THE PREVALENCE OF ABNORMAL CHEST RADIOGRAPH FINDINGS AMONG HIV INFECTED CHILDREN

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DECLARATION

This dissertation is my original work and has not been presented for the award of a degree in any other university.

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DEDICATION

To my father Dr. Arnold Rodrigues for being a great inspiration to my career and for his never ending support and guidance.
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<tr>
<td>AFB</td>
<td>Acid-Fast bacilli</td>
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<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
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<tr>
<td>ALARA</td>
<td>As Low as Reasonably Achievable</td>
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<tr>
<td>ART</td>
<td>Antiretroviral therapy</td>
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<td>CCC</td>
<td>Comprehensive Care Centre</td>
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<td>CMV</td>
<td>Cytomegalovirus</td>
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<td>CT</td>
<td>Computed Tomography Scan</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>HRCT</td>
<td>High resolution Computed Tomography scan</td>
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<td>IRIS</td>
<td>Immune Reconstitution Inflammatory Syndrome</td>
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<td>KNH</td>
<td>Kenyatta National Hospital</td>
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<td>LIP</td>
<td>Lymphocytic interstitial pneumonia</td>
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<td>MDH</td>
<td>Mbagathi District Hospital</td>
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<tr>
<td>PJP</td>
<td>Pneumocystis jiroveci pneumonia</td>
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<tr>
<td>PMTCT</td>
<td>Prevention of Mother To Child Transmission</td>
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<td>TB</td>
<td>Tuberculosis</td>
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<td>WHO</td>
<td>World Health Organization</td>
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DEFINITION OF TERMS

1. **Pulmonary opacity or infiltrate**: an area of lung with increased density; appears radio-opaque

2. **Consolidation** is a dense, homogeneous opacity that obliterates adjacent heart and diaphragm borders (silhouette sign). Air filled bronchi may become visible tubular lucencies also known as air bronchograms.

3. **Other infiltrate** is an in-homogenous opacity involving the lung parenchyma that includes patchy or reticular or reticulonodular opacities with or without areas of atelectasis and peribronchial thickening.

4. **Atelectasis** refers to incomplete expansion or collapse of the lung parenchyma resulting in volume loss. It is characterised by an overall increase in lung density with reticular opacities, bronchovascular crowding and displacement of interlobar fissures.

5. **Interstitial or reticular opacities** are linear opacities in the lung caused by thickening of alveolar supporting tissues or interstitium which contains connective tissues, blood vessels, bronchial walls and lymphatics. May result in a diffuse reticular network of interlacing linear opacities. They are defined by the sizes of the intervening spaces into fine (<2mm), medium (3-10mm) or coarse (>1cm).

6. **Peribronchial thickening or cufing** is present when there is increased density or haziness of the walls of the smaller bronchi (away from the immediate hilar area) so that they become visible as circles or parallel lines.

7. **Lobar pneumonia** is a homogenous consolidation affecting one or more lobes of the lung

8. **Bronchopneumonia** is a patchy opacification of one or more secondary lobules of a lung

9. **A pulmonary nodule** is a small, rounded opacity within the lung measuring less than 3 cm in diameter. They are well-defined with sharp margins and are surrounded by normal aerated lung.

10. **A pulmonary mass** is an opacity measuring greater than 3cm.

11. **Hilar lymphadenopathy** is increase in density, enlargement or lobulation of the hilum.
12. **Pleural effusion** is a homogeneous opacification or radiodensity seen in the lateral costophrenic sulcus with a concave interface towards the lung (pleural meniscus) which appears higher laterally than medially on frontal radiographs. About 175ml of pleural fluid is required for this characteristic appearance.

13. **Comprehensive Care Centre** - out-patient clinic that is funded to provide free-of-charge healthcare services to registered HIV infected clients. Health care services include regular clinical evaluation, follow-up and dispensing of anti-retroviral drugs medical management of co-morbidities, nutritional advice, maternal health care and women’s health services, and counseling. It also provides subspecialty referrals, substance abuse and mental health support services.

14. **HIV Exposed** - infants and children born to mothers living with HIV until HIV infection in the infant or child is reliably excluded and the infant or child is no longer exposed through breastfeeding. For those<18 months of age, HIV infection is diagnosed by a positive virological test six weeks after complete cessation of all breastfeeding. For a HIV-exposed children >18 months of age, HIV infection can be excluded by negative HIV antibody testing at least six weeks after complete cessation of all breastfeeding.

15. **HIV Infected** - A child with a confirmed HIV antibody test.
ABSTRACT

Background
Human Immunodeficiency virus infected children are highly susceptible to opportunistic infections of the respiratory system which are the most common cause of morbidity and mortality. The chest radiograph is the most frequently requested examination. Its applications include screening, diagnosis and monitoring response to medication of respiratory illnesses.

Objective: To determine the prevalence of abnormal chest radiograph findings among HIV infected children.

Setting: Kenyatta National Hospital and Mbagathi District Hospital general paediatrics wards and Comprehensive Care Clinic.

Design: A hospital based cross-sectional study.

Study Justification: The prevalence of abnormal chest radiograph findings of HIV infected children in our setting has not been documented. This study provides baseline data that can be used to develop future diagnostic algorithms.

Participants: HIV infected children age 1 month to 15 years admitted in KNH or MDH general paediatric ward or on follow-up at the CCC outpatient clinic.

Study Procedure: HIV infected children who met the inclusion criteria including informed consent from their guardian(s) were recruited. A structured questionnaire was used to collect data on patient demographics, clinical symptoms and chest radiograph findings through guardian/parent interviewing and chest radiograph assessment. The chest radiographs were interpreted by two independent qualified radiologists.
Sampling procedure: Consecutive and convenient sampling.

Study Duration: Four months (November 2014 and February 2015).

Results: A total of 123 HIV infected children were studied. Normal chest radiographs were found in 54/123 (43.9%) while 69/123 (56.1%) had abnormal chest radiographic findings. Pulmonary opacities were identified in the majority of patients with abnormal chest radiographs (66.7%) while 28% showed lymphadenopathy. In the pulmonary opacities, “other infiltrate” (60.9%) was found to be more common than consolidation (39.1%). Pleural effusions were not common while cavitory lesions and pneumothorax were not identified.

There was no significant association between the radiographic findings and the children’s age and sex.

The most common symptom was cough (86%), of which 22% was productive of sputum. A significant number of children had features of respiratory distress (48.8%) as well as weight loss (32%) and night sweats (23%). The findings of this study correlated well with similar studies in Africa.

Conclusion: HIV infected children, especially those below the age of 5 years, are highly susceptible to chest infections. This was seen in the high incidence of cough and severe respiratory distress as well as the significant number of abnormal chest radiograph findings. The chest radiograph has been shown to be a useful study in detection of pulmonary disease in symptomatic children with HIV and the radiologist can assist in narrowing the differential diagnosis. The high prevalence of ‘other infiltrate’ in this study may indicate that the causative pathogen may not respond to standard antibiotic regimes; however more clinical studies to confirm this is required.
**Recommendation:** Due to the non-specific nature of abnormal chest radiograph findings in children with HIV, correlation with the level of immune suppression as well as the clinical and laboratory findings is vital. The addition of baseline chest radiographs to our local protocols may enable early diagnosis of chest infections especially pulmonary tuberculosis as well as establish whether abnormal chest radiograph findings in symptomatic children are new lesion.

**Study Limitations:** The chest radiograph findings were not compared to laboratory findings and level of immune suppression due to budgetary constraints.
INTRODUCTION
In 1999, the Government of Kenya declared HIV and AIDS to be a national disaster. Since then the number of children infected with HIV has risen dramatically in the developing countries. In 2006, there were 2.3 million children under the age of 15 years worldwide who were HIV infected (3). By 2011, 91% of the 3.4 million children living with HIV were in sub-Saharan Africa (4).

Approximately 260,000 children died of HIV related causes in 2009. A large proportion of these children died before the age of 5 with half of them dying before the age of 2 years. The mean age of mortality was 6 months (2). The United Nations Agency for International Development (UNAID) Global report 2012 documented that whereas access to HIV and AIDS treatment was on the rise, the proportion of eligible children receiving Anti-Retroviral therapy (ART) was much lower. This meant that more children continued to die as a result of HIV and AIDS (5).

HIV infected children have an increased susceptibility to developing infections. Severe infections of the respiratory tract have been found to be a major cause of morbidity and mortality in this age group (6, 7).

Chest radiography is often used as one of the main diagnostic investigations for patients with chest infections. It is available in most resource poor settings including the public sector. Although the radiological findings in children with HIV with chest infections can be non-specific, correlation with clinical findings can narrow down the possible diagnosis and aid in initiating treatment early (8, 9). Patients with HIV infection may have atypical chest radiographic findings in comparison to non-HIV infected patients with chest infections. These features include an increased frequency of lymphadenopathy, pulmonary tuberculosis and PJP (10, 11).

This study assessed the prevalence of abnormal chest radiograph findings in HIV infected children with the view of aiding radiologists and paediatricians with an approach that can be used to narrow down the diagnoses thereby assisting in the investigation and management of these patients.
LITERATURE REVIEW

The first case of HIV in Kenya was identified in 1984 (12). Since then, women have been found to be 30% more likely to be living with HIV than men; with women aged 15-24 years being four times more likely to be infected than men. These are young women of child bearing age who are also the primary care providers. This means that children have a high chance of acquiring HIV from their infected mothers during pregnancy, at birth and during breastfeeding (13).

Mother-to-child HIV transmission has remained the primary route of HIV infection for children. Accessibility to measures to reduce this transmission has remained a challenge in Africa. Without Prevention of Mother to Child Transmission (PMTCT) services, there is a 30-40% chance that a mother will pass the virus to her child. After birth practices such as prolonged breastfeeding (more than the recommended 6 months) increases the likelihood of a child acquiring HIV (13).

By the year 2010 it was estimated that there were over 97,000 HIV exposed newborns in Kenya. Considering an HIV transmission rate of 40% without any PMTCT interventions, then approximately 38,900 were estimated to be HIV infected (13). Early infant diagnosis of HIV became possible due to the introduction of the HIV paediatric programme in 2005 in Kenya. This has enabled early initiation of ART. Children below the age of 2 years who have a positive DNA PCR are started on therapy regardless of their WHO clinical stage, CD4 count or CD4 percentage, while HIV infected children above the age of 2 years are started on ART using age-related CD4 counts or WHO clinical stage 3 or 4 disease (2).

HIV infected children are increasingly susceptible to respiratory infections. This is due to the fact that HIV causes a cellular immune deficiency state due to the depletion of helper T-lymphocytes (CD4 cells). The loss of CD4 cells results in the development of opportunistic infections and neoplastic processes. Due to the decrease in cellular immunity, the infections tend to reflect pathogens that are common to the geographic region. For example, persons with AIDS in the USA tend to present with organisms.
such as Pneumocystis jiroveci pneumonia while in developing countries tuberculosis will be more common (14). Many respiratory illnesses such as upper respiratory infections, bacterial pneumonia, TB, non-Hodgkin lymphoma, obstructive airway disease also occur in immunocompetent individuals. However, these conditions are by far more common in HIV infected individuals. The incidence of these respiratory illnesses increases as the CD4 levels decrease (15).

Patients in whom there is a clinical suspicion of pulmonary illness will usually have selected laboratory tests and chest radiography performed. In settings where the availability of laboratory tests and infrastructure are limited, the chest radiographs have played a crucial role in assessing the diagnosis of chest infections and has been increasingly used especially to determine the likely presence of pulmonary tuberculosis as part of the clinical scoring. Where sputum induction and polymerase chain reaction are not available, and chest radiographs have been used as part of the basis for starting anti-TB therapy and assessing response to treatment (8). This is because the chest radiograph has been found to be more available than CD4 counts in the majority of low resource areas of this country (16).

As part of the Kenyan protocols, chest radiographs are also useful as a baseline study before initiation of ART in patients with who have had previous contact with persons with pulmonary TB or have respiratory symptoms (11, 17).

**Spectrum of Abnormal Chest Radiograph Findings**

It is recognised that there are no strict radiological definitions for chest radiographic changes seen in HIV related pulmonary disease. The radiological findings can be variable and proper interpretation can help narrow down the diagnosis. Although it is difficult to determine the etiological cause of chest x-ray abnormalities as they are non-specific (18), chest radiographs have been shown to be 42-73% accurate in predicting the causative agent in paediatric pneumonia highlighting the important role of this examination (19).
A significant number of chest radiographs in HIV infected children are abnormal which confirms the chest as one of the most common sites of infection in HIV patients (6). In South Africa, 46% of the 92 HIV infected children reviewed had abnormal chest radiographs (21) while more than 76% of HIV infected children reviewed in a study in South Nigeria had abnormal chest radiographs (22). A study done in 2002 at KNH on HIV infected children and adults, age-range from 2-67 years showed that 58% had abnormal chest radiographs (24) and in 366 HIV infected children with WHO-defined community-acquired severe pneumonia, reviewed in Durban, South Africa, 99% had abnormal chest radiographs (23).

Age-related chest radiographic findings in paediatric HIV were shown to exist by Atalabi et al in Nigeria (22). Children aged 1-5 years had the highest occurrence of abnormal chest radiographic findings (82%); followed by children above the age of 5 years (77%). Before the age of 1 year 60% of children had abnormal chest radiographs. Lymphadenopathy was also least common before the age 1 year while it was seen more commonly in children between the ages of 1-5 years than in those above 5 years. The relatively lower incidence of abnormal findings in children below the age of one year is likely due to the higher morbidity and mortality seen in HIV infected children before 2 years of age (3). The higher incidence of abnormal findings in children below the age of five years in comparison to those above five years of age is likely due to their immature immune system and underlines the need for early diagnosis and initiation of treatment.

The predominant age related radiological difference between children and adults is seen in pulmonary TB. Young children tend to develop primary TB while older children and adults develop latent TB. There is a decrease in the prevalence of lymphadenopathy with increasing age. Children below the age of 3 were found to have a higher prevalence of lymphadenopathy (100%) than those between the ages of 4-15 years (88%). Furthermore there is an even lower prevalence of lymphadenopathy in young adults below the age of thirty (43%). Only 10% of patients with pulmonary TB in their 6th decade have been found to have lymphadenopathy (25).
In contrast parenchymal opacities are more prevalent in older children (78%) and the adult population (84%) in comparison to children below the age of 3 years (51%). Pleural effusions are not common in children below the age of 2 years and are more prevalent in adults with pulmonary TB (25).

Lymphadenopathy was found in 45.3% of patients in the Nigerian study (22); with bilateral perihilar lymphadenopathy being the most frequent pattern of adenopathy. The right hilum was more commonly involved than the left which is consistent with literature on pulmonary tuberculosis (25). Also noted was that lymphadenopathy was seen in only 1% of subjects in the South African study (21). The sample size and age distribution in these two studies did not differ greatly and the only difference that can be inferred is that the South African study by du Plessis et al (21) included chronically ill patients due to convenient sampling. The 2002 KNH study found 6.3% of patients (children and adults) had hilar or mediastinal nodes (24) however this study did not further analyse the proportion of lymphadenopathy in the children versus the adult population.

Lung parenchymal lesions were the most common finding in a South African study and were found in 34% of patients (21). They were predominantly air space opacities with focal presentation being more common than diffuse changes. In the Nigerian study (22), 37% of patients had parenchymal lesions with a predominance of unilateral reticulonodular opacities. Thirteen percent had homogenous right sided opacities. In the study carried out by Jeena et al (23) on HIV infected children with severe pneumonia, consolidation was found in 50% of patients while ‘other infiltrates’ (patchy consolidation) in 49.2%. These patients with ‘other infiltrates’ were found to respond poorly to the WHO regimen of oral amoxicillin or parenteral penicillin. The authors concluded that these ‘other infiltrates’ may have represented PJP or viral infections (23). Features such as cavitation, miliary opacities were not common.

Pleural pathology is not a common feature in paediatric chest in HIV and was seen in less than 1% of patients in the Nigerian study (22) and in 1% in the South African study (21). In contrast, in the KNH study, pleural effusion was seen in 15.6% of patients which is most likely related to the majority (75%) of patients being adults (24).
The Role of the Chest Radiograph in the Diagnosis of Bacterial Pneumonia

Bacterial pneumonia has been found to be the most common respiratory cause of death in children in Africa. *Streptococcus pneumoniae* is the most common bacterial pathogen isolated from HIV-infected children with severe pneumonia (6). The main imaging used to diagnose pneumonia is chest radiography worldwide; however the interpretation of chest radiographs has been shown to vary between clinicians as well as amongst radiologists. As a result standardization of chest radiograph interpretation was found to be necessary (34). This has led to WHO developing an epidemiological tool to aid in the interpretation of paediatric chest radiographs for the diagnosis of pneumonia in epidemiological studies (34).

The WHO defined consolidation as a dense opacity that may be a fluffy consolidation of a portion or whole of a lobe, often containing air bronchograms. Other consolidations/infiltrates are defined by the WHO as linear or patchy inhomogenous airspace densities in a lacy pattern involving both lung fields featuring peribronchial thickening, perivascular cuffing, nodular or reticulonodular changes and multiple small areas of atelectasis and hyperinflation. A chest radiograph is considered to be normal when no abnormal opacities are seen (34). This epidemiological tool has however been found to be inadequate by Jeena et al (23) due to the increased prevalence of treatment failure with the standard WHO regimen of parenteral penicillin or oral amoxicillin in the HIV infected children with “other consolidates/infiltrates”.

The most common radiological finding in the HIV infected children with severe pneumonia was ‘end point consolidation’ and these responded well to the WHO recommended antibiotic regimen for severe pneumonia. This finding by Jeena is important as it implies that a change in the standard treatment regimen of pneumonia should be changed based on the chest radiograph findings. More studies are required for further verification.
Role of the Chest Radiograph in Diagnosing Pulmonary Tuberculosis

In 1993 the World Health Organization declared TB to be a global public health emergency. TB has since been found to be the most common cause of infection-related death worldwide (26). For patients with HIV infection, the risk of developing TB is 7-10% per year. Although children contribute little to the maintenance of the TB epidemic, they are greatly affected by it. The progression of the disease is determined by various factors and in the paediatric age group, the age and immune status of the child are key factors. Children below the age of 3 years as well as immunocompromised children and immune immature children are at the greatest risk (26).

Chest radiographs play a crucial role in diagnosis of pulmonary TB when in correlation with the clinical history and in the history of contact with persons with known TB infection. Chest radiographs are part of the current protocol for screening children with HIV for pulmonary TB prior to initiation of antiretroviral therapy especially those who have had contact with persons with PTB (2).

In HIV infected children, the WHO criteria for the diagnosis of TB (cough >2 weeks, failure to thrive, or weight loss) is less helpful (26). The diagnosis of pulmonary TB has been found to be problematic in children as obtaining sputum is a challenge and the yield from sputum induction and gastric lavage has been found to be low. Up to a third of patients are also found to have a normal ESR thereby limiting the usefulness of ESR in the diagnosis of TB in children. With the administration of the BCG vaccine, the Mantoux test has been found to be difficult to interpret in children with PTB (22). A study carried out in Lagos by Temiye et al involving 124 HIV positive children showed co-infection with TB to be the most common illness in these children aged below 15 years. None of the children out of 32 cases treated for TB in HIV had a positive Mantoux test (22). These findings underline the importance of the chest radiograph in clinical management as the presence of pulmonary opacities; though nonspecific will denote pulmonary disease.
Swingler et al found that chest radiographs have 67% sensitivity and 59% specificity in detecting mediastinal lymphadenopathy in suspected TB in children, when they compared contrast enhanced chest CT scans with plain chest radiographs of 100 patients (30). Milkovic et al (27) found 84% of children with tuberculosis to have lymphadenopathy while Leung et al (28) found 92% of patients to have similar findings. Mediastinal or hilar lymphadenopathy was found in 72% of patients with pulmonary TB by Woo Sun Kim et al (29).

Parenchymal changes were also a significant finding of TB in the paediatric age group. Leung et al (28) found 70% of the children to have parenchymal abnormalities more commonly seen on the right side. Sixty one percent of subjects in Milkovic et al 2005 study (27) also had parenchymal lesions on chest radiography. Woo Sun Kim et al study (29) was carried out on infants below the age of 1 year and the most common radiographic finding in this age group was air space consolidation (80%) with nodular lesions being seen on 28% of patients.

**Role of the Chest Radiograph in the Diagnosis of Pneumocystis jiroveci Pneumonia**

Pneumocystis jiroveci pneumonia is caused by the ubiquitous unicellular eukaryote Pneumocystis jiroveci (35). This is the most common opportunistic infection in persons with HIV infection and rarely causes infection in the general population. It causes a severe hypoxic pneumonia in children and if untreated leads to a high mortality in infants. It has been found that 29-67% of deaths due to respiratory illness in HIV infected African children are due to PJP (36).

The most common chest radiological findings are fine reticular interstitial opacities that are often perihilar in distribution (37). They may be diffuse or focal. Normal chest radiographs and pleural effusions are generally uncommon (38).

Sivit et al studied chest radiographs of children with perinatally transmitted HIV who had PJP aged 2-17 months. The most common findings were diffuse and patchy infiltrates. No lymphadenopathy was observed. Pleural effusion was seen in only 5% consistent
with most literature on PJP chest radiograph findings. One third of the subjects were found to develop a pneumothorax validating the need for chest x-rays in paediatric HIV management and follow up even though the initial radiograph may be normal (39). The chest radiograph plays a central role on the diagnosis of PJP as there is no specific laboratory test that is diagnostic.

**Role of the Chest Radiograph in the Diagnosis of Lymphocytic Interstitial Pneumonia**

Lymphocytic interstitial pneumonia (LIP) has been designated an AIDS-defining illness by the US Centre for Disease Control and Prevention when seen in children. It has been reported to occur as part of immune reconstitution syndrome. LIP has been found in 22-75% of paediatric patients with HIV who have pulmonary disease. Clinically, it presents with a syndrome of fever, cough, and dyspnoea.

The chest radiographic findings include bibasilar interstitial or micronodular infiltrates which coalescence into an alveolar pattern, often with mediastinal widening and hilar enlargement denoting pulmonary lymphoid hyperplasia (34). The chest radiograph aids in the presumptive diagnosis of LIP based on the persistence for 2 months or more of characteristic radiographic features.

**Role of the Chest Radiograph in the Diagnosis Immune Reconstitution Inflammatory Syndrome**

HIV immune reconstitution inflammatory syndrome (IRIS) is the paradoxical worsening of patient’s condition after initiation of ARTs due to the recovery of the immune system (10). It has an incidence of 10-20%. The most common causes are tuberculosis co-infection (BCG vaccine related), atypical pneumonia and CMV. Although the mortality due to IRIS is unknown there is an increase in mortality rate within the first 3 months of initiation of ART. On the chest radiograph IRIS may represent with enlargement of a pulmonary nodule and worsening of lymphadenopathy or pulmonary opacities. These features are non-specific and difficult to differentiate from other chest infections including TB making the clinical history critical in the diagnosis of IRIS (10).
The Role of the Chest Radiograph in HIV Associated Malignancies

There is an increased risk of developing malignancies in patients with HIV infection. This risk is also seen in children. Studies have shown a 40 times higher risk of developing malignancy in children infected with HIV than in uninfected children (40). The most common malignancies found in children with HIV/AIDS are Non Hodgkin Lymphoma, Kaposi’s sarcoma, and leiomyosarcoma. The incidence of cancer is higher in adults with HIV than in children and the type of HIV associated malignancy varies with age as well as geographical location. Leiomyosarcoma has been found to be more common in children than Kaposi sarcoma in the USA but Kaposi sarcoma is the most common paediatric HIV-related malignancy in Sub-Saharan Africa. In Zambia, Kaposi sarcoma accounts for almost 20% of all childhood cancers (40).

The main chest radiographic findings in Kaposi Sarcoma (KS) are perihilar interstitial nodules which may either be linear or ill-defined mostly involving the middle and lower lobes. These may eventually develop into dense air space consolidation. Lymphadenopathy is seen in 10-16% of patients while unilateral or bilateral pleural effusions are present in 30-90% (41). As chest radiograph findings may be non-specific; the diagnosis can only be considered in a suitable clinical setting such as cutaneous KS lesions. In centres were radionuclide scanning is available, thallium and gallium scans are used to differentiate between Kaposi sarcoma and a pulmonary infection (42).

Interpretation of the Chest Radiograph

It has been shown that despite radiologists coming from different backgrounds and environments and having used various reference materials, there is a high level of interobserver agreement when it comes to interpretation of chest radiographs. With the use of simple criteria and adequate standardized training of radiologists there is less ambiguity and variability in interpretation of chest radiographs (43). Another study has shown that when two independent paediatric radiologists were blinded to clinical information, there was good agreement on the diagnosis of pneumonia on chest x-ray among children with non-severe low respiratory infections (44).
American College of Radiology (ACR) and the Society for Paediatric Radiology (SPR) have designed practice guidelines for the performance of chest radiography (45). These guidelines are meant to help standardize care provided to patients and although recommended; there is an allowance for special patient needs and circumstances. Guidelines include informative and completed request form which include patient’s bio data, clinical history, signs and symptoms and documented formal training in paediatric radiology. The latter may not be feasible in our set up as the number of paediatric radiologist with formal training is limited. This study utilized board certified radiologists working at the KNH and MDH hospitals.

Antero-posterior (AP) and left lateral views of the chest radiograph are routinely done so as to fully evaluate the airways, lungs, pulmonary vessels, mediastinum, heart, pleura and chest wall and establish whether there is any pathology. Studies have shown that it is not necessary to perform routine lateral radiographs in children with respiratory infections as they only increase the diagnosis of pneumonia in a small percentage of cases (46-49). Supine views are reserved for very sick patients and are routinely done for young children who cannot stand.

**STUDY JUSTIFICATION**

Opportunistic chest infections are the leading cause of mortality in HIV exposed or infected children. In 2010 the in-hospital mortality of HIV infected children (13.9%) was more than twice that of uninfected children with severe pneumonia (5.3%); the majority of deaths being before the age of 2 years (50).

Chest radiographs have been in use for many years for the evaluation of paediatric chest conditions. It is an investigation tool that clinicians have found to be readily accessible and relatively cheap. Early diagnosis of chest infections can thus be made and guide the clinician in narrowing down the diagnosis and requesting only the necessary laboratory investigations. The use of chest radiographs as a baseline study has been found to be valuable before initiating on ART in both South Africa and Nigeria.
In Kenya the paediatric programme for HIV was initiated only in 2005. Guidelines for the prevention of Mother-to-child transmission as well as for the staging and management of HIV exposed and infected children were developed and have been revised to the current guidelines of 2013.

With the recent change in ART regimens especially in early initiation of therapy in infants, this study will aim to determine what is the current prevalence of abnormal chest radiograph findings in HIV exposed/infected children and suggest possible aetiologies. It is hoped that this study will form a data base on which future studies can be designed.

**STUDY OBJECTIVES**

To determine the prevalence of abnormal chest radiograph findings in HIV infected children the Kenyatta National Hospital, General Paediatric Wards and CCC.

Specific Objectives

1. To determine the prevalence of abnormal chest radiograph findings among HIV infected children in KNH and MDH general Paediatric wards and CCC out-patient clinic.
2. To describe the abnormal chest radiograph patterns (mediastinal, pulmonary and pleural pathology) among HIV infected children in KNH and MDH general Paediatric wards and CCC out-patient clinic.
RESEARCH METHODOLOGY

Study Design
A cross sectional study design was used to determine the prevalence of abnormal chest radiograph findings in HIV infected children between the ages 1 month to 15 years at Kenyatta National Hospital and Mbagathi District Hospital.

Study Area
This study was carried out in the general paediatric wards and Comprehensive Care Centres at the Kenyatta National Hospital and Mbagathi District Hospital.

Kenyatta National Hospital is the largest referral and teaching hospital in Kenya. It is located in Nairobi and is the second largest hospital in Africa with a bed capacity of 2000. There are four general paediatric wards each with a bed capacity of 60, although bed occupancy is often over 100%. In the year 2010 there were 160 HIV infected children admitted to the general paediatric wards. A total of 4,294 children attended the CCC between the months of August 2013 to August 2014.

Mbagathi District Hospital is the Nairobi County referral hospital. It is located in Dagoretti Constituency but serves patients from the whole Nairobi area and its environs. The bed capacity is 200 of which 32 beds are for paediatric patients. Bed occupancy in the paediatric wards is usually over 100%. There were 18 HIV infected children admitted to the general paediatric wards between January and June 2014 and 25 children were being reviewed monthly at the CCC.

Study Population
Children aged 1 month to 15 years admitted to the general paediatric wards or seen at the CCC at KNH and Mbagathi Hospital who were HIV infected.

Inclusion Criteria
- HIV infected children aged 1 month to 15 years with a positive HIV serology.
- Patients with written informed consent from the parent or guardian.
Exclusion Criteria

- Children with chest or cardiac congenital abnormalities
- Poor image quality of chest radiograph

Sample Size

Sample size determination was based on a similar study by Atalabi et al (22), which estimated the prevalence of abnormal chest radiographs in HIV infected children to be 76.7% at the University College Hospital in Ibadan which, like KNH, acts as a teaching and tertiary referral hospital.

From the Kenyatta National Hospital and Mbagathi Hospital, Radiology Department records, it was estimated that, on average, 200 HIV positive children were referred for chest radiography in a period of 6 months. In order to adjust the sample size into this finite population, the sample size calculation was adjusted using the finite population correction method as shown below;

\[ n' = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)} \]

Where:

- \( n' \) = minimum sample size
- \( N \) = Study population. This is the total number of HIV positive children referred for chest radiographs over a 6 month period = 200
- \( Z \) = Z statistic for a level of confidence which was put at 95% which gives a value of 1.96
- \( P \) = hypothesised prevalence of abnormal chest radiographs in HIV positive children (76%)
- \( d \) = Precision with a 95% confidence interval which gives a margin of error of ±0.05.
\[ n' = 200 \times 1.96^2 \times 0.76 (1 - 0.76) \]
\[ (0.05)^2 (200-1) + 1.96^2 0.5 (1-0.76) \]

\[ n' = 200 \times 3.8416 \times 0.18 \]
\[ 0.0025 \times 199 + 3.8416 \times 0.24 \]

\[ n' = 384.16 \]
\[ 0.4975 + 0.9216 \]

\[ n' = 117 \]

\[ n' = 117 \text{ participants} \]

**Sampling Method**
Consecutive sampling on all children who were HIV positive in the general wards or CCC of KNH and Mbagathi Hospital was carried out. The patients were screened by the primary physicians as well as two research assistants to determine eligibility and whether do patients meet the inclusion criteria. The screening was done between 8am to 5pm on weekdays and 9am to 2pm on weekends and public holidays due to feasibility.

**Study Procedure**
All HIV infected infants and HIV positive children aged 1 month to 12 years in the general paediatric wards and CCC of KNH and MDH were screened by the primary physicians and two research assistants. Any patient who met the inclusion criteria and the primary care giver provided a written informed consent (see Appendix 1) was recruited. An assent for children above the age of 7 years was also provided after confirming with their guardian they were aware of their HIV status (see Appendix 2).
The recruitment period was six months. The primary physicians requested chest radiographs based on their clinical evaluation of the HIV infected children e.g. exposure to care giver with TB, acute symptoms such as difficulty in breathing, fever or chronic symptoms such as weight loss (Appendix 3). Chest radiographs were not performed on asymptomatic patients or on any patient who the clinician did not find necessary to have a chest radiograph done.

A structured questionnaire was administered by the two research assistants to the caregivers. The questionnaire contained the socio-demographic details of the child; the clinical respiratory complaints and the most recent CD4 count (where available). The questionnaire had categorical variables to collect data on: lymphadenopathy, pulmonary opacities, pleural effusions, cavitary lesions, pneumothorax and presence of any other lesions (Appendix 3)

An erect postero-anterior (PA) view at a distance of 150-200cm with the anterior chest wall against the film cassette was taken for the older children using 70kVp and 2.0mAs. If the patient was unable to stay erect or unable to keep still, the chest radiograph was taken as antero-posterior (AP) supine. The chest radiographs were defined as adequate if the following criteria was met; minimal rotation, full inspiration with adequate penetration, and correctly labeled to include patients name, identification number, date of examination and side markers.

The radiographs was read and interpreted by two board certified independent radiologists.

The following conclusions obtained from interpretation using the defined terms were used during data analysis.

- Normal chest radiograph
- Abnormal chest radiograph:
  - Mediastinal/hilar pathology e.g. lymphadenopathy
  - Parenchymal pathology to include consolidation and other infiltrate.
  - Pleural pathology
If there is a difference in the chest radiograph findings between the two radiologists, the chest radiographs was discussed between them where possible and a consensus was reached.
A comprehensive written report was provided to the caregiver to return to their primary physician for further management of the patient.

ETHICAL CONSIDERATIONS

The study was conducted after getting the approval from the Research and Ethics Committee of Kenyatta National Hospital and the University of Nairobi.

**Autonomy**

The study was carried out only after informed consent has been sought from the caregiver. They were free to withdraw from the study at any stage without affecting the quality of care the children received. Assent to participate in the study was sought from the children over the age of 7 years.

**Informed Consent**

The parents/guardians of the patients had the details of the study fully explained to them before recruitment for the study followed by consent through signing of the written informed consent form.

Children above the age of seven years who already have full disclosure of their HIV status had the details of the study fully explained to them in simple terms that they could understand before recruitment for the study. They were asked to sign and assent form in the presence of their parent/guardian.

**Confidentiality**

Strict Confidentiality was observed throughout the entire study period, held in trust by participating investigators, research staff and the study institutions. The study participants were given study identification numbers and no personal identification data
was recorded. No information concerning the individual study findings will be released to any unauthorized third party without prior written approval of the study institution or the Ethics Research Committee.

**Risks**

Study participant were not unnecessarily exposed to radiation. No asymptomatic children were recruited for this study. The 0.1 millisievert dose received from a chest radiograph posed minimal risk to the patient. No experimental drugs or invasive procedures were carried out.

**Benefits**

Any diagnostic information which is found to be beneficial to the patient was shared with the managing clinician to aid in the management of the patient.

**Safety**

This study did not interfere with the treatment of a severely ill child.

**DATA MANAGEMENT AND ANALYSIS**

**Data Management**

Data collected through the data collection forms was entered into a *Microsoft Excel*™ database. Analysis was conducted using STATA version10 data analysis software which were password protection and backed-up into an external hard drive and CD. The hard drive and CD are under the safe custody of the principal investigator. Each data record entered into the database was assigned a unique identification number so as to protect the privacy of the patients. The data collection forms were filed and stored in a safe cabinet where verification of results can be done whenever necessary to ensure quality of data was maintained.
RESULTS
A total of 123 children who met the inclusion criteria were included in the study. Their age ranged between 1 month and 15 years. The median age was 24 months.

*Figure 1: Age Distribution*

**Socio-demographic Characteristics**
There were 61 males (49.6%) and 62 females (50.4%) enrolled in the study.

*Table 1: Distribution of children by age group (n=123)*

<table>
<thead>
<tr>
<th>Age categories</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 12 months</td>
<td>14 (43.8%)</td>
<td>18 (56.3%)</td>
</tr>
<tr>
<td>13-24 months</td>
<td>18 (54.5%)</td>
<td>15 (45.5%)</td>
</tr>
<tr>
<td>25 - 60 months</td>
<td>7 (36.8%)</td>
<td>12 (63.2%)</td>
</tr>
<tr>
<td>Above 60 months</td>
<td>22 (56.4%)</td>
<td>17 (43.6%)</td>
</tr>
<tr>
<td>Total</td>
<td>61 (49.6%)</td>
<td>62 (50.4%)</td>
</tr>
</tbody>
</table>
Clinical Findings

The predominant clinical presentation of the children included in this study was cough in 86%. The duration of the cough varied from 1 week to 6 months and in 22% of patients the cough was productive of sputum. Forty eight percent of children had dyspnea while weight loss (32%) and night sweats (23%) were also common symptoms found in these children. Chest pain was not a common feature found in only 8% of children.
Table 2: Characteristics of the children’s clinical symptoms (n=123)

<table>
<thead>
<tr>
<th>Patient Symptoms</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coughing</td>
<td>106 (86.2%)</td>
</tr>
<tr>
<td>Night sweats</td>
<td>29 (23.6%)</td>
</tr>
<tr>
<td>Sputum</td>
<td>27 (22%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>10 (8.3%)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>39 (32%)</td>
</tr>
<tr>
<td>Dyspnoeic</td>
<td>59 (48.8%)</td>
</tr>
</tbody>
</table>

CD 4 count (Median) 750 (min=71, max=1500)

Chest Radiograph Findings

There were 54 children (43.9%) with normal chest radiographs and 69 children (56.1%) with abnormal chest radiographic findings.

Pulmonary opacities were identified in the majority of patients (66.7%) and of these “other infiltrate” (60.9%) was found to be more common than consolidation (39.1%).

Thirty five patients (50.7%) had lymphadenopathy. Pleural effusions were not common while cavitary lesions and pneumothorax were not identified.

Occurrence of abnormal chest radiographs

A total of 69 (56.1%) of the radiographs were abnormal and 54 (43.1%) were normal as summarized in figure 3.
Comparison of Radiographic Features with age

The predominant feature in children below 12 months was pulmonary opacity (28%) with a higher incidence of “other opacity” than consolidation. Lymphadenopathy was identified in 22.9% of these children.

Lymphadenopathy (31%) was the most prevalent abnormal chest radiograph finding in children between 13-24 months. There was also a higher incidence of consolidation (35%) in this age group compared to “other infiltrate”.

Between the age of 25-60 months the predominant chest radiograph finding was consolidation(15%) and lymphadenopathy (14%) while in children above the age of 60 months the main findings were “other infiltrate” in 39% and lymphadenopathy in 31%.

Lymphadenopathy was most prevalent in children below 24 months. The children between 13-24 months had the highest incidence of consolidation while “other infiltrate” was most prevalent in children above 60 months. None of the children were diagnosed with cavity lesions and pneumothorax.

Table 3 summarizes the radiographic findings among the children.
Table 3: Radiographic findings among the participating children (n=69)

<table>
<thead>
<tr>
<th>Abnormal chest radiograph findings</th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphadenopathy</td>
<td>35(50.7%)</td>
</tr>
<tr>
<td>Pulmonary opacities</td>
<td>46 (66.7%)</td>
</tr>
<tr>
<td>Consolidation (n=46)</td>
<td>20(43.5%)</td>
</tr>
<tr>
<td>Other infiltrate (n=46)</td>
<td>28(60.9%)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>6(0.5%)</td>
</tr>
<tr>
<td>Cavity lesion</td>
<td>0</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>0</td>
</tr>
</tbody>
</table>

Difference in abnormal chest radiographs

There was no significant association between the radiographic findings and the children’s age as shown in table 4.

Table 4: Difference in abnormal chest radiographs by age groups (n=69)

<table>
<thead>
<tr>
<th>Age categories</th>
<th>Under 12 months</th>
<th>13-24 months</th>
<th>25 - 60 months</th>
<th>Above 60 months</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphadenopathy</td>
<td>8(22.9%)</td>
<td>11(31.4%)</td>
<td>5(14.3%)</td>
<td>11(31.4%)</td>
<td>0.986</td>
</tr>
<tr>
<td>Pulmonary opacities</td>
<td>13(28.3%)</td>
<td>13(28.3%)</td>
<td>6(13%)</td>
<td>14(30.4%)</td>
<td>0.555</td>
</tr>
<tr>
<td>Consolidation (n=46)</td>
<td>6(30%)</td>
<td>7(35%)</td>
<td>3(15%)</td>
<td>4(20%)</td>
<td>0.609</td>
</tr>
<tr>
<td>Other infiltrate (n=46)</td>
<td>8(28.6%)</td>
<td>6(21.4%)</td>
<td>3(10.7%)</td>
<td>11(39.3%)</td>
<td>0.324</td>
</tr>
</tbody>
</table>

Note
The Fisher exact test was applied to test the association between age-group and radiographic finding. A p-value of <0.05 was considered statistically significant.
IMAGE 1: Lymphadenopathy with right mid-zone consolidation

IMAGE 2: Bilateral “other pulmonary infiltrates”

IMAGE 3: Left pleural effusion
IMAGE 4: 4 month history of cough and weight loss with bilateral "other pulmonary infiltrates" on anti-TB therapy.

IMAGE 5: Bilateral "other pulmonary infiltrate" in a patient suspected to have LIP
DISCUSSION
In this study we found the majority of patients were below the age of 5 years (68%) and most of them below the age of 2 years (52%) with a median age of 24 months. These findings are similar to studies carried out in Nigeria (64%) and in South Africa (55%) where the majority of children included in their studies were below 5 years of age. This can be attributed to the fact that HIV testing is routinely done with consent to all newborns whose mothers are exposed as well as to all children of all ages admitted in any government hospital regardless of mother’s sero-status and the child’s clinical presentation. The routine testing allows early diagnosis HIV infections in children and ARV therapy commencement. During testing and counseling of the children, the mother is encouraged to have her test done, thereby increasing the number of adults who are aware of their immune status. If the mother is found to be HIV positive, she is reviewed by the physicians and enrolled for management at the hospital CCC.

There was no statistical difference in sex distribution in this study which is similar to other studies in Nigeria and South Africa.

The chest is the most common site of infection in children with HIV and this was reflected in the high proportion of patients with cough (86%). Severe respiratory infections are the major cause of death in HIV infected children. The pulmonary complications of HIV infection study (15) demonstrated that respiratory symptoms are common among HIV infected individuals with 27% of patients complaining of cough. They also reported that cough was significantly more common in HIV infected individuals than non HIV infected (40% vs 25%).

Only 22% of children enrolled in our study had a productive cough and this is in keeping with the fact that most young children do not expectorate sputum. Our study had a high proportion of children below the age of 5 years. Sputum production was found to be more prevalent in HIV infected individuals than in non HIV infected individuals in the pulmonary complications of HIV infection study (15). Patients with purulent sputum and a short duration of symptoms are likely to have bacterial pneumonia while the absence of sputum in a patient with low CD4 counts and symptoms of a few weeks is suggestive of PJP.
Dyspnea was identified in almost half of the patients (48.8%) and this may be attributed to the study being carried out in a hospital based setting with symptomatic and critically ill patients. Associated findings of lower chest wall in-drawing meeting the WHO criteria for severe pneumonia as well as central cyanosis or difficulty in breastfeeding/drinking (very severe pneumonia) were also present in these children. Study subjects in the pulmonary complications of HIV study showed a significant incidence of dyspnea (23%) and a significantly higher occurrence in HIV infected individuals than non HIV infected subjects (41% vs 7%).

Although most patients presented with acute symptoms, constitutional symptoms such as night sweats (23%) and weight loss (32%) were relatively common, as these are non-specific clinical features of HIV and HIV-associated infections such as tuberculosis.

A significant number of chest radiographs were found to be abnormal (56.1%). These findings are similar to the study carried out by Onyambu et al in 2002 in KNH on HIV infected children and adults where 58% had abnormal chest radiographs. This is attributed to the fact that the chest is the most common site of infection in HIV infection. The study by du Plessis et al in South Africa reviewed 92 HIV infected children and found 46% to have abnormal chest radiographs a slightly lower prevalence than our study. Other studies showed a higher prevalence of abnormal chest radiograph findings. More than seventy-six percent of HIV infected children in a study in south Nigeria had abnormal chest radiographs while of the 366 HIV infected children with WHO defined community acquired severe pneumonia reviewed in Durban, 99% had abnormal chest radiographs.

Age related chest radiographic findings in paediatric HIV were shown to exist by Atalabi et al in Nigeria (22). Their study findings compared favourably with our study with the highest occurrence of abnormal chest radiograph findings occurring in children aged 1-5 years of age; 78% in our study and (82%) in Nigeria. This was followed by the age of above 5 years in our study (58%) as well as in the study in Nigeria (77%). The higher incidence of abnormal findings in children below the age of five years in comparison to
those above five years of age is likely due to their immature immune system and highlights the need for early diagnosis and initiation of treatment. Before the age of 1 year there was no significant difference with 50% of these children having abnormal findings in our study and 60% in the Nigerian study. The lower incidence of abnormal findings in children below the age of one year is due to the higher morbidity and mortality seen in HIV infected children before 2 years of age (3) or earlier initiation of therapy. Further evaluation on the current mortality of HIV infected children in this age group may be required to fully determine this.

Lymphadenopathy was the second most common finding after pulmonary opacities in our study. We found 50.7% of HIV infected children had lymphadenopathy which is similar to the 45.3% of patients in the study from Nigeria. In contrast lymphadenopathy was only seen in 1% of subjects in the South African study and the 2002 study carried out in KNH which found only 6.3% of children and adults with HIV to have lymphadenopathy. Although the great difference in findings between the South African study and our study cannot be explained, the difference between our study and the 2002 KNH study is likely to be the higher proportion of adults reviewed in 2002 with only 26% of their patients being children. Adult pneumonia and latent pulmonary tuberculosis have a lower incidence of lymphadenopathy (10-30%) than children.

Lung parenchymal lesions were the most common finding in the South African study (21) involving 34% of patients. In our study we found a higher prevalence of lung parenchymal disease in 69.6% of children with HIV. The higher incidence is similar to the 2002 KNH study which found that 75% of patients (adults and children) to have pulmonary opacities.

When evaluating the lung parenchymal opacities the predominant finding in our study was “other pulmonary infiltrate” in 22% of patients and consolidation in 16%. These findings are similar to the Nigerian study (22). It is speculated that the higher incidence of “other infiltrate” in our study could represent viral infections, atypical pneumonia, tuberculosis, LIP or PCP.
In 21% of the patients there was a presumptive diagnosis of pulmonary tuberculosis dependent on the chest radiograph findings and the duration of symptoms. This is similar to Atalabi et al’s study in Nigeria where 20% of children had sputum confirmed AFB positive TB. Parenchymal disease is reported to be seen in 70% of children with tuberculosis (25). Although it is difficult to conclusively diagnose TB on chest radiograph findings alone due to their non-specific features, the radiological findings are often similar to those on non-HIV infected children.

Another possibility for the high prevalence of pulmonary opacities in our children is IRIS which may present with new or worsening pulmonary opacities as well as worsening of hilar lymphadenopathy or enlargement of pulmonary nodules. The children admitted to the wards who were found to be HIV positive would have ART initiation after basic workup and before being discharged through the CCC clinic. The relatively high CD4 counts in our study may be attributed to the early initiation of ART.

Pleural pathology was not a common feature in paediatric chest in HIV and was seen in less than 1% of patients in the Nigerian study (22) and only in 1% in the South African study (21). This is similar to our study which showed less than 1% of children with pleural effusions. In the KNH study, pleural effusion was seen in 15.6% of patients which could be because the majority (75%) of patients was adults (24). Pleural effusions in children are usually indicative of bacterial pneumonia. Pleural effusions are seen in 5-10% of children with tuberculosis (25).

Features such as cavitation, miliary opacities were not common in the South African and Nigerian study and there were no chest radiographs with cavitation or pneumothorax identified in our study. This is because cavitation is usually more commonly seen in adolescents and adults (25) and the majority of our patients were below 5 years of age.
CONCLUSION
Children, especially those below the age of 5 years, are highly susceptible to HIV associated chest infections. This is seen with the high incidence of cough and severe respiratory distress as well as the significant number of abnormal chest radiograph findings. Similar to other studies, there were a significant number of children who had a presumptive diagnosis of TB, which is endemic to our country and a cause of morbidity and mortality in immunocompromised patients. The predominance of pulmonary infiltrates over consolidation could be attributed to the presence of atypical pneumonia, viral infections, PJP as well as pulmonary TB. The findings of this study also correlated well to other studies in Africa.

The chest radiograph is shown to be a useful study in detection of pulmonary disease in symptomatic children with HIV and the radiologist can assist in narrowing the differential diagnosis. However further laboratory investigation is required to confirm the diagnosis as some of the chest radiograph findings are non-specific.

STUDY LIMITATIONS
1. There was no correlation of chest radiograph findings and laboratory findings to confirm the cause of chest radiograph abnormalities especially pulmonary TB.

2. Not all children recruited had current CD4 counts to allow correlation of chest radiograph findings and level of immune suppression.

3. Baseline chest radiographs are not part of the guidelines for management of HIV patients limiting the study to symptomatic patients with available chest radiographs.
RECOMMENDATIONS
Due to the non-specific nature of abnormal chest radiograph findings in children with HIV, correlation with the level of immune suppression as well as the clinical and laboratory findings is vital.

The addition of baseline chest radiographs to our local protocols may enable early diagnosis of chest infections especially pulmonary tuberculosis as well as establish whether abnormal chest radiograph findings in symptomatic children are new lesion such as those seen in IRIS after initiation of ART.

Follow-up studies are required to determine how the children with “other infiltrate” on radiograph respond to the standard WHO treatment regimen.
REFERENCES


50. Kibore MW, Were FM, Obimbo EM, Laving A. Prevalence of Human Immunodeficiency Virus Infection among Children Under Five Years with Severe or Very Severe Pneumonia in Kenyatta National Hospital. 2010
APPENDICES:

APPENDIX 1: CONSENT FORM

Patient’s Study Identification Number: ........................................

Date: ..............................

Study Title: THE PREVALENCE OF ABNORMAL CHEST RADIOGRAPH FINDINGS IN HIV INFECTED CHILDREN

Investigator: Dr. John Rodrigues

Tel Number: 0722-269254

Supervisors:

Dr. Gladys Mwango
Dr. Callen Onyambu

Investigators Statement:

We are requesting you and your child to kindly participate in this research study. The purpose of this consent form is to provide you with the information you will need to help you decide whether to participate in the study. This process is called ‘Informed Consent’. Please read this consent information carefully and ask any questions or seek clarification on any matter concerning the study with which you are uncertain.

Introduction:

HIV is a virus that attacks the human immune system. Without a strong immune system, the body is unable to protect itself from disease especially chest infections such as pneumonia and tuberculosis (TB). A chest x-ray may be requested by the doctor to help in the diagnosis of chest infections. The aim of this study is to find out what percentage of children with HIV have abnormal chest x-rays.
In this study if your child’s doctor sees it necessary to have a chest x-ray done then your child will have a chest x-ray performed which will be interpreted by two specialized doctors (radiologists). Children with previous chest x-rays will be asked to provide them for this study and review by our radiologists. One hundred and seventeen HIV infected children will be recruited for this study. We will then find out how many of these children have abnormal chest x-rays. A typed report of your child’s chest x-ray will be provided to you and your doctor to aid in the treatment of your child.

**Benefits**

The results of the research will be used by healthcare providers in the CCC, paediatric, and radiology departments to help improve the diagnosis of chest infections in HIV infected children. This study also aims to inform policy makers on a cheap, inexpensive, readily available diagnostic tool that can help in the screening and diagnosis of chest infections in HIV infected children in our country.

**Risks:**

The radiation dose received from a chest x-ray carries minimal risk to your child and is far less than the radiation you receive from the natural environment every year. There will be no invasive procedures carried out in the study that may harm your child.

Refusal to participate will in no way jeopardize the treatment of your child.

**Voluntariness:**

The participation in this study will be fully voluntary. There will be no financial rewards to you for participating in the study. One is free to participate or withdraw from the study at any point. Refusal to participate will not compromise your child’s care in any way.

**Confidentiality:**

Care will be taken during data collection and storage to guarantee confidentiality of you and your child through allocation of unique study identification numbers and no personal
identification data will be recorded. The data collection instruments will not contain patient identifiers. The data collected will be stored in a computer that will only be accessible to the principal investigator and research assistants using a password. Retrieval of this data will be through the use of the same password. No specific information regarding you, your child will be released to any person without your written permission or approval of the ethics research committee. We will however discuss general overall findings regarding all children assessed but nothing specific will be discussed regarding your child's condition.

**Problems or Questions:**

If you ever have any questions about the study or about the use of the results you can contact the principal investigator, **Dr. John Rodrigues** by calling **0722-269254**.

If you have any questions on your rights as a research participant you can contact the **Kenyatta National Hospital/ University of Nairobi – Ethics Research Committee (KNH/ UON - ERC)** by calling **2726300 Ext. 44355**.

I _________________________________ having received adequate information regarding the study research, risks, benefits hereby **AGREE / DISAGREE** (Cross out as appropriate) to the participation of my child in this study. I understand that our participation is fully voluntary and that I am free to withdraw at any time. I have been given adequate opportunity to ask questions and seek clarification on the study and these have been addressed satisfactorily.

Parents/Guardian’s Signature: _________________ Date ____________

I _________________________________ declare that I have adequately explained to the above participant, the study procedure, risks, and benefits and given him /her time to ask questions and seek clarification regarding the study. I have answered all the questions raised to the best of my ability.

Investigator’s Signature _________________ Date ________________
Appendix 1.1: Fomu ya Idhini
Nambari ya Utafiti: ........................................

Tarehe: .........................................................

Swala Kuu la Utafiti:

UHUSIANO KATI YA UGONJWA WA UKIMWI NA PICHA ZA KIFUA (CHEST X-RAY)
AMBAZO SI ZA KAWAIDA KATIKA WATOTO AMBAO WANATIBIWA KWA HOSPITALI KUU YA KENYATTA.

Mpelelezi Mkuu: Dkt. John Rodrigues
Nambari ya simu: 0722-269254

Wasaidizi Wakuu: Dkt. Gladys Mwango
Dkt. Callen Onyambu

TAARIFA YA MPELELEZI MKUU:
Tunawaomba wewe na mtoto wako kushiriki katika utafiti huu. Lengo la fomu ya idhini ni kupa taarifa unaohitaji kukusaidia kuamua kama unataka kushiriki katika utafiti huu. Tafadhali soma taarifa iliyo katika fomu ya idhini hii kwa umakini na pia uliza maswali usipoelewa taarifa yoyote.

KUANZISHWA
Ukimwi ni ugonjwa ambao unashambulia mfumo wa kinga wa mwili. Bila mfumo wa kinga, mwili hauwezi kujinga kutoka maambukizi hasa maambukizi ya kifua kama kisamayu na kifua kikuu. Picha ya kifua inasaidia daktari kufanya utambuzi wa maambukizi ya kifua. Lengo la utafiti huu ni kuangalia kiasi cha oicha amazo sio za kawaida kwa watoto ambao wana virusi vya ukimwi.
Katika utafiti huu, daktari wa mtoto wako akiaagiza pich ya kifua, picha hiyo itapigwa na kutafsiriwa na madaktari wawili wa picha (Radiologists.) Mtoto ambaye ana picha ya kifua ataombwa kutoa hiyo picha ili madaktari wa picha (Radiologist) waweze kuitafsiri. Watoto mia moja na kumi na saba wenye virusi vya ukimwi wataajiriwa katika utafiti huu. Ndipo tutakuwa kujua jinsi watoto wangapi wana picha ya kifua ambayo si ya kawaida. Ripoti ya picha ya mtoto wako itatolewa kwa wewe na daktari wako na misaada katika usimamizi wa mtoto.

**MANUFAA**

Matokeo ya upelelezi huu, yatasaidia madaktari katika kliniki ya CCC na vyumba vya watoto katika hospitali na pia madaktari wa picha kutambua maambukizi ya kifua kati ya watoto wenye virusi vya ukimwi.

Utafiti huu unatakea pia kuwajulisha watunganya sera kuhusu chombo cha uchuuunguzi kwa bei nafuu na inapatikana kwa urahisiambayo inaweza kusaidia kwa uchunguzi nakupima maambukizi ya kifua kati ya watoto wenye virusi vya ukimwi katika nchi yetu.

**MADHARA**

Kipimo cha mionzi kupokea kutoka na picha ya kifua (Chest X-ray) hubeba hatari ndogo kwa mtoto wako na ni chini ya mionzi kupokea kutoka katika mazingira ya kila siku. Hakutakuwa na utaratibu vamizi ambazo zinaweza kuathiri mtoto wako. Kukataa kushiriki katika utafiti huu si kuhatarisha matibabu ya mtoto.

**HIARI:**

Kushiriki kwa utafiti huu ni kwa hiari ya mtoto na mlezi wake. Hakuna gharama yoyote ya ziada itakayotokana kwa ajili ya kushiriki katika utafiti huu. Mgonjwa ama mlezi ana uhuru wa kutamatisha kuhusika wakati wowote bila madhara yoyote.
USIRI:


SHIDA AU MASWALI:

Ikiwa ungetaka kupata maelezo zaidi juu ya utafiti huu, tafadhali wasiliana na mpelelezi mkuu Dkt. John Rodrigues kupitia nambari ya simu 0722-269254 ama Hospitali Kuu ya Kenyatta Idara ya Utafiti kwa nambari ya simu 2726300 ugani wa simu 44355.

Mimi _______________________________ nimeelewa maana na jinsi utafiti huu utakavyofanywa na pia kuwa utafanywa kwa hiari yangu na nikona uhuru kutamatisha kuhusika kwa utafiti huu wakati wowote.

Sahihi ya Mlezi: .............................. Tarehe: ..............................

Mimi _______________________________ natangaza kuwa nimewaeleza walezi wa mgonjwa juu ya njia utafiti huu utafanywa, madhara na manufaa ya utafiti huu na pia nimewapa wakati wa kuuliza maswali na baadaye kuwapa majibu kwa kadri ya uwezo wangu.

Sahihi ya Mplelezi Mkuu.......................... Tarehe : ..............................
APPENDIX 2: ASSENT FORM

This informed assent form is for children between 7 and 12 years of age.

**Patient’s Study Identification Number:** .................................

**Date:** .............................

**Study Title:** THE PREVALENCE OF ABNORMAL CHEST RADIOGRAPH FINDINGS IN HIV INFECTED CHILDREN

**Investigator:** Dr. John Rodrigues

**Tel Number:** -0722-269254

**Supervisors:**

Dr. Gladys Mwango

Dr. Callen Onyambu

**Investigators Statement:**

We are requesting you to please participate in this research study. This form is to help you to understand why we are doing this research and then decide whether to participate in the study.

You can choose whether or not you want to participate. You can talk to anyone you feel comfortable with about the research such as your parents or your doctor. If you do not wish to take part in the research, you do not have to. You do not have to decide immediately.

If there are any words you do not understand, please ask us as well as any questions as we go along.
**Introduction:**

HIV is a virus that is a type of germ which can make children very sick by weakening the body's ability to fight diseases especially chest infections. When a child has HIV the doctor may ask for a picture of the chest called a chest x-ray to look for any disease in the chest so that the doctor can give the right medicine to make the child feel better.

In this study we are doing we will look at the chest x-rays of children with HIV and see how many of them are not normal. This will help us to learn more about children with HIV and see how we can help them in the future.

I ____(initial) understand that participation is voluntary

**Benefits and Risks**

The results of this research will be used by the doctors to help improve our ability in detecting chest infections in HIV infected children.

During the process of taking the chest x-ray we use radiation, which are waves of high energy that help us to see inside your body. These radiation waves are similar to those you receive from the sun. All radiation can be a little dangerous. The radiation you will get from the chest x-ray is a lot less than what you get from the sun in one year.

There will be no painful tests or procedures done.

I _____ (initial) understand the benefits and risks.

**Voluntariness:**

It is your choice whether or not to take part in this study. You can take time to think about it. Even if you decide not to take part, you will still get the treatment you need.

I __ (initial) understand that participation is voluntary.
**Confidentiality:**

We will not tell anyone else that you are in this study or share the information you give us with anyone other than the people involved in the study. We will use a number to store your information and only the researchers will know that number. Your information will be locked and only the doctors in the study will be able to see it. After finishing the study, we will tell more people such as doctors about what we found. Your name or your family’s details will never be revealed.

**Problems or Questions:**

If you ever have any questions about the study or about the use of the results you can contact the principal researcher, **Dr. John Rodrigues** by calling **0722-269254**.

If you have any further questions on your participation in this research and that you are protected from harm you can contact the **Kenyatta National Hospital/ University of Nairobi – Ethics Research Committee (KNH/ UON - ERC)** by calling **2726300  Ext. 44355**.

I have read this information (or had the information read to me). I have had my questions answered and know that I can ask questions later if I have them.

I agree to take part in the research.

Child’s Signature: ___________________________ Date___________

I _______________________________ declare that I have adequately explained to the above participant, the study procedure, risks, and benefits and given him /her time to ask questions and seek clarification regarding the study. I have answered all the questions raised to the best of my ability.

Investigator’s Signature ___________________________ Date_______________
Appendix 2.1: Aina ya kupata kibali.
Nambari ya Utafiti: ........................

Tarehe: .................................

Swala Kuu la Utafiti:

UHUSIANO KATI YA UGONJWA WA UKIMWI NA PICHA ZA KIFUA (CHEST X-RAY)
AMBAZO SI ZA KAWAIDA KATIKA WATOTO AMBAO WANATIBIWA KWA
HOSPITALI KUU YA KENYATTA.

Mpelelezi Mkuu:  Dkt. John Rodrigues
Nambari ya simu: 0722-269254

Wasaidizi Wakuu:  Dkt. Gladys Mwango

Dkt. Callen Onyambu

TAARIFA YA MPELELEZI MKUU:

KUANZISHWA
Ukimwi ni ugonjwa ambao unashambulia mfumo wa kinga wa mwili. Bila mfumo wa kinga,mwili hauwezi kujijinga kutoka maambukizi hasa maambukizi ya kifua kama
kisamayu na kifua kikuu. Picha ya kifua inasaidia daktari kufanya utambuzi wamaambukizi ya kifua. Lengo la utafiti huu ni kuingilia kiasi cha watoto wenye virusi vya ukimwi ambao wana picha ya kifua ambele sita kawaida.

Katika utafiti huu, daktari wako akiaagiza picha ya kifua, picha hio itapigwa na kutafsiriwa na madaktari wa picha (Radiologists). Kama una picha ya kifua ya hiv karibuni (Chini yamiezi sita iliyo picha) utaombwa kutoa hiyo picha ili madaktari wa picha (Radiologist) waweze kuitafsiri. Ripoti ya picha yako itatolewa kwa mzazi na daktari wako na misaada katika usimamizi wako.

Mimi ………………. (Awali) naelewa kwamba ushiriki ni kwa hiari.

MANUFAA NA MADHARA

Matokeo ya upelelezi huu, yatasaidia madaktari katika kliniki ya CCC na vyumba vya watoto katika hospitali na pia madaktari wa picha kutumbua maambukizi ya kifua kati ya watoto wenye virusi vya ukimwi.

Kipimo cha mionzi kupokea kutoka na picha ya kifua (Chest X-ray) hubeba hatari ndogo kwa binadamu na ni chini ya mionzi kupokea kutoka katika mazingira ya kila siku. Hakutakuwa na utaratibu vamizi ambazo zinaweza kuathiri. Kukataa kushiriki katika utafiti huu ni kuhusika wakati wowote bila madhara yoyote.

Mimi ………………. (Awali) naelewa kwamba ushiriki ni kwa hiari.

HIARI:

Kushiriki kwa utafiti huu ni kwa hiari yako. Wewe una uhuru wa kutamatisha kuhusika wakati wowote bila madhara yoyote.

Mimi ………………. (Awali) naelewa kwamba ushiriki ni kwa hiari.

USIRI:

Habari ambayo tutatupa juu yako, au familia yako itawe kwa siri. Tutatumia nambari ya utafiti ili muweke kuwatambulisha bila kutumia jina lako. Habari tutakayopata kutokana na
huu utafiti itawekwa kwa kompyuta na kuangaliwa tu na mplelezi mkuu na wasaidizi wake kwa kutumia nywila. Hakuna mtu atakayeruhusiwa kupata habari hizo bila ruhusa yako au ya idara ya utafiti ya Kenyatta.

**SHIDA AU MASWALI:**

Ikiwa ungetaka kupata maelezo zaidi juu ya utafiti huu, tafadhali wasiliana na mpelelezi mkuu Dkt John Rodrigues kupitia nambari ya simu 0722-269254 ama Hospitali Kuu ya Kenyatta Idara ya Utafiti kwa nambari ya simu 2726300 ugani wa simu 44355.

Nimekubali kushiriki katika utafiti huu.

Awali ya mtoto .......................... Tarehe ..............................

Mimi ..................................................natangaza kuwa nimemueleza mgonjwa juu ya njia utafiti huu utafanywa, madhara na manufaa ya utafiti huu na pia nimempa wakati wa kuuliza maswali na baadaye kumpa majibu kwa kadri ya uwezo wangu.

Sahihi ya Mplelezi Mkuu...
APPENDIX 3: QUESTIONNAIRE

CHEST X RAY FINDINGS IN HIV EXPOSED/INFECTED CHILDREN

ID:
Age:
Sex:

1. Is the patient symptomatic?
   Yes….   No….

2. Is the patient coughing?
   Yes….   No….
   Duration of cough….

3. Is the cough productive of sputum?
   Yes….   No….

4. Does the patient have chest pain:
   Yes….   No….

5. Is the patient dyspnoeic?
   Yes….   No….

6. Does the patient have any weight loss?
   Yes….   No….

7. Is the patient experiencing night sweats?
   Yes….   No….

8. What is the latest CD 4 count?
   Level:….
Radiological Findings

Normal chest radiograph

Abnormal chest radiograph
1. Is there lymphadenopathy?
   Yes….   No….
2. Are there any pulmonary opacities?
   Yes….   No….
   a. Consolidation
      Yes….   No….
   b. Other infiltrate
      Yes….   No….
3. Are there pleural effusions?
   Yes….   No….
   Right…. Left…. Bilateral….
4. Are there any cavitary lesions?
   Yes….   No….
5. Is there a pneumothorax?
   Yes….   No….
6. Are there any other lesions?
   Yes….   No….
   Specify….