PREVALANCE OF ABNORMAL LUNG FUNCTION TESTS AND ASSOCIATED CLINICAL FEATURES AMONG HIV INFECTED CHILDREN AGED 7-18 YEARS IN DAR ES SALAAM, TANZANIA

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By

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A Dissertation Submitted in (partial) Fulfilment of the Requirements for the Degree of Master of Medicine (Paediatrics and Child Health) of Muhimbili University of Health and Allied Sciences

Muhimbili University of Health and Allied Sciences
October, 2015

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled ***Prevalence of abnormal lung function tests and associated clinical features among HIV infected children aged 7-18 years in Dar es Salaam, Tanzania*** in (partial) fulfilment of the requirements for the degree of Masters of Medicine (Paediatrics and Child Health) Muhimbili University of Health and Allied Sciences.

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Date

DECLARATION
AND
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I **Yahya H. Binde** Declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

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DEDICATION

I dedicate this dissertation to my beloved parents, my mother, Khadija Mressa and my late father, Hussein Binde, who sacrificed a lot in raising and shaping me to become the person I am to today. I also dedicate it to my aunt, Theresia Mghanga who has been always there for me throughout the struggle in my career. May God bless you.

ABSTRACT

Background: HIV/AIDS is still a major health burden in Sub-Saharan Africa and the whole world at large. Recent data from African countries shows the prevalence of chronic lung disease (CLD) is high in children living with HIV/AIDS. With the initiation of antiretroviral medications early in infancy, many HIV infected children are expected to live longer, hence prone to other comorbid conditions including chronic lung disease. There is no study which has been done in Tanzania to assess the abnormal lung function tests in children living with HIV/AIDS. Hence this study will provide the baseline information about the magnitude and risks factors for chronic lung disease.

Objective

To determine the prevalence of abnormal lung function tests and associated clinical features among HIV infected children aged 7-18 years in Dar es salaam, Tanzania.

Methodology

This was a hospital-based cross-sectional study design, carried out in two centres, Infectious Disease Centre and Muhimbili National Hospital care and treatment clinics (CTC). Both clinics are situated within Ilala Municipality in Dar es Salaam Tanzania. Study duration was nine months. Study population included all HIV infected children aged 7-18 years who attend both centres. A structured questionnaire was used for collection of data. After the history was obtained, children underwent physical examination before assessment of lung functions by spirometry.

Data were analysed using Statistical Package for Social Science (SPSS) version 20. Continuous variables were expressed as mean, standard deviation, median and interquartile ranges. Chi-square and fisher's exact test were used to compare categorical variables. Student's T-test and Mann Whitney U test were used to determine if there was any significant difference between the groups with normal and abnormal functions. A P-value of <0.05 was considered statistically significant.

Results:

A total of 121 children aged 7-18 years were included in this study. There was predominance of adolescents 82 (67.8%). Males were 75 (62%) and over half of the children 67 (55.4%) were orphans. The prevalence of abnormal lung function tests was found to be 17.4% (95% CI=10.7-24.8). Pulse oximetry findings showed that, none of the study participants were hypoxic at rest or post exercise. Physical findings revealed a history of chronic cough in half, lung crepitations in 19%, and peripheral cyanosis in 14% of the study participants. All these signs were associated with abnormal lung function tests ($p=0.021$, $p<0.01$, $p<0.01$ respectively). Most children 15 (71.4%) had advanced WHO HIV clinical disease stage (III & IV). However CD4 cell count did not affect the lung function tests ($p=0.560$). The median duration of HIV infection since diagnosis and the median duration on Antiretroviral Therapy (ART) use were comparatively short, 246 weeks (IQR 128 - 418) and 243 weeks (IQR 123 - 356) respectively. Assuming that most children acquire HIV infection through vertical transmission, it implies that they were diagnosed late and hence late initiation on ART which may have contributed to the abnormal lung function tests.

Conclusion and Recommendation:

The prevalence of abnormal lung function tests in HIV infected children is relatively high. This implies that chronic lung disease may go undetected and can contribute to high morbidity and mortality in this population. Presence of chronic cough, peripheral cyanosis and lung crepitations have shown to be important features in HIV infected children with lung function impairment.

HIV infected children presenting with chronic cough, peripheral cyanosis and lung crepitations should undergo lung function tests for early detection of chronic lung disease. Further studies should be done to identify the actual cause of chronic lung disease among HIV infected children. This will allow timely and appropriate management which may improve their quality of life.

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ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
BMI	Body Mass Index
CLD	Chronic Lung Disease
COPD	Chronic Obstructive Pulmonary Disease
CTC	Care and Treatment Centre
FEV_1	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
HIV	Human Immunodeficiency Virus
ILD	Interstitial Lung Disease
IQR	Interquartile Range
LIP	Lymphoid Interstitial Pneumonitis
MDH	Management and Development for Health
MNH	Muhimbili National Hospital
NGO	Non-Governmental Organization
PCP	Pneumocystis pneumonia
PTB	Pulmonary tuberculosis
SD	Standard deviation
SSA	Sub-Saharan Africa

DEFINITIONS OF TERMS

For the purpose of this study, the following definitions of terms were used:

Adolescent: Any person between the age of 10 and 19 years

Abnormal lung function test: Defined as Forced Expiratory Volume in 1 second (FEV_1) <80% of the predicted value.

Chronic cough: Cough lasting for ≥ 14days.

***Delayed ART initiation*:** ART initiation more than 2weeks from the time of HIV diagnosis.

***Exercise*:** Regarded as climbing 2 flight of stair case unassisted

Increased work of breathing: difficulty in breathing accompanied by use of accessory muscles of respiration

Moderate stunting: Height for age -2 and -3 Standard deviation

***Moderate wasting*:** BMI between -2 and -3 Standard deviation

Normal growth: Height for age above -2 and median

***Normal nutritional status*:** BMI between -2 and 1 Standard deviation

Obese: BMI above 2 Standard deviation

Orphan: A child who lost either parent or both parents

Over weight: BMI between 1 and 2 Standard deviation

Recurrent fever: 3 or more episodes of fever within 6 months

Recurrent pneumonia: ≥2 episodes of pneumonia attacks within 6 months

***Severe immunosuppression*:** CD4 cell count <350/mm^3

Severe stunting: Height for age below -3 Standard deviation

Severe wasting: BMI below -3 standard deviation

Vertical transmission: Transmission of HIV from mother to Child

Very sick child: Child with features of severe sepsis (tachycardia, tachypnoea, fever/hypothermia) accompanied by evidence of hypoperfusion or dysfunction of at least one organ system.

CHAPTER ONE

1.0 INTRODUCTION AND LITERATURE REVIEW

Globally, HIV/AIDS still remains to be a major health problem affecting all age groups. About 34 million people in the year 2011 were estimated by UNIAIDS to be living with HIV/AIDS (1).

Sub-Saharan Africa is still leading in the global HIV burden. It is estimated that about 69% of people living with HIV/AIDS worldwide are in Sub-Saharan Africa (1).

In Tanzania, a Sub-Saharan country, HIV/AIDS prevalence is high (5.1%) and has affected both social and economic aspects. In year 2011, an estimated 1.6 million Tanzanian people were living with HIV/AIDS and among them 1.3 million were aged 15 years or older (2).

Children have not been spared, by the year 2011; 3.4 million children were living with HIV/AIDS worldwide. There were 330,000 new infections and 230.000 deaths attributed to HIV/AIDS. Most of the deaths came from Sub-Saharan Africa (3).

The high incidence of HIV/AIDS in children depends on the rate of HIV infection among women of reproductive age, their fertility rate and the effectiveness of mother to child transmission of HIV infection programme (4).

HIV infection can be acquired through unprotected sexual intercourse, exposure to infected blood products, sharing sharp objects and through mother to child transmission (5). In Sub-Saharan Africa, sexual transmission has been found to be a predominant mode of transmission followed by mother to child transmission (6,7). Early HIV diagnosis and treatment is therefore critical for the survival and quality of life improvement among HIV infected children (8–10).

Chronic lung diseases continue to be underdiagnosed although they are among the leading causes of chronic morbidity and mortality worldwide (11). According to the 2030 global disease projections, chronic lung diseases are estimated to be among the top three leading causes of morbidity and mortality in the world (12).

Following HIV infection, different systems of the body can be affected. Chronic lung disease which is preceded by recurrent chest infection can be life threatening and needs urgent assessment. Studies have shown that the prevalence of chronic lung disease in HIV infected children is higher compared to HIV negative children (13). This could be due to a direct damage to lung tissue by the virus itself or as a result of immune suppression with subsequent recurrent airway infection and inflammation.

Several studies have demonstrated increased risk of chronic lung disease in HIV infected individuals with history of recurrent bacterial pneumonia, pneumocystis pneumonia (PCP), pulmonary tuberculosis (TB), cigarette smoking and malnutrition (14,15). Currently it has been shown that ART initiation is related to down-regulation of pulmonary diseases and consequently improving the quality of life among HIV infected individuals (15).

In Zimbabwe, it was shown that among admitted adolescents (aged 10 - 18years), 46% were HIV positive and had low median CD4 count of 151 cells/µl. The adolescents in this group were more likely to be stunted, orphans and born to a HIV positive mothers. Respiratory and cardiovascular diseases were the commonest causes for admission. Older children and adolescents presenting with HIV infection have low immunity as evidenced by advanced WHO clinical disease staging and low CD4 cell count. This is possibly a result of delayed HIV diagnosis and ART initiation often for more than a decade (16,17).

In a study done in the United State of America (USA), respiratory symptoms including cough, sputum production, chest pain and difficulty in breathing were more common in HIV positive individuals as compared to HIV negative individuals (18). Radiological abnormalities with features suggestive of post tuberculosis lung disease were highly prevalent in HIV positive children as well. Computerized tomography

scan among this group revealed features of bronchiectasis, abnormal wall thickening, consolidation and nodular lesions which are suggestive of chronic obstructive pulmonary disease (COPD) (19). Underlying pathophysiologic mechanism(s) is/are unknown.

Some studies have shown that CD4 cell count is significantly related to abnormality in lung function tests (FEV_1) and FEV_1/FVC ratio (20,21). However these findings differ in other studies. For example, in Zimbabwe it was revealed that although FEV_1 < 80% among HIV infected children was high in both sexes, it was neither influenced by their CD4 cell count nor their ART duration (19).

Currently, abnormal lung function test (FEV_1) have been shown to be an important predictor of increased respiratory mortality (22). In children with chronic cough, exercise has been shown to be associated with low FEV_1/FVC ratio, which could be due to reduced airway flow as a result of bronchospasm (23).

In children, spirometry findings are affected by age, sex, and height. In a study done among white children in United Kingdom, it was found that children below 152.6cm height, portrayed a slight difference in lung function test among boys and girls of the same height with slightly increase in boys than in girls. As these children approached puberty there was a significant improvement in performance in lung function tests in both sexes, however this was more pronounced in boys than girls. These finding can be explained by hormonal changes after puberty with increased muscle power and thoracic dimension which are more remarkable in boys than in girls of the same age (24,25).

LUNG FUNCTION TESTS IN CHILDREN

Lung function tests are important diagnostic tests, which can provide information on how well the lungs are functioning. These can be used to evaluate a child with known or suspected respiratory disease and monitor response to treatment. These tests include; spirometry, peak expiratory flow rate, nitric oxide exhalation test, muscle pressure, diffusion capacity measurements, arterial blood gases and pulse oximetry.

Spirometry has been used for screening, diagnosis and monitoring of patients with chronic lung diseases (26,27). It is easy to operate, less expensive and it is recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) for diagnosis of chronic lung diseases (28). Spirometry is the most useful instrument for evaluation of chronic lung diseases in children above six years. Although can be done in younger age but due to difficulty in understanding the instructions and cooperation required for performing the expiratory manoeuvres, the age above six years was found to be more appropriate (29). Other factors which can influence the results obtained from the spirometry includes personal and technical issues. The most important parameters in spirometry are: the forced expiratory volume in 1 second (FEV_1) which is the maximum volume delivered in one second after maximum inspiration and the forced vital capacity (FVC) which is the maximum forceful volume produced during expiration after full inspiration (30).

For the purpose of this study the presence of post bronchodilator FEV_1<80 of the predicted value with FEV_1/FVC ratio <70 indicate obstructive lung disease while FEV_1<80 of the predicted value with normal FEV_1/FVC ratio indicate restrictive lung disease which is based on GOLD (28).

HIV associated chronic lung diseases in children

Lymphoid interstitial pneumonitis (LIP):

This has been linked with hyperplasia of the mucosal associated lymphoid tissue. For the case of immunocompromised patients, LIP is presumed to be an outcome of lymphoid proliferation due to HIV or EBV viruses (31,32). A study which was done in South Africa showed that among children with chronic lung disease, LIP was only found in HIV positive. In these children, LIP was the most common chronic lung disease (33). Management of LIP include oxygen therapy to correct hypoxia, low dose steroid with bronchodilator in case of wheeze and chest physiotherapy. Broad spectrum antibiotics may be considered if there is co-infection with bacterial (4).

***Bronchiectasis*:**

This condition is characterized by abnormal and irreversible dilatation of the airway (bronchus) causing chronic cough, air way obstruction and recurrent respiratory tract infection (34). In developed countries cystic fibrosis is the most common non-infectious cause of bronchiectasis. In most African countries post infection with viruses, bacteria, tuberculosis, mycoplasma are the leading cause of bronchiectasis. However the incidence has dropped due to introduction of antibiotics and immunization programs (35,36). In the HIV era, bronchiectasis has been linked with recurrent pneumonia attacks and ongoing unmanaged lymphoid interstitial pneumonitis (LIP) infection (37). Normally bronchiectasis is managed with broad spectrum antibiotics, bronchodilator, chest physiotherapy, sometimes surgery might be indicated in case of segmental lung damage (4).

Pulmonary tuberculosis (TB)

HIV infection pose more than 3 times high risk of developing TB infection. It also worsens the progress of Tb infection to Tb disease (38). Studies have shown that TB which occurs as co-infection with HIV increases the risk of chronic lung disease. This is mostly due to the consequence of TB treatment or recurrent TB infection (39,40). Management of pulmonary tuberculosis include six months course of anti-tuberculosis medications (38).

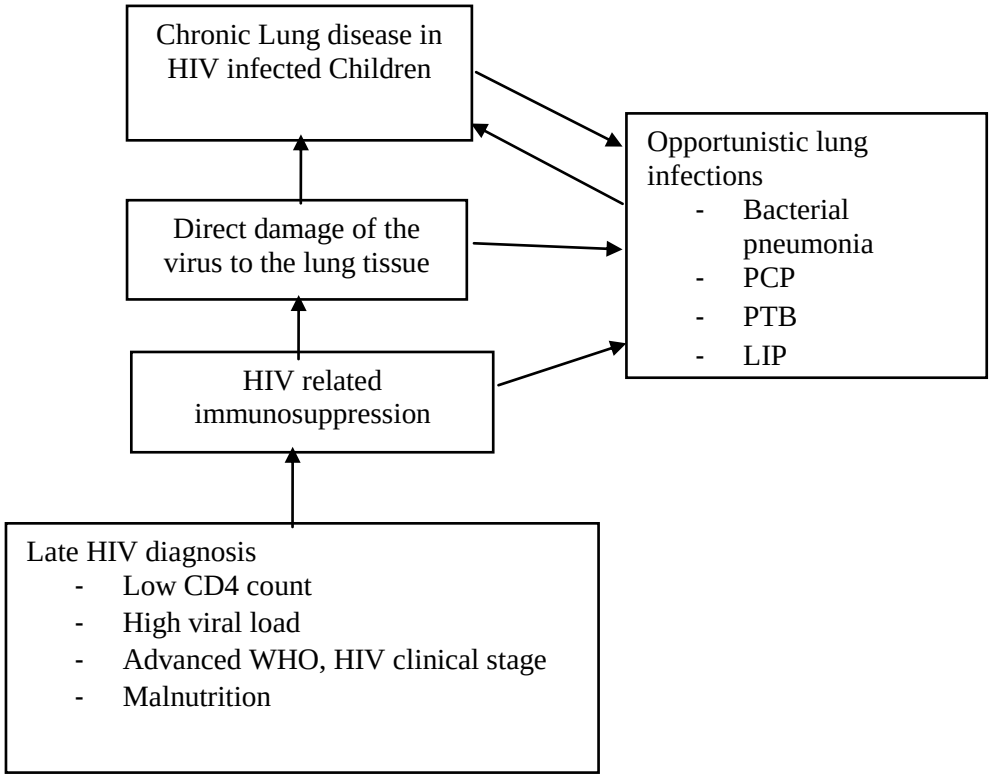
***Other pulmonary infections*:**

Recurrent pneumonia secondary to bacterial infection commonly *Haemophilus influenza*, *Streptococcal pneumonia* and viral, fungal or mixed infections are important risks linked to chronic lung disease in children. The most frequently observed respiratory infections pre ART era, are bacterial pneumonia, Pneumocystis pneumonia and respiratory candidiasis (41). Treatment of pulmonary infection is individualised and may involve broad spectrum antibiotics, antifungal, or high dose Co-trimoxazole for PCP. Oxygen therapy and chest physiotherapy may be indicated as well (4).

***Bronchiolitis obliterans**:*

This is a rare form of chronic lung disease. Its occurrence is linked with bronchial fibrosis resulting to substantial air trapping and patients will present with dyspnoea. Adenovirus and mycoplasma infections in early childhood have been related to the development of this condition later on in life (42,43). Management of bronchiolitis obliterans includes oxygen therapy in case of hypoxia, antibiotics, steroids, bronchodilators and chest physiotherapy (44).

1.1 Conceptual framework



HIV infected children are expected to be at high risk of acquiring respiratory tract infections including pneumonia, pulmonary tuberculosis, and other lung opportunistic infections like PCP and LIP. As the result of recurrent and chronic respiratory infections due to opportunistic organisms lead to the destruction of lung parenchyma and predispose the child to chronic lung disease. Another possibility is the effect of direct damages of the virus its self to the lung parenchyma cells.

1.2 Problem statement

Children with HIV infection are now living longer after introduction of free ART to all infected children. Studies in developed countries and some countries in Sub-Saharan Africa (SSA) have demonstrated chronic lung disease to be a significant problem among this population. Chronic lung disease in SSA is largely contributed by complications of infectious diseases such as pulmonary tuberculosis (PTB). Tanzania is one of the countries where both HIV and PTB are endemic, hence likely to have high magnitude of abnormal lung function tests among HIV infected children. Adolescent pose more risk because mostly acquire HIV infection vertically and have lived with HIV for a significant period of time.

1.3 Rationale

Few studies have been done in Sub-Saharan Africa on chronic lung disease among children with HIV infection. This study will provide us with valuable information regarding the gravity of this problem in our country. Also information concerning risk factors for chronic lung disease will be obtained hence planning for an early intervention to improve the quality of life to these children. Moreover this study will give indication as to whether there is a need for routine screening for lung function tests for HIV infected children. This may be necessary so that appropriate management is provided to subsequently reduce morbidity and mortality among HIV infected children in our country.

1.4 Research questions

1) What is the magnitude of chronic lung disease among HIV infected children in Dar es Salaam, Tanzania?
2) Is late WHO, HIV clinical disease stage associated with chronic lung disease?
3) Does prolonged use of ART reduce the incidence of chronic lung disease?

1.5 Study Objectives

1.6.1 Broad objective

To determine the prevalence of abnormal lung function tests and associated clinical features among HIV infected children aged 7-18 years in Dar es Salaam, Tanzania.

1.6.2 Specific objectives

1. To determine the prevalence of abnormal lung function tests among HIV infected children aged 7-18 years.
2. To determine the relationship between abnormal lung function tests and clinical findings among HIV infected children.
3. To determine the relationship between duration of HIV confirmation and abnormal lung function tests.
4. To determine the relationship between abnormal lung function tests and ART duration.

CHAPTER TWO

2.0 METHODOLOGY

2.1 Study design

This was a hospital based cross-sectional study.

2.2 Study area

This study was conducted at Infectious Disease Control (IDC) and Muhimbili National Hospital (MNH) Care and Treatment Centre (CTC) clinics. All these clinics are situated in Dar es Salaam, Tanzania. They are situated about 5km distance apart and receive patients from all districts of Dar es Salaam city. Both clinics provide free care and treatment to HIV infected children as part of National AIDS Control Programme (NACP) policy. Both clinics adhere to the national guidelines for the management of HIV and AIDS. They enrol all HIV exposed children and those with confirmed HIV infection. Basic routine investigations includes; CD4 cell count, viral load, haemoglobin level, renal function tests, liver function tests and chest x-ray.

IDC clinic provides HIV testing, counselling, care and treatment for adult and children aged 0-18 years. The IDC paediatric clinic is managed jointly by investigators from the Geisel School of Medicine at Dartmouth and Muhimbili University of Health and Allied Sciences (MUHAS). It receives support from Management and Development for Health (MDH), a local Non-Governmental Organization (NGO) serving as a developmental partner for HIV/AIDS activities in Dar es Salaam. The clinic has two medical doctors and four nurses. It operates on the five working days and has an adolescent club once every month. In addition the clinic has pharmacy and laboratory services. It serves approximately 900-1000 children in a year.

Also as mentioned above, some of the participants were recruited from the CTC clinic at Muhimbili National Hospital (MNH). MNH is the national referral hospital which attends about 1000-1200 outpatient per week and has a 1500 beds capacity. The paediatric department receives about 6000-7000 referrals per year in different sub specialties including infectious diseases dealing in HIV and TB. The clinic has three medical doctors and five nurses who attend patients. It has pharmacy and

laboratory facilities and it operates on the five working days and has adolescent club once every month.

2.3 Study population

All HIV infected children attending CTC clinics at IDC and MNH from May 2014 to Feb 2015.

2.3.1 Inclusion criteria

- All children with HIV/AIDS aged 7-18 years attending CTC clinics at IDC and MNH.
- HIV positive children whose parents/guardians agreed a written informed consent.
- HIV positive adolescents who gave assent.

2.3.2 Exclusion criteria

- HIV positive children who were very sick or had severe anaemia at the time of recruitment.
- Children with congenital / acquired heart disease/heart failure.
- Children with spinal deformity.

Children who were very sick were excluded because they might not have been able to perform the test; whilst those with existing congenital anomalies were prone to have abnormal lung function tests.

2.4 Sample size estimation

A minimum sample size was computed by using the following formula with an assumption that 33% of HIV infected children have abnormal lung function tests as observed from a study done in Malawi (45). We employed the formula for finite population because the two CTC clinics have a turnover of approximately 400 children aged 7-18years who regularly attend clinic in nine months**.**

$$n = \frac{Nz^2\,pq}{d^2(N-1)+z^2pq}$$

Where; n = estimated minimum sample size of participants interviewed.

N=Population size who were expected to attend clinics during study time (400).

z= 1.96 approximated to 2 (at 95% confidence interval).

P= Proportion of CLD among HIV infected children in Malawi was estimated to be 33% (45).

q=1-p.

d= is the accepted margin of error (in this study taken to be 7%).

$$\frac{400 \times 1.96^2 \times 0.33(1-0.33)}{0.07^2(400-1) + 1.96^2 \times 0.33\ (1-0.33)}$$

The minimum sample size was therefore 121 participants.

2.5 Study duration

The study was conducted over a period of 9 months from May 2014 to February 2015.

2.6 Sampling procedure

A total of 121 children with HIV infection aged 7-18 years attending CTC clinics at MNH and IDC were recruited. Children were allowed to receive their routine HIV care, then those who met the eligibility criteria were grouped and assigned a unique number to each one. The numbers were thoroughly mixed and the researcher without looking selected n numbers which represented the population assigned to that number. This population was then included in the sample.

2.7 Data collection method and procedures

A structured questionnaire designed for the purpose of the study was used to collect socio-demographic and clinical information on the participants. Children were enrolled at the time of their regularly scheduled clinic visits, during which history was obtained, physical examination was done and lung function tests were performed. Baseline demographic and clinical characteristics of interest including

name of the participant, date of birth, sex, level of education, were recorded as indicated in Appendix 1.

Children/parents/guardians were asked about history of chronic cough, shortness of breath, exercise tolerance, chest pain or tightness, cigarette smoking, presence of audible wheezing as well as duration of symptoms to determine if specific symptoms were acute, sub-acute, or chronic. Thorough physical examination was conducted by a doctor. Participant's weights, height, body mass index (BMI) and vital signs, were taken. Inspection, palpation and percussion of chest were done. Inspection was focused on the shape of the chest wall, deformity, and increased work of breathing such as nasal flaring, suprasternal, intercostal or subcostal retractions and abdomino-thoracic breathing. Palpation was focused on swelling and tenderness of the chest, tracheal position and chest expansion. Percussion of the chest wall was done to assess for pain, tenderness, resonance and dullness. Auscultation was focused on quality of breathing sounds. Additional signs of chronic lung disease such as digital clubbing and cyanosis were evaluated.

2.8 Data Measurement

2.8.1 Weight

Weight was taken by using a solar cell weighing scale (SECA) with the participant putting on light clothes and removing shoes. Weight was taken to the nearest 10g. Calibration of the scale was done daily before starting the exercise and weekly using a fixed weight of 1kg. Measurements were taken in standing position.

2.8.2 Height

Height was taken using a height board fixed on the wall against a flat stepping floor. Children were asked to remove their shoes and step on the floor against the board with the head piece placed at the head at 90^{o} while the head is in neutral position. The readings were recorded to the nearest 0.1cm.

2.8.3 Body Mass Index

Body mass index (BMI) was calculated using the following formula

$$BMI = \frac{\text{Weight (kg)}}{\text{Height (m)}^2}$$

2.8.4 Oxygen saturation

Oxygen saturation was measured by using a portable pulse oximetry machine (Nonin Medical, Inc. Plymouth, MN USA Model 9590 Oximeter 1.5V×2AA IEC LR03). Readings were recorded from the index fingertip. A reading <90% at room air was regarded as severe hypoxia (46).

2.8.5 Lung function tests

Lung function tests were assessed by using spirometry, Breeze 6.4.1 package with Med graphics pneumotachomer (Medgraphraphic Cardiorespiratory Diagnostics, St.PaulMN USA). FEV_1, FVC and FEV_1/FVC ratio were computed using standard for African children (47). Calibration of the machine was done daily before starting the exercise. Children who tested in the abnormal range (FEV_1 <80% of the predicted value) were regarded as having abnormal lung function tests.

2.8.6 Blood investigation

Blood for CD4 cell count analysis for each participant whose most recent CD4 cell count was more than 6 months was collected. About 2 millilitres of venous blood was taken from antecubital fossa using a sterile disposable syringe. The sample was collected in sterile EDTA K 3 tubes with lavender tops and mixed adequately by inverting four times. CD4 cell count was measured by using BD Bioscience's BD FACSCalibur (Becton, Dickson and Company, USA) system at the IDC laboratory. Aseptic technique during the procedure was observed.

2.8.7 Procedures for lung function

Baseline lung function tests (spirometry) and oxygen saturation was done to all participants. Paediatric oriented /friendly spirometry was used. Children were encouraged to blow out maximally by using pictorial and verbal motivations. A nose

clip was used during the manoeuvre. A minimum of three attempts were done and two reproducible values were taken and the machine chose the best value. All measurements were taken in standing position.

At baseline O_2 saturation of ≥ 90%, and FEV_1 of >75%, study subject performed a standardized exercise. Standardized exercise was defined as a 2 flight stair case climb, each stair 15cm height and 30cm width (48). Oxygen saturation and spirometry were then repeated immediately. Then Bronchodilator (albuterol metered dose inhaler 90mcg/puff, manufactured by IVAX Pharmaceuticals Ireland, Waterford Ireland) 4puffs with corrugated spacer was administered to determine the presence of reversible abnormal lung function test which may signify asthma. After 10minutes of albuterol administration, oxygen saturation and spirometry were repeated.

When the baseline oxygen saturation was <90% or FEV_1<75%, the subsequent exercise portion was deferred and then albuterol was given and oxygen saturation and spirometry repeated 10 minutes later. The dose of albuterol was fixed across all age group.

Participants who tested in the abnormal range defined as FEV_1 <80% predicted were regarded as having abnormal lung function tests and a referral to Muhimbili National Hospital was offered for those identified at IDC for further evaluation and management.

Participants who failed to give reproducible values were given a chance to repeat the same day and if necessary in their subsequent clinics.

2.9 Data analysis

Analysis was done using Statistical Package for Social Science (SPSS) version 20.

- Frequency charts were used for categorical variables.
- Mean and median were used for continuous variables.
- Chi-square and fisher's exact test were used to determine the association between categorical variables as appropriate.
- Student's T-test was used to compare if there is a significant difference between the means for continuous variables.
- Mann Whitney U test was used to compare the difference in medians.
- P value of <0.05 was considered as statistically significant.

2.10 Ethical considerations

Ethical clearance was sought from Muhimbili University of Health and Allied Sciences (MUHAS) Directorate of Research and Publications (Ref.No.MU/PGS/SAEC/Vol.IX/). Permission to conduct the study was obtained from the Director of Ilala Municipal and the Director of Hospital services at Muhimbili National Hospital.

Potential participants and their parent/guardian(s) were informed about the study and consent was obtained. Verbal assent was obtained from older children after obtaining the consent from their parents. Children who had abnormal lung function tests were closely followed up and further evaluations were done at Muhimbili National Hospital. For all data analyses, no subject identifiers are provided or included. Paper and electronic data were stored in a research office, which was secured through locking mechanisms. Paper files were stored in locked filing cabinets and computer data were stored in a secure, password-protected computer.

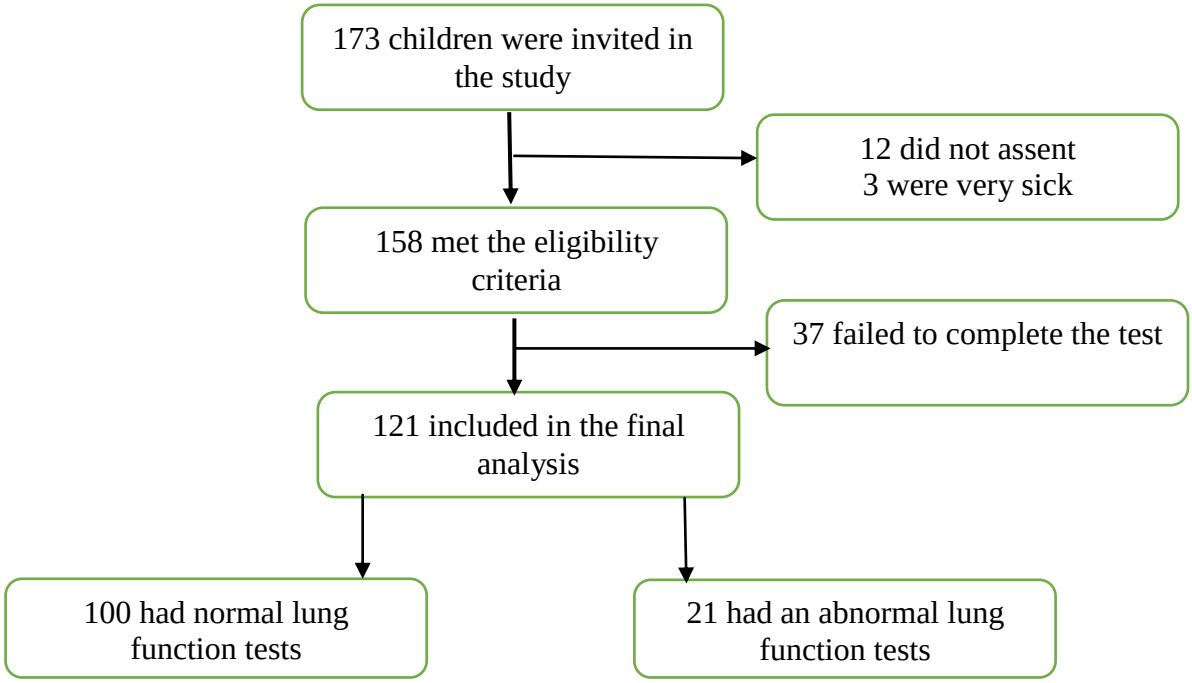
CHAPTER TWO

3.0 RESULTS

In this study, 173 participants were invited, of whom 121 children met the inclusion. About 12 participants (6%) did not give assent because they were not comfortable to perform the tests

Figure 1.

Figure 1: Flow chart of the study participants



3.1 Socio-demographic characteristic

Among one hundred and twenty one participants, 82 (67.8%) were adolescents aged between 13 to 18 years. Majority were males representing 75(62%). More than half, 71(58.7%) of the participants were in primary school. Orphans were 67(55.4%) whereby 20 (29.9%) had lost both parents and 24 (35.8%) had lost their mothers. Majority of the children 109 (90.1%) were on ART at the time of recruitment as shown in Table 1.

About 37(23%) of the eligible participants were not able to complete lung function tests. Females were 21(56.8%) and orphans 17 (45.9%) whereby majority had lost either both their parents or their mother 16 (94.4%). Type of orphan status and gender were statistically significant between participants who completed the tests and those who failed. Other variables including clinical presentations were not statistically different between the two groups. ANNEX 1, 2 &3

Table 1: **Socio-demographic characteristics of the study population (n=121).**

Character	Specific variable	Frequency (n)	Percentage (%)
Age (years)			
	Less than 12	39	32.2
	13 to 15	52	43
	16 to 18	30	24.8
Sex			
	Male	75	62
	Female	46	38
Orphan			
	Yes	67	55.4
	No	54	44.6
Type of orphan			
	Both parents	20	29.9
	Mother	24	35.8
	Father	23	34.3
Education level			
	Primary school	71	58.7
	Secondary school	50	41.3
Taking ART			
	Yes	109	90.1
	No	12	9.9

With regard to the anthropometric measurements of this population, 55.4% had normal weight, 40.5% were underweight and 4.1% were overweight. Looking at the growth pattern status, 67.8% had normal growth while 32.2 were stunted. Figure 2&3.

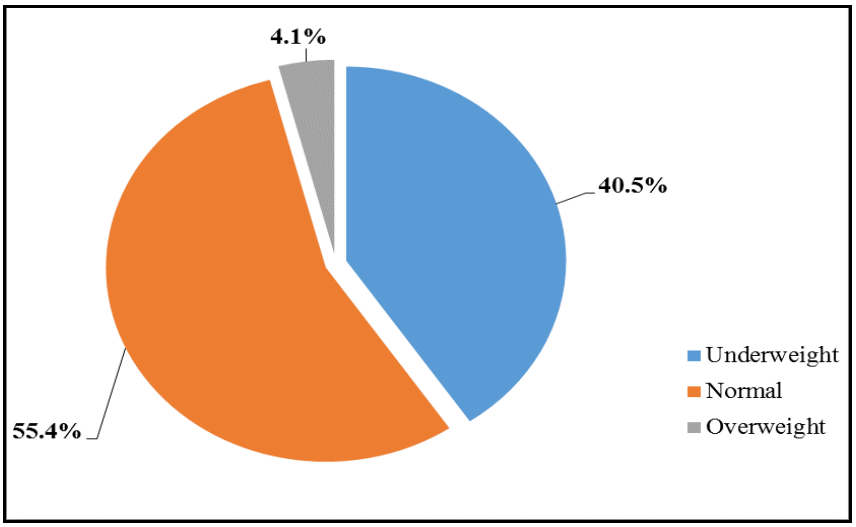


Figure 2: Distribution of nutrition status based on BMI values

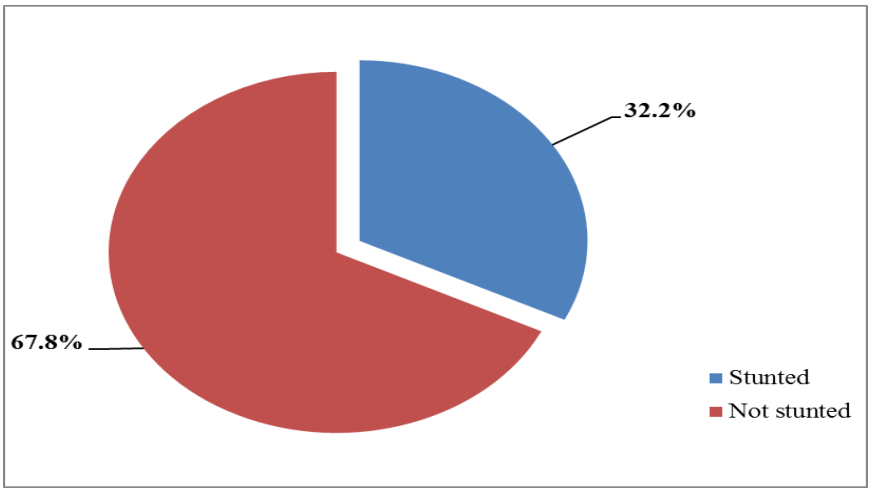


Figure 3: Distribution of growth pattern based on height for age values

3.2 Prevalence of abnormal lung function tests

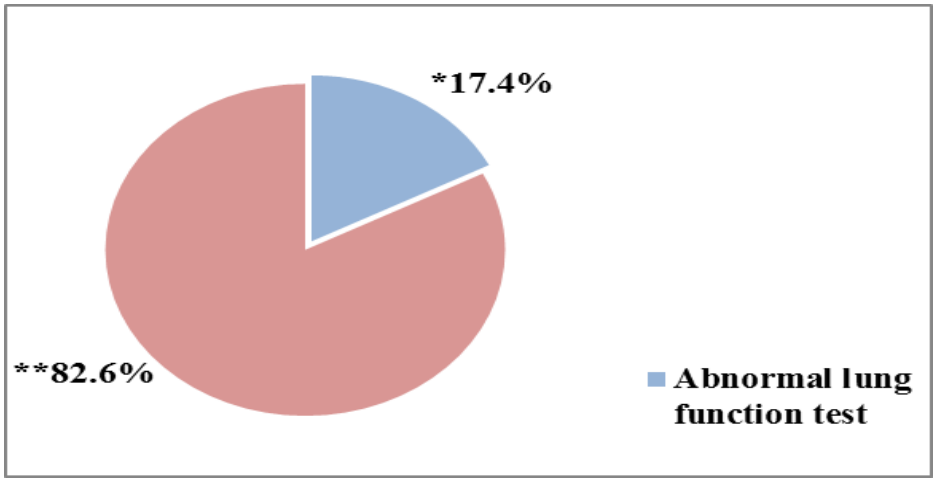
Among the enrolled participants, 21(17.4%; 95% CI=10.7-24.8) were found to have abnormal lung function tests shown by FEV_1% of <80% at base line and after exercise challenge. Of those who had abnormal lung function tests, no participant had a significant reversibility post bronchodilator administration. All participants in this study had normal oxygen saturation both at rest and post exercise of >90%. Figure 4.

3.3 Abnormal lung function tests and clinical features

Common respiratory symptoms and signs were compared among those with abnormal and normal lung function tests**.** For those with abnormal lung function tests, 10 (47.6%) presented with chronic cough, 4(19%) crepitation, and 3(14.3%) had peripheral cyanosis, all were statistically significant (P<0.05). Table 3.

Underweight and stunting were important findings in this group, about 10(47.6%) were underweight and 12(57.1%) were stunted, but both were not statistically significant (P=0.224, P=0.252 respectively). Also majority of children 15(71.4%) had advanced WHO clinical stage (III and IV) disease**.** However, there was no significant difference between children who had normal compared to abnormal lung function tests with regard to their WHO,HIV clinical disease stage and current CD4 cell count (P=0.067, P=0.560). Table 2 & 3.

Figure 4: Distribution of lung function test among the study participants



95% CI for percentages (10.7– 24.8), n=121

Table 2: Clinical characteristics of study participants with lung function tests (n = 121)

	LUNG FUNCTION TEST		Total	*Fisher's exact test* p-value
	Abnormal (n, %)	Normal (n, %)		
Chronic cough				
Yes	10 (47.6)	23 (23)	33 (27.3)	
No	11 (52.4)	77 (77)	88 (72.7)	***0.021**
Previous history of TB				
Yes	7 (33.3)	22 (22)	29 (24)	
No	14 (66.7)	78 (78)	92 (76)	***0.269**
Passive cigarette smoking				
Yes	2 (9.5)	14 (14)	16 (13.2)	
No	19 (90.5)	86 (86)	105 (86.8)	**0.736**
Shortness of breath				
Yes	3 (14.3)	9 (9)	12 (9.9)	
No	18 (85.7)	91 (91)	109 (90.1)	**0.435**
Exercise intolerance				
Yes	3 (14.3)	12 (12)	15 (12.4)	
No	18 (85.7)	88 (88)	106 (87.6)	**0.723**
Chest pain				
Yes	2 (9.5)	10 (10)	12 (9.9)	
No	19 (90.5)	90 (90)	109 (90.1)	**0.947**
Weight loss				
Yes	4 (19)	12 (12)	16 (13.2)	
No	17 (81)	88 (88)	105 (86.8)	**0.476**
Recurrent fever				
Yes	3 (14.3)	9 (9)	12 (9.9)	
No	18 (85.7)	91 (91)	109 (90.1)	**0.435**
Wheezing				
Yes	2 (9.5)	6 (6)	8 (6.6)	
No	19 (90.5)	94 (94)	113 (93.4)	**0.626**
Cyanosis				
Yes	3 (14.3)	0 (0)	3 (2.5)	
No	18 (85.7)	100 (100)	118 (97.5)	**<0.01**
Crackles				
Yes	4 (19)	1 (1)	5 (4.1)	
No	17 (81)	99 (99)	116 (95.9)	**<0.01**
CD4 count				
Less than 350	3 (14.3)	22 (22)	25 (20.7)	
More than 350	18 (85.7)	78 (78)	96 (79.3)	**0.560**
HIV clinical staging				
One	3 (14.3)	11 (11)	14 (11.6)	
Two	3 (14.3)	42 (42)	45 (37.2)	
Three	11 (52.4)	40 (40)	51 (42.1)	**0.067**
Four	4 (19)	7 (7)	11 (9.1)	

Chi-square test

Table 3: Association between lung function tests and nutrition status (n=121).

Nutrition status based on	LUNG FUNCTION TEST		Total	p-value
	Abnormal (n,%)	Normal (n,%)		
BMI category				
Underweight	10 (47.6)	39 (39)	49 (40.5)	
Normal	9 (42.9)	58 (58)	67 (55.4)	**0.244**
Overweight	2 (9.5)	3 (3)	5 (4.1)	
Growth pattern				
Stunted	12 (57.1)	70 (70)	82 (67.8)	
Not stunted	9 (42.9)	30 (30)	39 (32.2)	**0.252**

Fisher's exact test

3.4 HIV/ART duration and abnormal lung function tests

Median duration since HIV diagnosis among children with abnormal lung function tests was shorter 246 weeks (IQR 128-418) compared to 357weeks (IQR 240-421) of those with normal function tests. ART duration among those with abnormal lung function was also relatively shorter as well with median duration 243 weeks (IQR 123-356) compared to 319 weeks 193-403) in those with normal lung function tests.

Duration since HIV diagnosis and ART use showed no statistical significant difference (P=0.176 and P=0.111 respectively). There was no difference between mean increase and decrease in CD4 count cells from the baseline among children who had abnormal compared to those with normal lung function tests. (P=0.822). Table 4 & 5.

Table 4: Association between lung function tests and duration of HIV infection / ART use

Variable	Median (weeks)	IQR	p-value
Median duration since HIV diagnosis			
Abnormal	246	128-418	**0.176**
Normal	357	240-421	
Median duration on ART			
Abnormal	243	123-356	
Normal	319	193-403	**0.111**

***Mann Whitney U test**.

Table 5: Association between changes in CD4 count from baseline with lung function tests

	LUNG FUNCTION TEST		Total	p-value
	Abnormal	Normal		
***Increased CD4 count from baseline**	17 (17)	83 (83)	100	
****Decreased CD4 count from baseline**	4 (19)	17 (17)	21	**0.822**

***Mean increase in CD4 count from baseline was found to be 476.07 (SD=37.3)**

****Mean decrease in CD4 count from baseline was found to be 292.52 (SD=44.1)**

CHAPTER FOUR

4.0 DISCUSSION

In this study the prevalence of abnormal lung function tests and associated clinical features among HIV infected children aged 7-18 years were investigated. There was a significant number of children 21(17.4%; 95%CI=10.7-24.8) who presented with respiratory compromise among those attending our HIV care and treatment clinics. The wide confidence interval observed might have been contributed due to small sample size utilized. Similar findings with comparatively larger prevalence were reported in other studies done in paediatric population from Malawi and Zimbabwe (19,45). The discrepancy observed is possibly due to difference in the study populations used and quality of care. In Zimbabwe, the study participants were more of older children (10-19 years) compared to the current study (7-18 years). The percentage of ART use in Malawi and Zimbabwe were 72% and 69% respectively while in the current study 90% of children were on ART at recruitment. Other findings from a study involving HIV infected adults in Pennsylvania United State of America revealed that up 21% had chronic lung disease based on spirometry findings (49) .

A significant number of children 37 (23%) were not able to provide reproducible values from the spirometry due to poor effort. This group was characterized by younger age (<12years), orphan status, more likely to be female, and had low levels of education. These characteristics may contribute to fear, inability to understand instructions and low self-esteem. A study done by Beegle et al, showed that being an orphan is associated with poor health, high mortality and low self-esteem in a child (50). However, when comparing those who could reproduce the tests and those who failed, there was no significant difference in terms of their clinical features which were found to be significant in children who had abnormal lung function tests. This suggests that their lung function tests were similar to those who could reproduce the tests.

4.1 Abnormal lung function tests and clinical presentation

Chronic cough, presence of peripheral cyanosis and lung crepitations were significant clinical findings among children with abnormal lung function tests. Chronic cough has been shown to be the most prevalent symptom in HIV infected children with abnormal lung function tests. This is consistent with the study done in Nigeria by Onyedum (21). This finding suggests that, there is ongoing pathology in the respiratory system primarily caused by the immunosuppression such as HIV/AIDS leading to recurrent airway damage. It can also indicate other respiratory opportunistic infections like PTB, PCP and fungal infection. Previous studies done prior to ART era showed that individuals living with HIV infection were more likely to present with respiratory symptoms such as chronic cough, shortness of breath and chest pain compared to their counterparts HIV infection (18).

Cyanosis and hypoxemia are both features of advanced COPD in children resulting from prolonged hypoxia. However presence of only peripheral cyanosis, mostly reflects cardiac causes or vasoconstriction due to cold exposure (51,52). Three participants (14.3%) among those presented with abnormal lung function tests had peripheral cyanosis. This could be an incidental finding or implies an early presentation of cor pulmonale as a complication of COPD.

A large number of children 15 (71.4%) with abnormal lung function test were categorized as WHO, HIV clinical disease stage III and IV which represents an advanced HIV/AIDS disease progression. This is a group known to have an increased risk of opportunistic infections including pulmonary tuberculosis (PTB), pneumocystis pneumonia (PCP) and recurrent pneumonia. These are important risk factors which can predispose an individual to chronic lung disease development as was reported from a study done in South Africa (53). This is in keeping with findings in this study where children with abnormal lung function tests were also more likely to be in WHO, HIV clinical stage III and IV disease.

Despite the advanced disease stage in this study population, CD4 count levels did not appear to have an effect on their lung function tests similar to the study done in Zimbabwe (19). Contrary to other studies which showed CD4 cell count less than 200cells/µl were significantly associated with respiratory insufficiency values among HIV infected patients (21,54).

Stunting and wasting are features of malnutrition; together with HIV infection, make the individual even more at risk of acquiring chronic illnesses. However, despite a considerable number of stunted and wasted children in this study population, similar to findings reported from Zimbabwe (19) these studies showed no significant difference in presence of abnormal lung function tests were found among stunted and wasted children when compared to their well-nourished counterparts.

4.2 Abnormal lung function tests and duration of HIV / ART use

Taking an assumption that most of children acquire HIV infection through vertical transmission. In this study it was evident that most of children with abnormal lung function tests were diagnosed late in life and had been on ART for a shorter duration of time. This is the group with longer duration of HIV exposure and high risk of recurrent opportunistic respiratory infections. Such children are at risk of chronic lung disease development. Similar findings were reported from a study done by Crothers et al (15). Recent study by Rashida et al, found an association between delayed HIV diagnosis and chronic lung disease development in children(19).

Recent data in adult studies showed that the use of ART was independently associated with a low risk of development of chronic lung disease as evidenced by spirometry findings (55). Findings from this study and others cited above are in keeping with the literature that ART helps to restore the immune system, prevent occurrence of respiratory infections and subsequently prevent chronic lung disease. Hence it can be emphasized that early diagnosis and initiation of ART may delay the onset of chronic lung disease.

Current HIV/AIDS guidelines for management of HIV infected children in Tanzania recommends that all children with HIV infection, below the age of two years should be started on ART regardless of their clinical or immunological condition(56). Therefore if appropriately implemented the incidence of chronic lung disease can be reduced in this population group.

CHAPTER FIVE

5.0 STUDY STRENGTH AND LIMITATIONS

5.1 Study strength

Lung function tests were performed by two trained medical doctors, and the traces of the test values were reviewed by a paediatric pulmonologist from Dartmouth children's hospital in USA.

5.2 Study limitation

This was a cross-sectional study, hence it could not asses the causal effect between chronic lung disease progression and lung function parameters**.**

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The prevalence of abnormal lung function tests among this cohort of HIV infected children is high, indicating that chronic lung disease is one of the causes of morbidity in this population. Presence of chronic cough, peripheral cyanosis and lung crepitations have been shown to be important features in children with lung function impairments.

6.2 Recommendations

1. HIV infected children presenting with chronic cough, peripheral cyanosis and crepitation should be investigated for lung function tests for detection of chronic lung disease. This will allow proper management plan and hence improve their quality of life**.**

2. We recommend further studies to identify the actual cause and risks associated with chronic lung diseases among HIV infected children.

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APPENDICES

Appendix I: Questionnaire

Title: Prevalence of abnormal lung function tests and associated clinical features among HIV infected Children aged 7-18years in Tanzania

ID number……. **Age…….……** **Gender**: Male **[1]** female **[2]**

Personal History

Orphan: Yes **[1]** No **[2]**

If Yes: Both parents **[1]** Mother **[2]** Father **[3]**

Education level: Primary school **[1]** Secondary school **[2]** College **[3]**

Didn't attend school **[4]**

Respiratory History

Is there history of chronic cough (lasting >2weeks) : Yes [**1**] No [**2**]

Is there history of shortness in breath: Yes [1] No [2]

Is there history of exercise intolerance Yes[1] No [2]

Is there history of Chest Pain/ tightness: Yes [1] No [2]

Is there history of weight loss: Yes [1] No [2]

Is there history of recurrent fever (≥3times in 6months): Yes [1] No [2]

Is there history of wheezing: yes [1] No [2]

Is there history of cigarette smoking: yes [**1**] No [**2**]

If yes specify duration and number of sticks per day

……..

Is there history of passive cigarette smoking at home: [**1**] No [**2**]

Is there history of Tuberculosis: Yes [1] No [2]

If yes please specify month and year of diagnosis

……

If yes, did you finish Ant.TB: specify month and year……..

Is there history other chest infections……

For how long it was diagnosed: years **[ ]**moths **[ ]**weeks **[ ]**

Last Chest X-ray findings…….

When was it taken: years **[ ]** moths **[ ]** weeks **[ ]**

Any history of Asthma: Yes **[1]** No **[2]**

If yes specify any treatment/s receiving ……..

HIV History: Date of diagnosis: d/m/y……

ART status Yes **[1]** No **[2]**

CD4 count on initiation of ART…… date taken…….

Recent CD4 count……..... date taken…….

Lowest CD4 ever tested…… date taken……

Current ART regimen…….……

Date started ART…….

Opportunistic infections ……..

……

……

……

……

HIV clinical stage: Stage 1[ ] Stage 2 [ ] Stage 3 [ ] Stage 4 [ ]

Physical examination:

Height (cm):…… Height Z-score…….

Weight (Kg):……. Weight Z-score…….

MUC (cm):…… MUAC Z score…….

BMI:…… BMI Z score…….

Heart rate:……. Respiratory rate:……

Digital clubbing: yes **[1]** No**[2]**

Peripheral cyanosis: yes **[1]** No **[2]** Central cyanosis: yes **[1]** No **[2]**

Increased work of breathing: yes [**1]** No**[2]**

Presence of Rhonchi: yes**[1]** No**[2]**

Presence of crackles: yes**[1]** No**[2]**

Other Lung findings Yes **[1]** NO **[2]**

If yes specify:

……

……

Lung function Test

Pulse Oximetry

Base line O_2 saturation	Post exercise O_2 saturation	Post Albuterol O_2 saturation

Spirometry findings

Readings	FEV_1	FVC	FVE_1%	FVC%	FVE_1/FCV
Predicted value					
Baseline value					
Post exercise					
Post Albuterol					

Appendix II: Consent Forms (English Version)

ID NO……..

PERMISSION FOR A CHILD TO TAKE PART IN RESEARCH

Title: Prevalence of abnormal lung function tests and associated clinical features among HIV infected children aged 7-18 years in Tanzania

Introduction: Your child is being asked to take part in this study because we are screening for chronic lung diseases in HIV-infected children who receive care at this clinic.

Your decision whether or not to allow your child to take part will have no effect on the quality of your child's medical care. Please ask questions if there is anything about this study you do not understand.

What is the purpose of this study?

The purpose of this study is to learn more about the lung function of children and youth with HIV infection. Children with HIV infection from other African countries (Zimbabwe and Malawi) have been reported to have an increased amount of lung disease we will check children in this clinic to see if the same is true for children in Tanzania.

Will you benefit from taking part in this study?

Your child will be a volunteer and might not personally benefit from being in this research study. However, if lung disease is discovered, further evaluation and treatment may be possible. In addition, we hope to gather information that may help other children in the future.

What does this study involve?

Your child's evaluation as part of this study will be done during a regular clinic visit and may last up to 60 minutes. We will ask specific questions about your child's health and perform a standard physical examination. We will measure the amount of oxygen in your child's blood by simply placing a reading device on one finger. In addition, your child will be asked to blow into a special device that measures the strength of your child's lungs. We will do these two tests while your child is at rest and also after stair climbing exercise. Finally, we will ask your child to breathe in a drug (Albuterol) which helps expand airways and may improve breathing and then repeat the testing.

What are the options if you do not want to take part in this study?

Your child's participation in this study is completely voluntary. Your child will continue to receive regular care at the clinic regardless of whether he/she participates in the study.

What are the risks involved with taking part in this study?

This study involves minimal to no risks for your child. It is possible that a reaction to the Albuterol administration will occur rarely, such as a temporary fast heartbeat or sense of irritability. In addition, the exercise portion may make the child feel short of breath for a short period of time. Your child will be observed carefully in the clinic during this time.

You can report any problems to your doctor or to the director of this study**:**

Dr. Yahya Binde or Dr. Anna Kiravu at IDC (255 222-120875)

• **Leaving the study:** You may choose to stop taking part in this study at any time for any reason. If you decide to stop taking part, it will have no effect on your child's medical care.

• **New Information:** New information related to this study and specifically new information about your child will be made known to you when it becomes available.

How will your privacy be protected?

The information you and your child provide as well as the test results will be kept strictly confidential. The study information will be stored in protected computer files and in paper records stored in locked filing cabinets. Only study staff will have access to the information.

The information will be maintained indefinitely.

Who may use or see your health information?

By signing this form, you allow the research team to use your child's health information and give it to others involved in the research. The research team includes the study director plus others working on this study at MUHAS and Dartmouth.

Your permission to use your child's health information for this study will not end until the study is completed. You may ask for your child's study data at any time.

It is possible for a court or government official to order the release of study data including information about your child.

What if you decide not to give permission to use and share your personal Health Information?

If you do not allow use of your child's health information for this study, you may not take part in this study.

If you choose to stop taking part in this study, you may cancel permission for the use of your child's health information. You should let the researcher know if you want to cancel your permission. The study team will assist you in putting your wishes in writing. Information collected for the study before your permission is cancelled will continue to be used in the research.

Whom should you call about this study?

If you have questions about this study or need to report a study related injury, you can call your doctor or the research director for this study: Dr.Yahya Binde/Dr. Anna Kiravu at IDC **(255 222-120875)** during normal working hours.

If Dr. Kiravu/Dr.Yahya is not available, other staff members at IDC will be available to answer your questions during normal business hours.

What about the costs of this study?

There will be no costs for you if you agree to have your child participate in the study.

Will you be paid to take part in this study?

There will be no payment to you or your child for participation in the study.

What happens if you get sick or hurt from taking part in this study?

The sponsor of this research is the IDC. If you develop an illness or have an injury related to the Albuterol used in this research study, IDC will pay for the reasonable costs of medical treatment.

If you have any questions or concerns about the legal responsibility of these organizations, please call the MUHAS Research Ethics Committee (255 22 215 2489) or the Dartmouth College Committee for the Protection of Human Subjects at CPHS.Tasks@Dartmouth.EDU, or 603-646-6482 during normal business hours.

If you agree that your child take part in this study and you sign this consent form, you are not giving up any of your legal rights.

Your responsibilities as a person taking part in this study

(1) Be aware it is important for your safety that the study team knows about your child's medical history and current condition.

(2) Notify the study team immediately if your child suffers any injury or unexpected reaction to the study medication or procedures.

CONSENT

I have read the above information about ***Screening for Chronic Lung Disease among HIV-infected Youth in Tanzania*** and have been given time to ask questions. I agree to take part in this study and I have been given a copy of this signed consent form.

SIGNATURE

_____

Researcher or Designee Signature and Date Printed Name

_____

Legally Authorized Representative (Parent/legal guardian) and Date Printed Name

Appendix III: Consent Forms (Swahili Version)

Namba ya utambulisho……..

RIDHAA YA KUSHIRIKI KWENYE UTAFITI HUU

Title: Prevalence of abnormal lung function tests and associated clinical features among HIV infected Children aged 7-18years in Tanzania

Utangulizi: Mtoto wako anaombwa kushiriki katika utafiti kwasababu tunafanya uchunguzi wa magonjwa ya muda mrefu ya mapafu kwa watoto wanao pata huduma katika kliniki yetu. Uamuzi wako wa kumruhusu au kutomruhusu mtoto wako kushiriki hautakua na athari zozote kwenye ubora wa huduma ya mtoto wako. Tafadhali uliza swali kama kuna kitu usichokielewa kuhusu utafiti huu.

Je dhumuni la utafiti huu nilipi?

Dhumuni la utafiti huu ni kujua ufanyaji kazi wa mapafu ya watoto wenye maambukizi ya virusi vya ukimwi. Watoto wenye virusi vya ukimwi kutoka nchi nyingine za afrika (Zimbabwe na Malawi) wameripotiwa kuwa naongezeko la magonjwa sugu ya mapafu. Tutawachunguza watoto kwenye kliniki hii ili tuone kama hali ipo hivyo kwa watoto wa Tanzania.

Je utafaidika kwa mwanao kushiriki kwenye utafiti huu?

Mtoto wako atapimwa kwa ridhaaa yake na inawezekana kuwa binafsi asifaidike kwa kuwepo kwenye utafiti huu. Lakini kama ugonjwa wa mapafu utagundulika, atafanyiwa vipimo zaidi na kupatiwa matibabu inapowezekana. Zaidi tunatarajia kukusanya taarifa amabazo zitawasaidia watoto wengine siku za mbeleni.

Je Utafiti huu unahusisha nini?

Uchunguzi wa mtoto wako kama sehemu ya utafiti utafanyika wakati wa mahuthurio ya kawaida ya kliniki na unaweza kuchukua hadi dakika 60. Ni hudhurio moja tu ambao

upimaji utahitajika na utafanyika kwa ajili ya utafiti. Tutauliza maswali kuhusu afya ya mtoto na kumfanyia uchunguzi wa mwili. Tutapima kiwango cha oksijen kwenye damu ya mtoto wako, kwa kumuwekea kifaa cha kusomea kwenye kidole. Zaidi ya hapo mtoto ataambiwa apulize kwenye kifaa maalum, kinachopima uwezo wa mapafu ya mtoto.

Tutafanya vipimo hivi viwili wakati mtoto wako amepumzika na baada ya zoezi la kupanda ngazi. Mwisho tunamwambia apumue kwenye dawa(Albuterol) ambayo husaidia kupanua njia ya hewa na inaweza kuboresha upumuaji, halafu atarudia tena vipimo.

kwa wale ambao vipimo vitaonesha wana shida watafinyiwa X-ray ya kifua pia ili kujua tatizo.

Je itakuwaje kama hutataka kushiriki kwenye utafiti huu?

Kushiriki kwa mtoto wako kwenye utafiti huu ni hiari kabisa. Mtoto wako ataendelea kupata huduma katika kliniki hii bila kujali kama ameshiriki kwenye utafiti ama la.

Je kuna athari gani za kushiriki katika utafiti huu?

Utafiti huu hauna hatari au unahusisha hatari kidogo kwa mtoto wako . Inawezekana mara chache utoaji wa Albutarol ukaleta madhara, kama vile mapigo ya moyo kwenda haraka au akajisikia kuwashwa. Zaidi wakati wa mazoezi mtoto anaweza kuishiwa pumzi kwa muda mfupi. Mtoto wako ataangaliwa kwa ukaribu sana hapa kliniki muda wote huo.

Unaweza kuripoti matatizo yoyote kwa daktari wako au kwa mwendesha utafiti huu:
Dr.Yahya Binde au Dr. Anna Kiravu ofisi ya IDC (255 222-120875)

Kuondoka kwenye utafiti:_unaweza kuamua kusitisha kuendelea kushiriki kwenye utafiti huu muda wowote na kwasababu yoyote. Kama utaamua kuacha kushiriki hautaathiri huduma za afya kwa mtoto wako.

Maelezo mapya:

Maelezo mapya kuhusiana na utafiti huu na hasa maelezo mapya kuhusu mtoto wako utajulishwa mara tu ya takapokuwa yamepatikana.

Utunzajiwa siri?

Habari mtakazotoa wewe na mtoto wako pamoja na majibu ya vipimo yatatunzwa kwa usiri mkubwa. Habari zihusuzo utafiti zitatunzwa kwenye kompyuta zenye ulinzi na rekodi zilizopo kwenye makaratasi zitatunzwa kwenye makabati yanayofungwa. Ni wafanyakazi wanao husika na utafiti tu ndio watakaoweza kuona taarifa, na taarifa hizi zitatunzwa siku zote.

Nina nia naweza kutumia au kuona taarifa zako za afya?

Kwa kuweka sahihi kwenye fomu hii umeruhusu watafiti kutumia taarifa za afya za mtoto wako na kuwapatia wengine wanaohusika na utafiti huu. Watafiti ni pamoja na mwendesha utafiti pamoja na wengine wanao husika na utafiti huu ambao wapo chuo kikuu cha Muhimbili pamoja na Chuo cha Dartmouth (Marekani)

Ruhusa ya kutumia taarifa za afya za mtoto wako itaisha wakati utafiti utakapokamilika.

Unaweza kuomba taarifa za mtoto wako wakati wowote.

Inawezekana mahakama au afisa wa serikali akaamuru kuonyeshwa kwa taarifa za utafiti ikiwa ni pamoja na taarifa za mtoto wako

Je itatokea nini kama utaamua kutotoa ruhusa ya kutumia na kushirikisha wengine taarifa zako za afya?

Kama hautaturuhusu taarifa ya afya ya mtoto wako zitumike, hautaweza kushiriki kwenye utafiti huu.

Kama utachagua kuacha kushiriki katika utafiti huu, unaweza kufuta ruhusa ya matumizi ya taarifa za afya za mtoto wako. Watafiti watakusaidia kuweka matakwa yako kwenye maandishi. Taarifa zitakazo kuwa zimekusanywa kabla ya kufuta ruhusa zitaendelea kutumika kwenye utafiti.

Je utampigia nani kuhusu utafiti huu?

Kama una maswali kuhusu utafiti au ukiwa na haja ya kuripoti athari zitokanazo na utafiti, unaweza kumpigia daktari wako au mwendesha utafiti huu: **Dr Yahya Binde** au **Dr. Anna Kiravu ofisi ya IDC (255 222-120875) muda wa masaa ya kazi.**

Je kuna gharama juu ya tafiti huu?

Hakuna gharama kama utakubali mtoto wako ashiriki kwenye utafiti huu. DPP itasaidia gharama zote za utafiti .

Je utalipwa kwa kushiriki kwenye utafiti:

Hapatakuwa na malipo kwako au mtoto wako kwa kushiriki kwenye utafiti

Je kitatokea nini kama utaugua au kuumia kwa kushiriki kwenye utafiti huu?

Mfadhili wa utafiti huu ni DarDar Pediatric Program. Kama utapata ugonjwa au utaumia kutokana na Albutarol iliyotumika kwenye utafiti huu, IDC italipa gharama za kawaida za matibabu.

Kama unamaswali kuhusu wajibu wa kisheria wa vyuo hivi tafadhali piga simu kamati ya maadili ya tafiti chuo kikuu cha muhimbili (MUHAS) (255 22 215 2489) au chuo kikuu cha Dartmouth (603) 646-3053 wakati wa saa za kazi .

Kama utakubali mtoto wako ashiriki kwenye utafiti huu na ukasaini fomu hii ya ridhaa, haujiondolei haki yoyote ya kisheria.

Wajibu wako kama mshiriki wa utafiti huu

(1) Ufahamu kuwa ni muhimu kwa usalama wako kwa watafiti kujua kuhusu taarifa za kimatibabu za mtoto wako na matatizo ya hivi karibuni.

(2) Kufahamisha watafiti mara moja kama mtoto wako ameumia au amepata madhara yasiyo tarajiwa kutokana na madawa au vipimo.

Ridhaa

Nimesoma maelezo hapo juu kuhusu uchunguzi wa magonjwa ya muda mrefu ya mapafu kwa vijana wenye maambukizi ya virusi vya ukimwi hapa Tanzania na nimepewa muda wakuuliza maswali. Nakubali kushiriki katika utafiti huu na nimepewa fomu ya ridhaa hii iliyowekwa sahihi

Sahihi

_____

Sahihi ya mtafiti au kaimu na tarehe Jina kamili

_____

Sahihi ya mwakilishi wa kisheria (mzazi / mlezi) na tarehe Jina kamili

ANNEXIS

Annex 1: Characteristics of the study population

Character	Unable to perform lung function test n=37 (23.4%)	Able to perform lung function test n=121 (76.6%)	TOTAL 158 (100)	*p*-value
Age (years)				
Less than 12	20 (54.1)	39 (32.2)	59	
13 to 15	12 (32.4)	52 (43)	64	**0.063**
16 to 18	5 (13.5)	30 (24.8)	35	
Sex				
Male	16 (43.2)	75 (62)	91	
Female	21 (56.8)	46 (38)	67	**0.044**
Orphanage				
Yes	17 (45.9)	67 (55.4)	84	
No	20 (54.1)	54 (44.6)	74	**0.315**
Type of orphanage				
Both parents	7 (44.4)	20 (29.9)	27	
Mother	9 (50.0)	24 (35.8)	33	**0.047**
Father	1 (5.6)	23 (34.3)	24	
Education level				
Primary school	26 (70.3)	71 (58.7)	97	
Secondary school	11 (29.7)	50 (41.3)	61	**0.067**
ART use				
Yes	36 (97.3)	109 (90.1)	145	
No	1 (2.7)	12(9.9)	13	**0.165**

Annex 2: Gender, type of orphanage and lung function tests

Clinical characteristics	LUNG FUCNTION TEST		Total	*p*- value
	Abnormal n (%)	Normal n (%)		
Sex				
Male	13 (61.9)	62(62)	75(62)	
Female	8 (38.1)	38(38)	46(38)	**0.993**
Type of orphanage				
Both parents	3 (30)	17 (26.8)	20(29.9)	
Mother	3 (30)	21 (39.3)	24(35.8)	
Father	4 (40)	19 (33.9)	23(34.3)	**0.895**

Annex 3: Comparison of clinical features of the study population

Character	**Unable to perform Lung Function test N=37 (23.4%)**	**Able to perform Lung Function test N=121 (76.6%)**	**TOTAL Recruited 158 (100)**	***p*-value**
Chronic cough	7 (20)	33 (27.5)	40(25.8)	**0.372**
Shortness of breath	3 (8.3)	12 (9.9)	15 (9.6)	**0.777**
Exercise intolerance	4 (11.1)	15 (12.4)	19 (12.1)	**0.836**
Chest pain	3 (8.3)	12 (9.9)	15 (9.6)	**0.777**
Weight loss	6 (16.7)	16 (13.2)	22 (14)	**0.601**
Recurrent fever	3 (8.3)	12 (9.9)	15 (9.6)	**0.777**
Wheezing	2 (5.7)	8 (6.6)	10 (6.4)	**0.849**
Cyanosis	0 (0)	3 (2.6)	3 (2)	**0.356**
Crackles	3 (9.7)	5 (4.4)	8 (5.5)	**0.253**