WHO clinical diagnostic criteria for paediatric AIDS [28]. See *appendix II.*

## STUDY POPULATION

Children aged 12 years and below admitted to the general paediatric wards at the Kenyatta National Hospital.

## PATIENT SELECTION

The subjects of the study were selected from those admitted to two general paediatric wards not admitting on consecutive days. Those included were the known cases of HIV/AIDS who were admitted to these wards and those others who were admitted who met the WHO clinical diagnostic criteria for paediatric AIDS [28]. The investigator visited each of the two wards on its post-admission day. The doctor's admission notes for all the new patients were looked at. Those children noted to have had any major or minor components of the WHO clinical diagnostic criteria for paediatric AIDS, had a history taken and a physical examination done. Those, on whom a clinical diagnosis of AIDS was made, were offered a HIV ELISA test, which was done with pre and post test counselling of the parent or guardian. The known cases of HIV/AIDS did not have the test repeated if they had a KNH laboratory report confirming the HIV seropositivity. Those who had positive HIV ELISA test and clinical diagnosis of AIDS had a written informed consent obtained from the parent or guardian for participation in the study. Upon discharge, these patients were referred to patient support centre KNH, or to the nearest HIV support group within the community for follow up.

## INCLUSION CRITERIA

1. Children who had been admitted as known cases of HIV/AIDS.

2. Children admitted who met the WHO clinical diagnostic criteria for paediatric AIDS and had a positive HIV ELISA test.

## EXCLUSION CRITERIA

1. Children whose parents or guardians did not give consent or withdrew from the study after they had given consent.

2. Children who died before completion of investigations.

3. Re-admissions who were recruited in the study in a previous admission.

**PROCEDURES**

1. Each child who met the selection criteria and consent was given had a history taken and a general examination which included anthropometric measurements done. A physical examination was also done.

2. Blood was drawn from a peripheral vein after skin preparation with antiseptic, using a 2 millilitre syringe and a 23 gauge needle; 0.5 millilitres of blood was put in an ethylene diamine tetra acetic acid (EDTA) bottle and taken to the haematology laboratory for a full haemogram.

3. Plain postero-anterior view chest x-ray and sometimes antero-posterior view, especially in infants, was booked and done on all the study patients at the x-ray department. These were examined by the investigator and reported with the help of a radiologist. The films were later re-examined by a cardiologist.

4. Twelve lead surface electrocardiography (ECG) and rhythm strip was done on all the study subjects in the cardiology department by the investigator assisted by the ECG/echocardiography technologists and then read by the investigator with the help of a cardiologist.

5. Echocardiography was considered as a gold standard for the diagnosis of heart disease in this study. This was supported by physical examination, chest x-rays and electrocardiographic tracings. Echocardiography was done using General Electric ultrasound machine model 6800. Subcostal, parasternal, apical and suprasternal views were used. The modalities of echocardiography used were two-dimensional real time, M-mode, pulsed wave Doppler and continuous wave Doppler echocardiography. Transthoracic echocardiography was done on all the study patients in the cardiology

department by the investigator assisted by the ECG/echocardiography technologists and/or a cardiologist. Two-dimensional real time echocardiography was used to assess the cardiac measurements, visual contractility and any abnormal finding like pericardial effusion, valvular abnormality and masses. M-mode echocardiography was used to assess the relative chamber sizes and to calculate the indices of cardiac contractility. Spectral pulsed wave Doppler with sample specimen taken at the tips of the mitral valve leaflets was used to assess diastolic function. The figure below shows how the pulsed wave Doppler looks in normal and in abnormal diastolic function. The first wave is the E (excursion) wave and the second one is the A (apposition) wave.



| Normal | Restrictive | Pseudo normalised | Reversed |
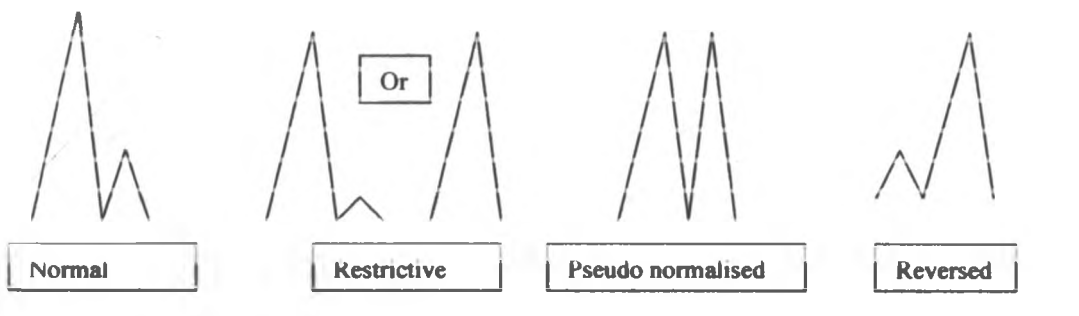
Continuous wave Doppler was used to assess tricuspid regurgitation. Pulmonary pressures were derived from tricuspid regurgitation using the Bernoulli's equation;

$P = 4V^2$: where P is the pulmonary pressure and V is the maximum velocity of the tricuspid regurgitation. A value of 5mmHg was added on top of the tricuspid regurgitation gradient to estimate the pulmonary pressures. The echocardiographic findings were recorded on videotape and interpreted later with the help of a cardiologist.

6.  Management of the patient's primary condition was not interfered with.

## STUDY DEFINITIONS

- Echocardiography was used as the gold standard for structural and functional abnormalities. Cardiac abnormality was said to be present when echocardiography was abnormal, with or without abnormal ECG or chest x-ray. Electrocardiography was used to demonstrate rhythm disorders or conduction disorders. Cardiac abnormality was also said to be present when the ECG showed these two abnormalities and the echocardiography was normal. The cardiac abnormalities included: pericarditis with or without pericardial effusion, dilated cardiomyopathy, ventricular dysfunction, conduction defects, and valvular abnormalities.

- Pericardial effusion is the presence of fluid in the pericardial space demonstrable on 2D-echocardiography. It could be anterior, posterior or circumferential. Cardiac tamponade is said to be present when there is pericardial effusion with diastolic collapse of the right atrium or right ventricle with poor inspiratory collapse of the inferior vena cava.

- Dilated cardiomyopathy is the dilatation of the heart chambers with poor contractility of the ventricles. Two-dimensional echocardiography shows reduced ejection fractions of less than 50%, reduced stroke volume and increased end systolic volume and end diastolic volume.

- Pulmonary hypertension is said to be present when the mean pulmonary pressure is higher than 16mmHg. Two-dimensional echocardiography shows dilated pulmonary trunk, dilated right ventricle and the pulmonary and tricuspid valves may be regurgitant.

- Left ventricular dysfunction has both systolic and diastolic components. Systolic

17

dysfunction is present when the 2D-echocardiography shows decreased stroke volume and increased end systolic volume and end diastolic volume. Diastolic dysfunction is said to be present when there is abnormal filling pattern of the left ventricle. This is assessed by using pulsed wave Doppler echocardiography; could be restrictive, pseudonormalised or reversed.

- ECG was considered normal when no abnormality was noted. ECG tracings were read using a standard method with scoring criteria [29]. The tracing was probably within normal limits (PWNL) when one minor abnormality was noted. A borderline tracing (BT) was considered if two minor abnormalities were noted. Probably abnormal tracing (PAT) was considered when one major abnormality was noted. A tracing was considered definitely abnormal (DAT) if two major abnormalities were noted.

- Anaemia – Haemoglobin level less than 10g/dl. For purposes of this study, the severity of the anaemia was graded as follows:

| Severity | Hb level (g/dl) |
|----------|-----------------|
| Mild     | 7-10.0          |
| Moderate | 4-6.9           |
| Severe   | <4              |

- Diarrhoeal disease – GIT disease characterized by increased frequency (>3/24hours), fluidity and volume of stools, and often accompanied by vomiting.

- Malnutrition – in this study meant severe forms of under nutrition: marasmus, kwashiorkor and marasmic kwashiorkor.

## DATA MANAGEMENT

### SAMPLE SIZE

The formula for sample size calculation used was $n = \dfrac{Z^2 (1-\alpha/_2)\, P\, (1-P)}{d^2}$

(Fischer's formula for prevalence studies)

$n$ = minimum sample size.

$Z = 1.96$ is the normal deviate corresponding to a confidence interval of 95 percent.

$\alpha = 0.05$ is the power of he study (5%)

$P$ = estimated prevalence of cardiac disease in HIV infection, 50 percent from other studies [7, 13].

$d = 10$ percent, the required absolute precision of prevalence.

Thus $n = \dfrac{1.96^2 \times 0.975 \times 0.4 \times 0.6}{(0.1)^2} = 93.6$

Minimum sample size = 94.

### DATA ANALYSIS

The data collected was entered in a computer database and analysed using the statistical program for social sciences (SPSS package) version 10.0 and EPI INFO version 6.0. The results were presented in bar graphs, pie charts and tables. Differences in frequencies were assessed using the Chi-square method or the Fischer's exact test.

## ETHICAL ISSUES

The study was carried out only after consent had been obtained from the department of Paediatrics, University of Nairobi and the KNH ethical and scientific committee. The HIV test results and patient records were handled with the strictest confidence.

# RESULTS

During the study period of December 2002 through May 2003, ninety nine consecutive patients who met the clinical criteria for inclusion into the study were recruited. There were a total of 55 males (56%) and 44 females (44%), giving a sex ratio of 1.25:1. There were more males than females in all the age groups. More than half of the children in the study, 52 (52%) were in the age group 1-5years. The median age of the study subjects was 36months; mean age 4years 1month, with range 3months to 12years. This is shown in figure 1 below.

**Fig. 1: The distribution of age and sex in the study subjects.**
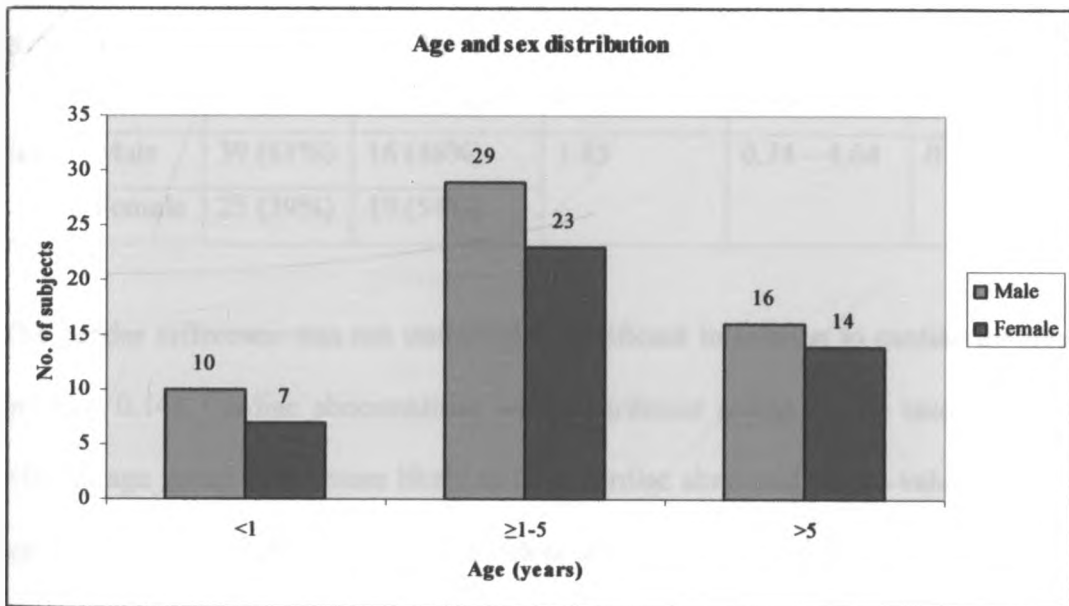
Echocardiography was used as the gold standard for demonstrating structural and functional cardiac defects. Electrocardiography was used for rhythm disorders. Other evaluations included history, physical examination, laboratory tests and chest radiography. Using the above criteria, 64 (65%) subjects were considered to have abnormal cardiac findings while the remaining 35 (35%) were considered normal. Table 1 shows the distribution of their cardiac involvement in terms of their age and sex.

**Table 1:  The distribution of cardiac disease according to age and sex.**

|  |  | Cardiac abnormality | | Odds ratio | 95%CI OR | p-value |
|---|---|---|---|---|---|---|
|  |  | Present (n = 64) | Absent (n =35) |  |  |  |
| Age (yr) | <1 | 9 (14%) | 8 (23%) | 0.55 | 0.17 – 1.79 | 0.27 |
|  | 1-5 | 39 (61%) | 16 (46%) | 1.53 | 0.62 – 3.80 | 0.32 |
|  | >5 | 16 (25%) | 11 (31%) | 0.92 | 0.35 – 2.47 | 0.87 |
| Sex | Male | 39 (61%) | 16 (46%) | 1.85 | 0.74 – 4.64 | 0.14 |
|  | Female | 25 (39%) | 19 (54%) |  |  |  |

The gender difference was not statistically significant in relation to cardiac involvement (p-value 0.14). Cardiac abnormalities were distributed across all the study age groups, with no age group being more likely to have cardiac abnormalities (p-values: 0.27, 0.32, and 0.87). From the above table, the development of cardiac abnormality was independent of the age and the sex of the subjects.

## Echocardiographic findings.

Echocardiography was mainly used to demonstrate structural and functional cardiac abnormalities. When the echocardiographic window was limited, CXR, ECG and clinical findings were used. This was done in 3 subjects who had poor echocardiographic windows which had made the echocardiographic study difficult. A number of subjects had multiple abnormalities. The main specific echocardiographic findings were as shown in Table 2 below. The commonest echocardiographic finding was left ventricular dysfunction, which was found in 35 (35%) subjects. Many children had more than one echocardiographic abnormality. See *appendix IV* for copies of sample echocardiographs.

## Table 2: Tabulation of the echocardiographic findings of the study subjects.

| Echocardiographic features | Number (n = 99) | Percentage (%) |
|---|---|---|
| Normal | 35 | 35 |
| Left ventricular dysfunction | 35 | 35 |
| Pericarditis/pericardial. effusion | 27 | 27 |
| Dilated cardiomyopathy | 21 | 21 |
| Pulmonary hypertension | 15 | 15 |
| Valvular abnormalities | 5 | 5 |

## Electrocardiographic findings.

Twelve-lead electrocardiography was performed in all the study subjects. Sixty three subjects had ECG tracings that were abnormal; while the other 36 had normal ECG tracings. The abnormal ECG tracings were further classified as: definitely abnormal tracings (16), or probably abnormal tracings (40). Borderline tracings (7) were grouped

under abnormal tracings. The commonest ECG abnormality was sinus tachycardia which was noted in 59 (60%) subjects. This was followed by right ventricular hypertrophy in 35 (35%) subjects and abnormal T waves in 21 (21%) subjects. Left ventricular hypertrophy was only seen in 14 (14%) subjects. Other abnormal rhythms included sinus bradycardia in 1 (1%) 8year old patient, isolated ventricular ectopics in 1 (1%) 10year old patient, and wandering pacemaker in 3 (3%) patients aged 8months, 3years and 4years. Some subjects had more than one specific ECG finding. See *appendix V* for copies of sample electrocardiographs.

Forty nine (77%) of the 64 patients with cardiac abnormalities, had both abnormal electrocardiographs and abnormal echocardiographs. Fifteen subjects (23%) had abnormal echocardiographs and normal electrocardiographs. None of the subjects were classified as having cardiac abnormality based on ECG alone since those who met the ECG criteria of rhythm disorders also had structural abnormalities picked on echocardiography.

## Clinical presentation.

The main complaints of the study subjects were; fever in 80 (81%), cough in 68 (69%), and dyspnoea in 63 of them (64%). None of these patients were found to have cardiac murmurs on examination. Many of the study subjects had multiple signs; pallor was noted in 71 (72%) subjects, tachypnoea in 32 (32%) subjects, basal rales in 28 (28%) subjects, tachycardia in 21 (21%) subjects, fever in 16 (16%) subjects and other signs in 23 (23%) subjects. Other signs included central cyanosis, ankle oedema, pericardial friction rub,

gallop rhythm and cardiomegaly. Evidence of congestive cardiac failure (a combination of tachypnoea, tachycardia, basal rales and hepatomegaly) was noted in 8 (8%) subjects. Figure 2 below shows the diagrammatic representation of the signs found in the study subjects.

**Fig. 2: Diagrammatic representation of the distribution of clinical signs in the study subjects.**



Distribution of signs in the study subjects.

■ 23
■ 16
□ 21
□ 28
■ 32
□ 71

pallor
tachypnoea
basal rales
tachycardia
fever
others
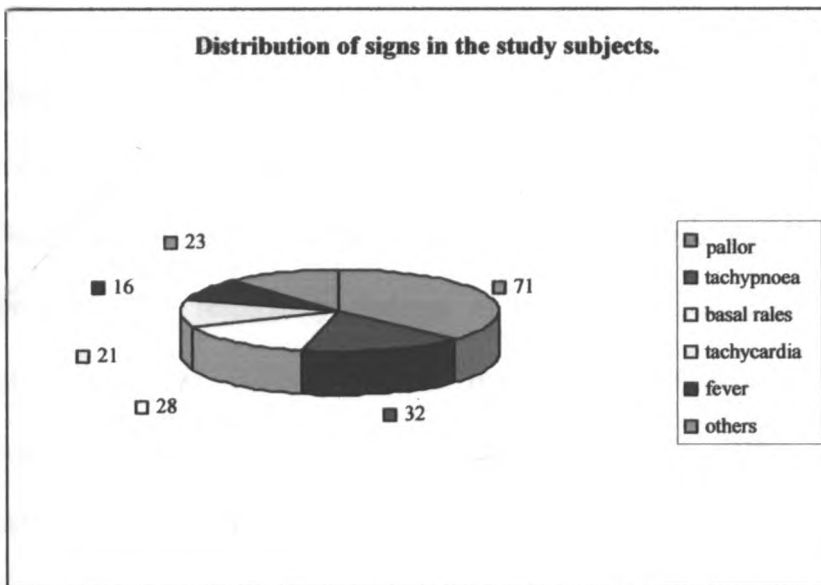
*The numbers shown are those of actual subjects with the sign shown, and are not mutually exclusive, such that one subject could have had more than one sign.*

The diagnoses at admission included severe pneumonia, tuberculosis, diarrhoeal disease, malnutrition, meningitis, and stroke. Other diagnoses included malignancy, malaria, measles, eczema and cellulitis. Diagnosis of pneumonia, tuberculosis or diarrhoeal disease was found in more than three-quarters, 78 (79%) of the study subjects. These three

diagnoses including anaemia which was also very common (found in 74% of subjects), are confounders rather than independent variables since they influence cardiac function.

## Laboratory findings

Anaemia in this study was found to be very prevalent, and was found in 73 subjects (74%). Normal haemoglobin level was found in only 26 (26%) subjects. The subjects who had anaemia were sub classified into: mild anaemia in 57 (58%), moderate anaemia in 13 (13%) and severe anaemia in 3 (3%) subjects.

## Radiographic findings.

Chest x-rays were done in 96 subjects and not done in 3 subjects. Radiographic findings were normal in 12 (12%) subjects. The abnormal radiographic findings showed predominantly respiratory findings of pneumonia, pulmonary tuberculosis or pleural effusion in 62 (63%) subjects. None had predominantly cardiac findings like cardiomegaly or pulmonary oedema. Twenty two (23%) subjects had combined respiratory and cardiac findings. Some subjects had more than one chest radiographic feature. See *appendix VI* for photographs of sample chest radiographs.

Fever, cough, dyspnoea and anaemia were found in at least two-thirds of subjects with cardiac abnormalities. Table 3 below compares some clinical characteristics with echocardiographic findings. None of the clinical features or diagnosis was significantly related statistically to the presence of a cardiac abnormality.

**Table 3: Comparison of proportions of subjects with cardiac abnormalities with their clinical characteristics**

| Subject characteristics | Cardiac abnormality | | Odds ratio | 95%CI OR | p-value |
|---|---|---|---|---|---|
| | Present (n = 64) | Absent (n = 35) | | | |
| Fever | 50 (78%) | 30 (86%) | 0.06 | 0.17 – 2.02 | 0.36 |
| Cough | 46 (72%) | 22 (63%) | 1.51 | 0.57 – 3.97 | 0.36 |
| Dyspnoea | 43 (67%) | 20 (57%) | 1.54 | 0.60 – 3.91 | 0.32 |
| Tachypnoea | 22 (34%) | 10 (29%) | 1.31 | 0.49 – 3.54 | 0.56 |
| Tachycardia | 16 (25%) | 5 (14%) | 2.00 | 0.60 – 7.02 | 0.21 |
| Wasting | 27 (42%) | 14 (40%) | 0.91 | 0.36 – 2.29 | 0.83 |
| Anaemia | 50 (78%) | 23 (66%) | 1.86 | 0.68 – 5.13 | 0.18 |
| Pneumonia | 18 (28%) | 16 (46%) | 0.46 | 0.18- 1.20 | 0.08 |
| Malnutrition | 6 (9%) | 1 (3%) | 3.52 | 0.39 – 80.84 | 0.23 |
| Tuberculosis | 17 (27%) | 5 (14%) | 2.17 | 0.66 – 5.57 | 0.16 |

The clinical characteristics of the subjects were compared with the specific Echocardiographic findings in a sub-analysis. Patients with anaemia had a 4 fold increased risk of having left ventricular dysfunction (odds ratio 4.1, 95% CI 1.2 – 15.6; p-value 0.01). Patients with tachycardia had a 3 fold increased risk of left ventricular dysfunction (odds ratio 3.2, 95% CI 1.1 – 9.7; p-value 0.02). Patients with dyspnoea had a 10 fold increased risk of having right ventricular dysfunction (odds ratio 10, 95% CI 1.3 – 213.1; p-value 0.01); as well were patients with tachypnoea (odds ratio 4.0, 95% CI 1.1 – 14.4; p-value 0.01). None of the other clinical features or diagnoses was significantly related to the presence of other specific cardiac abnormalities.

**Logistic regression model.**

To increase the power of the study and to explore clinical correlates to cardiac disease as diagnosed on echocardiography, the clinical characteristics used for comparison above were entered into a logistic regression model. The results of that analysis are presented in Table 4 below.

**Table 4: Diagrammatic representation of the logistic regression model of the subject characteristics as predictors of cardiac disease.**

| Variables in the Equation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95.0% C.I.for EXP(B) | |
| | B | S.E. | Wald | df | Sig. | Exp(B) | Lower | Upper |
| FEVER | .590 | .666 | .785 | 1 | .376 | 1.803 | .489 | 6.646 |
| COUGH | .784 | .750 | 1.091 | 1 | .296 | 2.190 | .503 | 9.534 |
| DYSPNOEA | .765 | .759 | 1.018 | 1 | .313 | 2.150 | .486 | 9.508 |
| TACHYPNOEA | .125 | .603 | .043 | 1 | .835 | 1.133 | .348 | 3.694 |
| TACHYCARDIA | .975 | .648 | 2.261 | 1 | .133 | 2.651 | .744 | 9.449 |
| PNEUMONIA | -1.864 | .755 | 6.091 | 1 | .014 | .155 | .035 | .681 |
| TB | -.495 | .802 | .382 | 1 | .537 | .609 | .127 | 2.932 |
| ANAEMIA | .921 | .534 | 2.973 | 1 | .085 | 2.512 | .882 | 7.155 |
| WASTING | .511 | .495 | 1.065 | 1 | .302 | 1.667 | .631 | 4.402 |
| Constant | -1.923 | 1.253 | 2.356 | 1 | .125 | .146 | | |

a. Variable(s) entered on step 1: FEVER, COUGH, DYSPNOEA, TACHYPNOEA, TACHYCARDIA, PNEUMONIA, TB, ANAEMIA, WASTING.

After controlling for all other factors, none of the clinical parameters entered into the regression model came out independently as of statistical significance to the development of cardiac abnormality. The outcome of this regression model suggests a diagnosis of pneumonia is protective to the development of cardiac disease, p-value of 0.01.

DISCUSSION

This study was carried out to determine the cardiac manifestations in children with AIDS at the Kenyatta National Hospital. The study was to determine the prevalence. clinical features and predictors of heart disease in these patients. The prevalence of cardiac involvement in patients with AIDS in this study was found to be 65%. heart disease being found in 64 subjects of the 99 studied. Though on the higher side of the range. this prevalence was similar to that reported by Cecchi (6.5%). Adriano (76%) and Longo-Mbenza (45.8%) [4. 5. 9]. All the three studies were however done in adults as opposed to our study which dealt with children. The first two studies quoted were both prospective and the entry point to the studies was a suspicion of heart disease in those patients with AIDS. Longo-Mbenza's study was also prospective but like ours had the entry point as AIDS. Fewer studies have been done in children as compared to those done in adults. Haddad Hardy [7] studied 25 children prospectively with follow up cardiac evaluation and reported a cardiac involvement prevalence of 32%. In his study. 20% of the children had clinical features of congestive cardiac failure. In our study. we found congestive cardiac failure in 8 subjects (8%). a rate much lower than what he found. May be had we done a prospective rather than cross sectional study. we could have found a higher prevalence on follow up. Bannermann [13] did a cross sectional study in 50 children and reported a cardiac involvement prevalence of 60%. In his study. the children were younger with a median age of 9months and he only concentrated on chronic lung infection and cor pulmonale.

The commonest echocardiographic feature noted was left ventricular dysfunction, which was found in 35 (35%) subjects. This prevalence was within the range reported by Currie (6.4%) [12] and Joshi (60%) [14]. Both of these were prospective studies in adults. In his study of children, Haddad Hardy found dilated cardiomyopathy to be the commonest cardiopathy which occurred in (32%) of his subjects [7] while Longo-Mbenza reported pericarditis and/or pericardial effusion to be the commonest (27.7%) [9].

In our study left ventricular dysfunction which has both systolic and diastolic dysfunction was found in 35 (35%) subjects. Its components in the study were LV systolic dysfunction and LV diastolic dysfunction. LV systolic dysfunction (ejection fraction <50%) was found in 6 subjects (6%), and LV diastolic dysfunction was found in 34 subjects (34 %). Some subjects who had LV diastolic dysfunction also had LV systolic dysfunction and thus the systolic and diastolic dysfunctions were not mutually exclusive. The components of the diastolic dysfunction revealed were: restrictive diastolic filling in 26 subjects, reversed filling pattern in 2 subjects and pseudo normalised filling pattern in 6 subjects (*see diagram in the procedures section, page 16*). LV systolic dysfunction in these subjects was probably secondary to myocarditis at that time which was demonstrable on ECG or myocarditis which occurred in the past.

Pericarditis with or without effusion was demonstrated in 27 (27%) subjects. This was comparable with that reported in other studies by Cecchi [4], Adriano [5], Haddad Hardy [7], Longo-Mbenza [9], and DeCastro [10] with prevalence range of 14.8-30%. Haddad Hardy studied subjects with similar ages as our study (3months to 11years) but had a

smaller number of 25 subjects. He reported pericarditis in 20% of them. The other four studies were all done in adults.

Our finding of dilated cardiomyopathy prevalence of 21% is lower than that of 32% reported by Haddad Hardy [7]. Haddad Hardy and Oleske [8] reported dilated cardiomyopathy to be the commonest cardiac manifestation; this was not the case in our study. However the prevalence of dilated cardiomyopathy found in our study fell within the range reported by other workers [4, 5, 6, 7, 8, 9, 10, 12, 14] with prevalence range of 4.4-32%.

Pulmonary hypertension with right ventricular dysfunction was found in 15 (15%) subjects. This was comparable with that reported in other studies (4-48%) by Cecchi [4], Currie [12] and Bannermann [13]. Four of these 15 subjects had severe pulmonary hypertension (>60mmHg) and dilated right ventricles with poor RV systolic function. Seven had mild and 4 had moderate pulmonary hypertension. These latter two groups had only mild RV dysfunction. Pulmonary hypertension which is commonly due to lung fibrosis secondary to chronic lung infections in these patients may increase progressively with time. This leads to cor pulmonale, which as it worsens may result in fatality. This may explain their proportionately lower numbers in the older age groups. Two-thirds of those subjects who had pulmonary hypertension and RV dysfunction had normal haemoglobin levels (not shown) or mild anaemia, and only 1/3 had moderate to severe anaemia. This may be explained by the fact that they are chronically hypoxemic with

production of erythropoietin and resultant erythrocytosis, hence the higher haemoglobin levels.

Isolated valvular lesions were found in 5 (5%) subjects. Thickening of the mitral valve was found in all these 5 subjects; in two of them the tricuspid valve was also thickened. This agrees with the range reported in other studies; De Castro (4.1%) [10] and Joshi (16.6%) [14]. Cardiomegaly with normal cardiac function as diagnosed on CXR and ECG was found in 2 (2%) subjects.

Conduction defects (first degree heart block) were demonstrated in 1 subject (4%). This subjects had a normal haemoglobin (11.2g/dL) and marked leucopenia ($1.5 \times 10^9$/L). This patient however had left ventricular systolic dysfunction. This proportion was much lower than that reported in other studies (32-35%) by Haddad and Roberto [7, 12]. They found various degrees of heart block without giving proportions of each conduction defect.

In none of the study subjects was a cardiac neoplasm found. Small lesions or tumours may have been missed on echocardiography especially those who had large effusions or poor echocardiographic windows. There was no recognizable congenital heart defect/abnormality demonstrated.

In this study, 69 (70%) children were 5years or below. It is likely that many died by the age of 5years from opportunistic diseases, explaining the fewer numbers above that age. Those subjects who were older were sicker compared to those below 5years of age.

The diagnoses for the subjects at admission as noted were pneumonia, pulmonary tuberculosis and diarrhoeal disease, contributing about 70%. Two other common diagnoses were malnutrition and meningitis. Many of them had multiple diagnoses and the main diagnosis was the one recorded. More than half 55 (56%) of the subjects had been admitted at least once in the past, the diagnoses being more or less similar to those of the index admission. Pneumonia, tuberculosis and severe malnutrition could have interfered with cardiac function and act as confounders in its assessment. Congestive cardiac failure in its presentation may have been misinterpreted as pneumonia at admission only to be realised at echocardiographic evaluation.

Anaemia was noted to be very common in the study subjects, it was found in 73 (74%) of them. The commonest degree of anaemia found was mild anaemia in 57 (78%) of those who were anaemic. The anaemia was mainly microcytic with a mean MCV of 76.3fl, and a mean Hb of 8.8g/dl. This was probably due to Iron deficiency. No other tests were done to establish other possible causes of the anaemia. In the studies reviewed, none of them reported anaemia being an independent factor in the cause of cardiac dysfunction. In those studies the prevalence of anaemia and its type were not given since it was not studied specifically. Anaemia affects the heart in at least two ways: tachycardia and a hyperdynamic state, both due to hypoxemia. There is initially left ventricular hypertrophy as a compensatory mechanism then later progressive chamber dilatation due to increased circulatory volume. As the dilatation progresses, the valves may become incompetent from being stretched.

The significance of clinical characteristics as predictors of cardiac disease is not clear as they may on their own, be signs or symptoms of cardiac disease. A sub analysis (not shown) was done to evaluate the significance of these clinical characteristics. Anaemia and tachycardia were found to be significantly related to left ventricular dysfunction, p-values 0.01 and 0.02, odds ratios 4.06 and 3.19, and 95% confidence intervals 1.16 – 15.56 and 1.07 – 9.67. Dyspnoea and tachypnoea are symptoms of lung infection which when chronic may cause pulmonary hypertension and subsequent right sided cardiac failure. The two symptoms were significantly related statistically to RV dysfunction, p-values 0.01 and 0.01, odds ratios 10 and 3.98; and 95% confidence intervals 1.27 – 213.1 and 1.13 – 14.44. Dyspnoea and tachypnoea could have also been symptoms of cardiac failure, and thus acted as confounders. Other studies have not addressed clinical characteristics as predictors of abnormal cardiac structure and function.

From the regression model, the clinical characteristics were found be insignificant as predictors of cardiac disease. A diagnosis of pneumonia however was found to have a protective role, p-value 0.01, odds ratio 0.155 and 95% confidence interval of 0.035 – 0.681. The biological plausibility of this is not clear and is difficult to explain. This has not been put below as a conclusion for that reason. A prospective study may be useful in evaluating this significance.

**Strengths of the study.**

1. This study had a large number of subjects as compared to other studies which only had a few.

2. All the subjects had full cardiac evaluations and their chest x-rays, electrocardiographs and echocardiographs were reviewed by a consultant paediatric cardiologist.


**Study limitations**

1. The study subjects were very sick patients and thus there was delay in doing the investigations which required the patient to be taken out of the ward. Some of these patients died prior to completion of their investigations leading to their loss to the study.

2. Children admitted at KNH are generally very sick and would have a higher incidence of end organ disease.

3. Post mortem was not done on those who died. This could have additionally revealed more cardiac findings not discovered in life, and further laboratory work up would have demonstrated presence or otherwise of HIV in the cardiac tissue.

4. CD4 counts were not done in these patients due to its cost. This may have been useful in relating the degree of immunosuppression and the cardiac findings.

5. Fever, anaemia and severe wasting may have contributed to the alteration of cardiac function and acted as confounders

## Conclusions

1. There is a high prevalence of cardiac disease in patients with AIDS (65% in this study).

2. Clinical characteristics are poor predictors of heart disease as diagnosed on echocardiography.

3. Anaemia and tachycardia was significantly correlated to left ventricular dysfunction and likewise, dyspnoea and tachypnoea to right ventricular dysfunction.

## Recommendation

Cardiac evaluation by echocardiography should be done on all patients with AIDS since clinical characteristics are not reliable predictors for cardiac complications. In resource poor settings like ours where echocardiography cannot be done readily, chest x-ray, ECG and cardiologist evaluation are recommended.

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**APPENDIX I**

**QUESTIONNAIRE**

A: PATIENT'S DATA

1. Date   [ ] [ ]    [ ] [ ]    [ ] [ ]

2. Name  _____.

4.  Hospital number   [ ] [ ] [ ]    [ ] [ ]    [ ] [ ]

4. Study number [ ] [ ] [ ]    Code [ ] [ ] [ ]

5. Sex [ ] Male=1, Female = 2

6. Age in months   [ ] [ ] [ ]

**B. PRESENTING COMPLAINT(S) DURING THE ADMISSION**

Code complaint: Present=1, absent=2

Code duration: less than 1 week=1, 1-2 weeks=2, 3-4 weeks=3, more than 4 weeks=4

| Complaint | Present/Absent | Duration |
|---|---|---|
| Fever | | |
| Cough | | |
| Dyspnoea | | |
| Chest pain | | |
| Diarrhoea | | |
| Vomiting | | |
| Poor appetite | | |
| Failure to gain weight | | |
| Mouth lesions | | |
| Discharging ear(s) | | |
| Skin rash | | |
| Lethargy | | |
| Convulsions | | |

Others (specify) _____.

Diagnosis at admission _____.

## C. PAST MEDICAL HISTORY

1. Has the child been admitted in hospital in the past one year? [ ] Yes=1  No=2

2. If YES to question C1, state the number of times [ ] code 1=1, 2=2, 3=3, 4 or more =4

3. If YES to question C1, state the diagnosis at each admission by history and/or discharge summary.

Code

1=chest infection

2=Recurrent or persistent diarrhoea

3=other febrile illness

4=other (specify)

| Admission | Diagnosis |
|-----------|-----------|
| 1 | |
| 2 | |
| 3 | |
| 4 | |

4. Has the child received any transfusion of blood or blood products [ ], Yes=1, No=2

If yes, how many times? [ ].

5. Has the child ever had a procedure done on him/her by the traditional healer? [ ] Yes=1, No=2

(Circumcision, tooth extraction, ear piercing, injections or cuts).

6. Has the child been involved in any sexual intercourse or sexual abuse? [ ], Yes=1, No=2

7. Is this a street child or a child prostitute? [ ], Yes=1, No=2.

## D. SYSTEMIC ENQUIRY

1. Has the child had oral thrush in past one year? [  ] Yes=1, No=2

(White flaky plaques in the oral mucosa or on the tongue, that leaves a red raw area when removed or rubbed).

If yes, state the duration of the longest episode [  ]. More than 4 weeks, =1, less than 4 weeks, =2.

2. Has the child had any skin lesions in the past one year? [  ]. Yes=1, No=2.

3. Has the child had discharging ear(s) in the past one year? [  ]. Yes=1, No=2

If yes, state the duration of the longest episode [  ]. More that two weeks, =1, less than 2 weeks, =2.

4. How are child's milestones? [  ].

Retarded=1, Appropriate=2

5. Does the child get convulsions? [  ] Yes=1, No=2

If yes, state the type._____

6. CHILD - Has there been effort intolerance? [  ], Yes=1, No=2

INFANT - Has there been feeding difficulties or excessive sweating? [  ], Yes=1, No=2.

## E. PHYSICAL EXAMINATION

1. Weight in kilograms [  ] [  ]. [  ]

2. Height in centimetres [  ] [  ] [  ]. [  ]

3. Head circumference in centimetres [  ] [  ]. [  ]

4. Temperature at time of examination in degrees Celsius [  ] [  ]. [  ]

5. Left mid arm circumference [  ] [  ]. [  ]

FOR THE SIGNS WHICH FOLLOW 6 THROUGH 25 STATE PRESENT OR ABSENT

code

Present=1

Absent=2

6. Generalised lymphadenopathy [  ] (lymphnodes larger than 0.5 cm diameter in more than three anatomical sites).

7. Pallor      [  ]

## RESPIRATORY SYSTEM

8. Tachypnoea (High respiratory rate for age) [  ]          RR _____ /min

9. Chest in drawing (intercostal and/or subcostal retraction) [  ]

10. Basal rales on chest auscultation.   [  ]


## CARDIOVASCULAR SYSTEM

11. Cyanosis [  ]                                          HR _____ /min

12. Ankle oedema      [  ]                                 BP _____/mmHg

13. Tachycardia (high heart rate for age) [  ]             (where appropriate)

14. Pericardial friction rub [  ]

15. Gallop rhythm [  ]

16. Cardiomegaly (downward and /or outward displacement of cardiac apex) [  ]


## CENTRAL NERVOUS SYSTEM

17. Lethargy [  ]

18. Irritability   [  ]

19. Decreased level of consciousness [  ]

 20. Cranial nerve palsies [  ]

21. Motor deficits [  ]

22. Neck stiffness [  ]

23. Disorders of movement [  ]

### ENT

24. Discharging ear(s) [  ]

### SKIN

25. Skin lesions [  ]

Other significant findings _____


## F. LABORATORY RESULTS

1. HIV ELISA test _____.

2. Haemogram:

Hb _____g/dl   Red cell count _____ x$10^{12}$/L.

MCH _____pg/cell MCV____fl   MCHC ____g/dl

White cell count ____x10$^9$/L

        WBC differential Count   x 10$^9$/L    percentage

        Neutrophils                  _____ _____ .

        Lymphocytes               _____ _____.

        Monocytes                 _____ _____.

        Eosinophils                _____ _____.

        Basophils                 _____ _____.

        Band forms               _____ _____.

        Plateletes counts _____x10$^9$/l

## CHEST X-RAY FINDINGS

Code: features present=1, features absent=2

### Heart shadow

1. Right ventricular enlargement [  ]

2. Left ventricular enlargement [  ]

3. Right atrial enlargement [  ]

4. Left atrial enlargement [  ]

5. Pericardial effusion [  ]

### Lung fields

6. Pneumonia [  ]

7. Increased vascular markings [  ]

8. Pulmonary oedema [  ]

9. Pleural effusion [  ]

10. Pulmonary tuberculosis [  ]

## H. ELECTROCARDIOGRAPHIC (ECG) FINDINGS

1. Heart rate [  ], Normal=1, Tachycardia=2, bradycardia=3

2. Rhythm _____ QRS axis _____

3. Right ventricular hypertrophy [  ] Present=1, absent=2

4. Left ventricular hypertrophy [  ] present=1, absent=2

5. Right atrial enlargement [ ] present =1 absent=2

6. Left atrial enlargement [ ] present =1 absent=2

7. ST segment _____.

8. T wave _____.


## I: ECHOCARDIOGRAPHIC FINDINGS

MEASUREMENTS (M-MODE)


LA ____cm                 AO ____cm                 RVD ____cm

LVDD____cm                LVSD____cm                EF____%

LVPWD____cm               IVS____cm                 FS____%

HR ____beats per minute   SV____ml                  CO____L/min


TWO DIMENSIONAL ECHOCARDIOGRAPHY

| VALVES | MORPHOLOGY | FUNCTION |
|---|---|---|
| Mitral |  |  |
| Aortic |  |  |
| Tricuspid |  |  |
| Pulmonary |  |  |

Atrial septum          _____.

Ventricular septum     _____.

Wall motion            _____.

Pericardial effusion   _____.

## DOPPLER FINDINGS

Pulmonary pressure _____ mmHg.

Diastolic function _____

## CARDIAC INVOLVEMENT REVEALED

Code demonstrated=1, not demonstrated=2

1. Pericarditis and/or pericardial effusion [ ]

2. Myocarditis and/or "cardiomyopathy" [ ]

3. Left ventricular dysfunction [ ]

4. Right ventricular dysfunction or cor pulmonale [ ]

5. Conduction defects [ ]

6. Cardiac neoplasm/mass [ ]

7. Cardiomegaly [ ]

8. Valvular abnormalities [ ]

9. None [ ]

**APPENDIX II**

**WHO CLINICAL CASE DEFINITION FOR PAEDIATRIC AIDS (1986) [28]**

MAJOR SIGNS

1. Weight loss or abnormally slow growth

2. Chronic diarrhoea lasting for more than a month

3. Prolonged fever lasting for more than a month

MINOR SIGNS

1. Generalised lymphadenopathy

2. Oropharyngeal candidiasis

3. Repeated common infections eg. otitis media and pharyngitis

4. Persistent cough

5. Generalised dermatitis

6. Confirmed maternal HIV infection

Diagnosis of AIDS is made if a child has at least 2 major signs and 2 minor signs in the absence of known causes of immunosuppression.

# APPENDIX III

## NORMAL RESPIRATORY RATES

| Age | Rate (breaths /min) |
| --- | --- |
| Less than 2 months | Less than 60 |
| 2 months to 12 months | Less than 50 |
| 1 year - 5 years | Less than 40 |
| 5-12 years | Less than 30 |

## NORMAL HEART RATES [40]

| Age | Rate (beats/min) |
| --- | --- |
| Neonate | 110-150 |
| 1 month - 1 year | 90-135 |
| 1-5 years | 85-115 |
| 5-12 years | 70-100 |

## ECG CHANGES IN CARDIAC ENLARGEMENT AND HYPERTROPHY [29]

RA enlargement: p wave taller than 2.5 mm (0.25 mV)

LA enlargement: P wave duration more than 120 ms (3mm) in lead II or $V_1$.

RV hypertrophy -Right axis deviation (QRS axis >positive 100 degrees)

-Tall R wave in $V_1$ (R wave at least the size of the S wave), aVR and $V_2$ more than 10mm (1mV).

LV hypertrophy -Tall left precordial R waves and deep right precordial S waves.

$SV_1$ + ($RV_5$ or $RV_6$) at least 35mm, OR $RV_5$ or $RV_6$ at least 25mm.

-Left axis deviation (QRS axis> negative 30 degrees)

-RaVL at least 11mm, OR RaVF at least 20mm or $R_1$+$S_{III}$ at least 25mm.

# APPENDIX IV SAMPLE ECHOCARDIOGRAMS



1. Massive pericardial effusion with thickened pericardium. There were features of cardiac tamponade. Subject underwent pericadiocentesis and the repeat echocardiography showed no effusion.
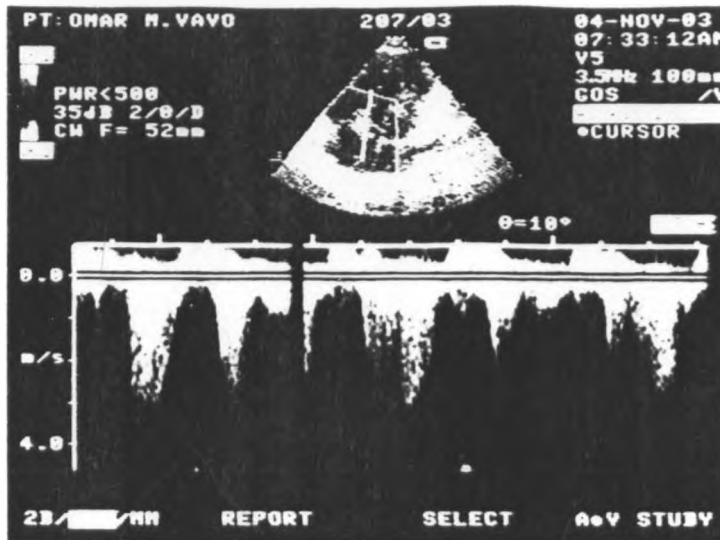
2. All cardiac chambers are dilated. There is tricuspid regurgitation ~3m/sec. the estimated pulmonary pressure is ~45-50mmHg.
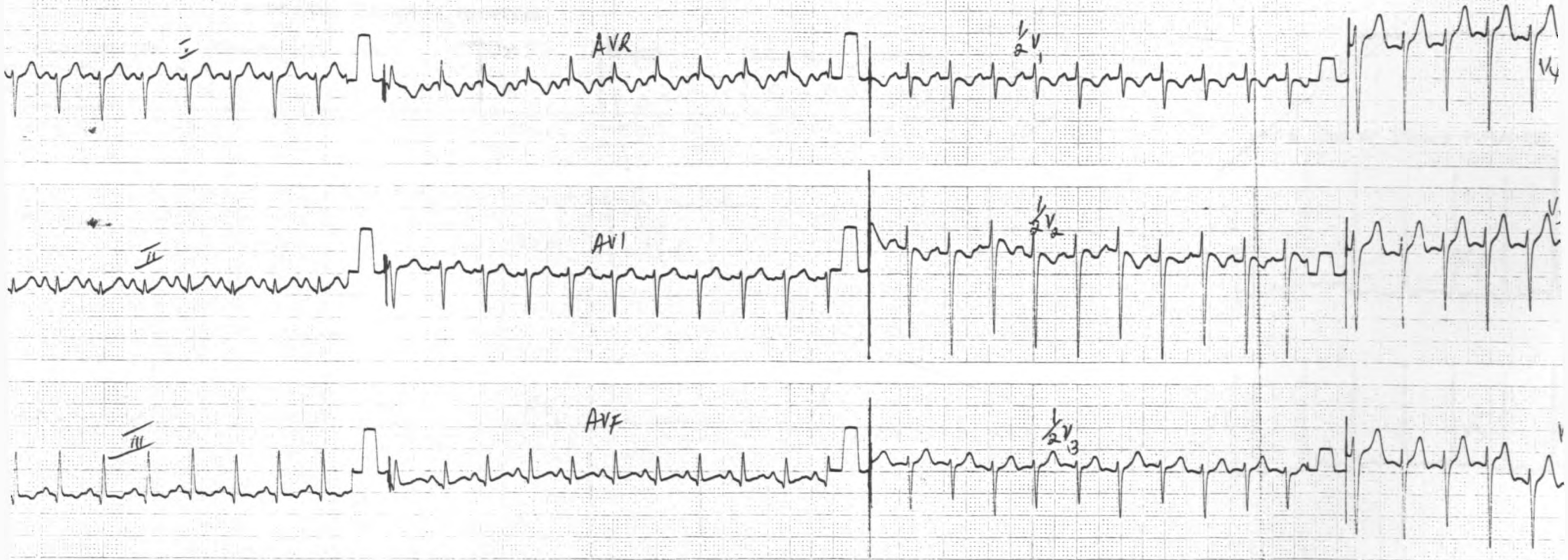
# APPENDIX V: SAMPLE ELECTROCARDIOGRAMS.

O1

### KENYATTA NATIONAL HOSPITAL

KNH 381

| E.C.G. REPORT | NAME Collins | AGE O91 | WARD | E.C.G. No. | UNIT No. |
|---|---|---|---|---|---|
| Date: 6/05/2003 | Omondi | 5.yrs | BB | 1514. | 0857452 |

mm/mV  25mm/s  F:HUM+MYO         aVR-L-F  10mm/mV  25mm/s  F:HUM+MYO         V1,2-3  5mm/mV, 25mm/s  F:HUM+MYO         V4,5-6  10mm/mV  25mm



Sinus rhythm. Tachycardia, HR ~150/min. Right axis deviation. Right atrial enlargement. Severe right ventricular hypertrophy.

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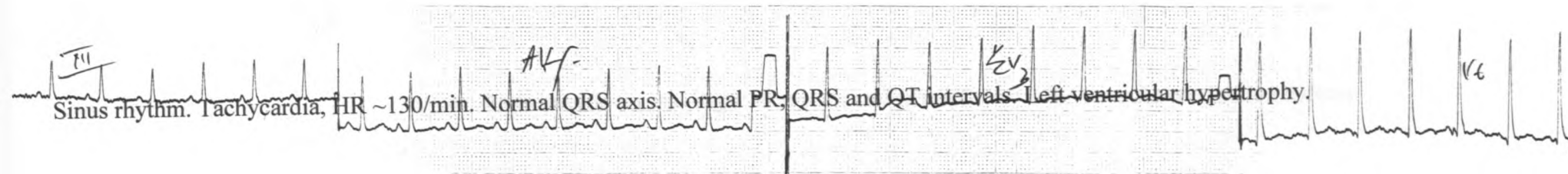| E.C.G. REPORT | NAME Samuel | AGE | WARD | E.C.G. No. | UNIT No. |
|---|---|---|---|---|---|
| e: 28/05/2003 | Odhiambo | 8 | 3c | 1630 | Q862412 |

0mm/mV  25mm/s  F:HUM+MYO  |  aVR-L-F  10mm/mV  25mm/s  F:HUM+MYO  |  V1-2-3  5mm/mV  25mm/s  F:HUM+MYO  |  V4-5-6  10mm/mV  25mm/s  F:HUM+MYO

Sinus rhythm. Tachycardia, HR ~130/min. Normal QRS axis. Normal PR, QRS and QT intervals. Left ventricular hypertrophy.

E.C.G. REPORT | NAME _Antony_ | AGE | WARD | E.C.G. No. | UNIT No.
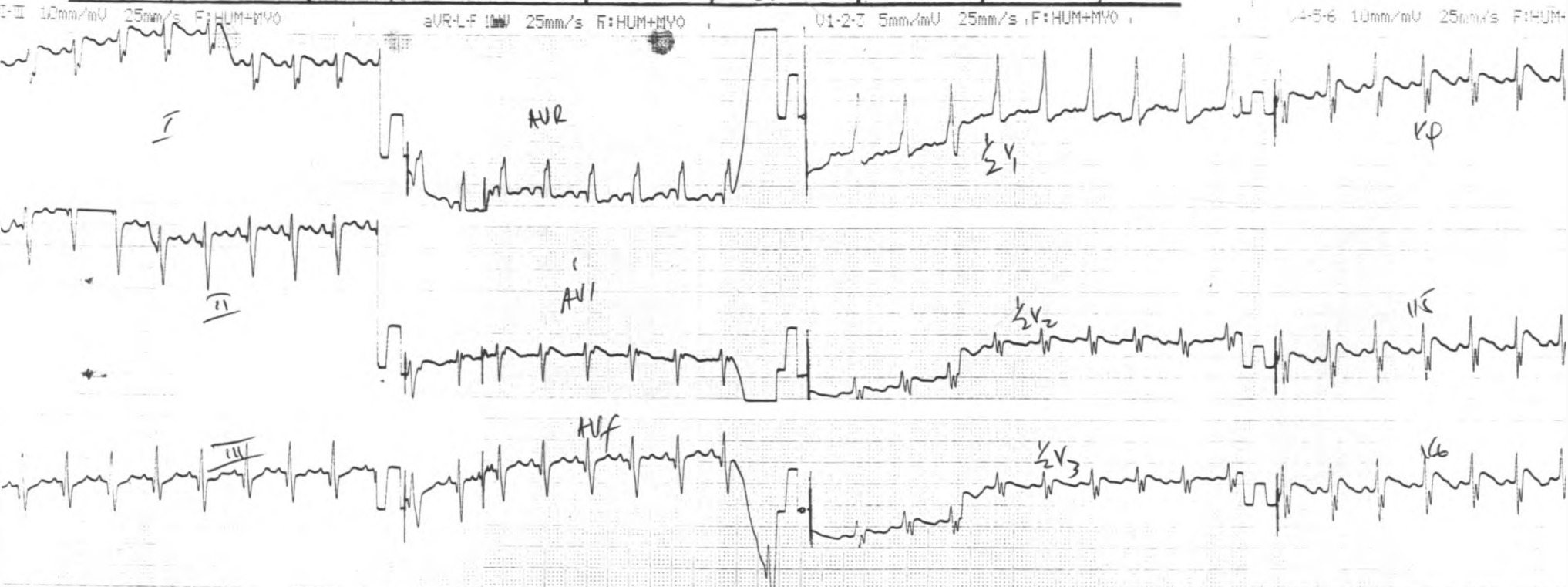
Date: 5/02/2003

I-II 10mm/mV 25mm/s F:HUM+MYO     aVR-L-F 1mV 25mm/s F:HUM+MYO     V1-2-3 5mm/mV 25mm/s F:HUM+MYO     V4-5-6 10mm/mV 25mm/s F:HUM

SUMMARY:

LPS

CLASS: WNL. PWNL BT. PAT. DAT.

REPORTED BY DR. _____

Sinus rhythm. Tachycardia, HR ~150/min. Right axis deviation. Right ventricular hypertrophy with non specific conduction defects.

53

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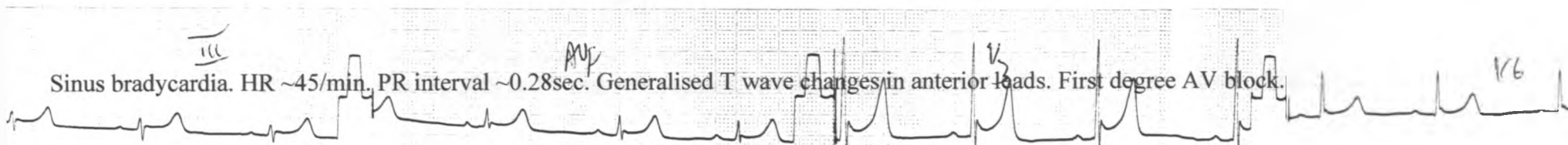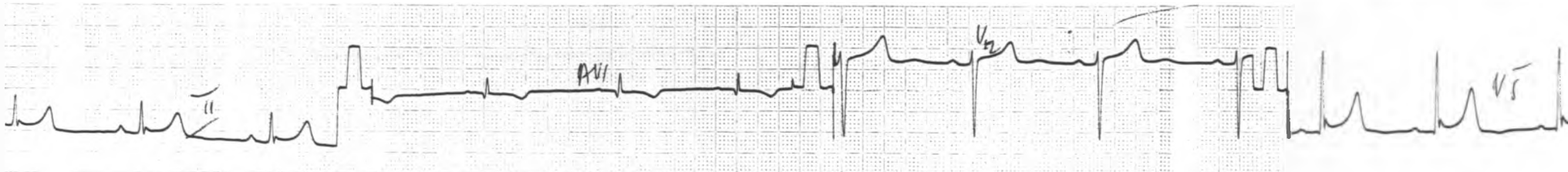| E.C.G. REPORT | NAME *Charles* | AGE | WARD | E.C.G. No. | UNIT No. |
|---|---|---|---|---|---|
| Date: 22/11/2002 | Mwuni K. | 8 | 30 | 3308 | D842502 |

0mm/mV 25mm/s F:HUM+MYO    aVR-L-F 10mm/mV 25mm/s F:HUM+MYO    V1-2-3 10mm/mV 25mm/s F:HUM+MYO    V4-5-6 10mm/mV 25mm/s F:HUM+

I    AVR    V1    V4

II    AVL    V2    V5

III    AVF    V3    V6

Sinus bradycardia. HR ~45/min. PR interval ~0.28sec. Generalised T wave changes in anterior leads. First degree AV block.

CLASS: WNL. PWNL BT. PAT. DAT.

54

| E.C.G. REPORT | NAME David | AGE | WARD | E.C.G. No. | UNIT No. |
|---|---|---|---|---|---|
| Date 28/00/00    013 | Miiunha. | A. | Mfk | 1335 | 0652897. |

I

AVR

V1

V4

II

AVL

V2

V5

III

AVF

V3
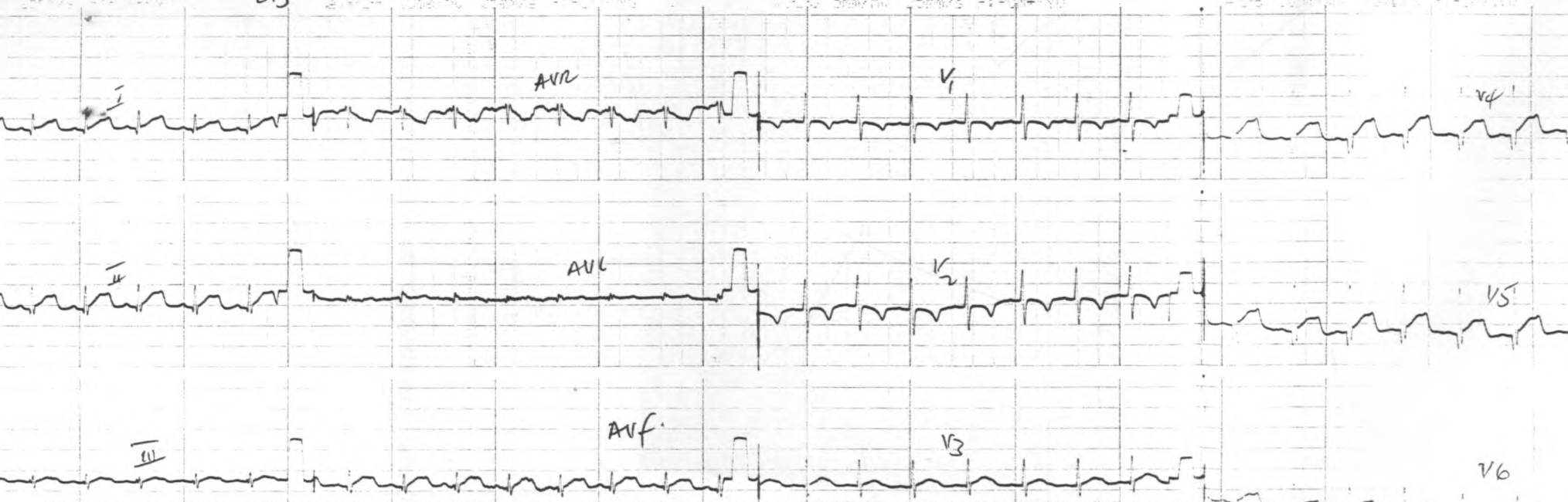
V6

Sinus rhythm. HR ~120/min. Normal P, QRS and T axis. ST segment elevation in I, II, III, aVF, aVR, and V4-6. Likely pericarditis.

SUMMARY:

CLASS: WNL. PWNL BT. PAT. DAT.

REPORTED BY DR. _____

LPS

55

# APPENDIX VI

## SAMPLE CHEST X-RAY PICTURES

CXR 1



There is cardiomegaly with right ventricular prominence. Cardiothoracic ratio (CTR) is 8:13.5. Bilateral nodular opacities are noted.

     **Conclusion:** Bronchopneumonia with cardiomegaly.

     **Echocardiography:** Diastolic dysfunction with echogenic myocardium.

CXR 2.



There is partial collapse of the right lung. There are bilateral pneumonic infiltrates.

The heart and bony cage are normal.

**Conclusion:** Right pnemothorax with Bronchopneumonia.

**Echocardiography:** mild pulmonary hypertension, pressures 35-40mmHg.

CXR 3.



There are bilateral reticulonodular opacities and air-bronchogram effect. The mediastinum is widened. The heart and bony cage are within normal limits.

**Conclusion:** Tuberculosis.

**Echocardiography:** moderate pulmonary hypertension, pressures 45-50mmHg.

CXR 4.



There are bilateral basal opacities with cystic changes in the right base. The cardiac shadow and bony cage appear normal.

**Conclusion:** pulmonary tuberculosis with right basal bronchiectatic changes.

**Echocardiography:** severe pulmonary hypertension, pressures 65-70mmHg with mild dilatation of the right ventricle.

CXR 5.



There is a right upper lobe mass with pressure effect. The heart size and shape and the bony cage are normal.

**Echocardiography:** normal findings.

CXR 6.



There is left sided pleural effusion. Patchy opacities are noted in the right lung field with right sided mediastinal shift.

**Conclusion:** Tuberculosis.

**Echocardiography:** normal findings.

**APPENDIX VII**

**CONSENT FORM**

IP NO.      [ ]   [ ]   [ ]   [ ]   [ ]   [ ]   [ ]

STUDY NO. [ ]   [ ]   [ ]              Code  [ ]   [ ]   [ ]

I, DR. KIPTUM of the Department of Paediatrics, University of Nairobi, am investigating children admitted to KNH general paediatric wards to determine the cardiac presentations in children with AIDS.

The study involves certain specific questions and examinations of your child and investigations done will include; HIV screening, blood cell counts, chest x-ray, electrocardiography and echocardiography. The results of these tests will be availed to your child's primary doctor(s) so that early specific treatment can be started for any abnormality detected.

The results of the study will be treated with strict confidence.  You may quit the study at any stage without any obligation, and the management of your child will not be interfered with at the least.

I agree to be part of this study.

NAME _____ SIGNATURE _____
                Parent/Guardian

WITNESS SIGNATURE _____ Date _____

(Dr. Kiptum)

**KENYATTA NATIONAL HOSPITAL**
**P.O. Box 20723, Nairobi**
Telegrams: "MEDSUP", Nairobi
Email: knh@healthnet.or.ke

Ref.........KNH-ERC/01/917                                    Date..14 February 2001

Dr. D.l. Kiptum
Dept. of Paediatrics
Faculty of Medicine
University of Nairobi

Dear Dr. Kiptum,

RE: **REVISED RESEARCH PROPOSAL** "A PROFILE OF CARDIAC MANIFESTATIONS
IN CHILDREN WITH ACQUIRED IMMUNODEFICIENCY SYNDROME   AT   KENYATTA
                NATIONAL   HOSPITAL"   (P809/8/99)

I am pleased to inform you that the KNH-Ethical & Research Committee
has reviewed and approved the revised version of your research proposal.
However you are requested to define the number of cases that will
constitute the control group.

Meanwhile the Committee takes this opportunity to wish you fruitful
research and look forward to receiving a summary of the research
findings and recommendations.

Yours sincerely,


PROF. A.N. GUANTAI
SECRETARY, KNH-ERC

cc   Prof. K.M. Bhatt
     Chairman, KNH-ERC

     Deputy Director (C/S), KNH

     Supervisors:   Dr. C.A. Jowi, Dept. of Paediatrics, UON
                    Dr. Mbori-Ngacha, Dept. of Paediatrics, UON

     The Chairman, Dept. of Paediatrics, UON

     The Dean, Faculty of Medicine, UON