

**RADIOGRAPH PATTERNS OF PULMONARY TUBERCULOSIS IN RELATION  
TO CD4 LEVELS IN HIV-POSITIVE ADULTS AT MOI TEACHING AND  
REFERRAL HOSPITAL**

**BY**

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## Declaration

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## **Dedication**

This research work is dedicated to Florence, Joy, Emmanuel and Nathan, the most special people in my life.

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## Abstract

**Background:** Pulmonary tuberculosis (PTB) is the commonest clinical presentation of tuberculosis. It has been declared a global public health emergency by WHO. It's the commonest opportunistic infection and cause of death in people infected with HIV. Chest radiography is useful in diagnosis and assessing response to therapy. Chest radiograph features in people with PTB and HIV co infection are atypical and are affected by CD4 levels. Some recent literature suggests that some of the features are changing in different geographic locations.

**Objective:** To determine chest radiograph features in relation to CD4 counts in adult patients with smear positive PTB and HIV co infection at MTRH

**Study design:** A cross sectional study

**Setting:** Chest clinic at MTRH, Kenya

**Subjects:** Newly diagnosed smear positive, HIV positive patients aged 16 years and above

**Methods:** 115 patients (using Fischer's formula with finite population adjustment) were studied between October 2011 and November 2012. Data on demographics, clinical presentation, physical examination findings, CD4 counts and chest radiograph findings were collected and analysed using STATA version 12. Descriptive statistics were carried out for continuous variables using mean, median, standard deviation and inter-quartile range. Frequency tables were generated for categorical variables. The chi square test and Fishers' exact test were used to test for any associations. A p-value < 0.05 was considered statistically significant.

**Results:** 55% of those studied were male. The mean age was 36 years. 58% of the patients had CD4 counts below 200cells/mm<sup>3</sup>, 61% of whom were male. The most common radiograph patterns, in order of frequency, were pulmonary infiltrates (60%), cavitations (25.2%), normal (23.5%), interstitial pattern (19.1%), consolidation (13.9%), pleural effusion (13%), scarring (9.6%), miliary pattern (9.6%) and hilar lymphadenopathy (1.7%). Normal radiographs and miliary pattern showed a significant association with CD4 counts below 200cell/mm<sup>3</sup> (p=0.001 and 0.014 respectively). Consolidation, scarring and pleural effusion had a significant association with CD4 counts above 350cells/mm<sup>3</sup> (p=0.001, 0.024 and 0.006 respectively). The other radiograph patterns showed no significant association with CD4 level.

**Conclusion:** Pulmonary infiltrates is the most common radiographic pattern in patients with smear positive PTB/HIV co infection. Normal radiographs and miliary pattern are significantly associated with CD4 counts below 200cells/mm<sup>3</sup>, while consolidation, scarring and pleural effusion have a significant association with CD4 counts above 350cells/mm<sup>3</sup>.

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## Abbreviations

<b>AAFB</b>	Acid Alcohol Fast Bacilli
<b>AIDS</b>	Acquired Immune Deficiency Syndrome
<b>AMPATH</b>	Academic Model Providing Access To Health Care
<b>BCG</b>	Bacillus Calmette Guerin
<b>CD4</b>	Cluster of Differentiation 4
<b>CT SCAN</b>	Computed Tomography Scan
<b>CXR</b>	Chest x-ray
<b>DOT</b>	Directly Observed Therapy
<b>HAART</b>	Highly Active Anti-retroviral Therapy
<b>HIV</b>	Human Immunodeficiency Virus
<b>IREC</b>	Institutional Research and Ethics Committee
<b>MTB</b>	Myocobacterium tuberculosis
<b>MTRH</b>	Moi Teaching and Referral Hospital
<b>PA</b>	Postero-Anterior
<b>PPV</b>	Positive Predictive Value
<b>PTB</b>	Pulmonary tuberculosis
<b>RNA</b>	Ribonucleic acid
<b>SPO2</b>	Oxygen saturation in circulation
<b>SD</b>	Standard Deviation
<b>TB</b>	Tuberculosis
<b>WHO</b>	World Health Organization
<b>ZN</b>	Ziehl-Neelsen

## Definitions

***Pulmonary Tuberculosis***

This refers to a chronic bacterial infection of the lungs caused by *Mycobacterium tuberculosis* species. In this study, pulmonary tuberculosis refers to those patients for whom a sputum ZN staining is positive for the bacilli.

***PTB/HIV Co-infection***

This refers to patients with the dual infection of PTB and HIV

***Chest X-ray features of PTB***

This refers to characteristic findings noted on the plain chest x-ray of patients meeting the inclusion criteria. The Postero-anterior view will be used unless otherwise stated.

***Smear positive PTB***

This refers to the sputum that contains bacilli that retain the Carbol Fuchsin during ZN staining, hence appearing red on microscopy.

***CD 4 counts***

This is the measure of the amount of T helper cells in peripheral blood.

## CHAPTER 1: INTRODUCTION

### 1.1 Background

Human Tuberculosis (TB), a global public health emergency<sup>1</sup>, is a chronic bacterial infection caused by *Mycobacterium tuberculosis*. Other mycobacteria such as *Mycobacterium bovis*, *Mycobacterium africanum* and *Mycobacterium microti* can also cause similar disease<sup>1,2</sup>. In individuals who have compromised immunity, such as in uncontrolled diabetes, human immuno-deficiency virus (HIV) infection and malignancy, normally opportunistic mycobacteria such as *M. Kansasii* and *M. intracellularis* may cause similar infection<sup>2-4</sup>.

Tuberculosis is the commonest complication and cause of death in human immunodeficiency virus (HIV) infected patients. The human immunodeficiency virus (HIV) belongs to the *Lentivirus* genus of the *Retroviridae* family of viruses. It is a single stranded positive sense RNA virus belonging to Group VI of viruses.<sup>5</sup> There are two identified species, HIV-1 and HIV-2. HIV-1 is by far the most common species and of importance epidemiologically. HIV infection, now a pandemic, is a major problem all over the world particularly in Sub-Saharan Africa. Despite having only 10% of the world's population, Sub-Saharan African bore about 22.4 million out of the 33.4 million people living with HIV/AIDS the world over as of 2008. Then, the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated new infections at 2.7 million with Sub-Saharan Africa recording 1.9 million, a staggering 67% of the world figure. AIDS-related deaths worldwide were 2.0 million with 72% (1.4 million) being in Sub-Saharan Africa. It is also estimated that only 14% of adults and children (nearly 3 million people) in need of antiretroviral therapy in the region are receiving such services, a significant improvement from 2%, 5 years earlier.<sup>6</sup>

Kenya mirrors the situation in the rest of Sub-Saharan Africa. HIV prevalence as of 2007 is reported at 7.1%, this means an estimated 1.4 million adults between the ages of 15 and

64 years were living with HIV/AIDS, 51.4% being resident in Nyanza and Rift Valley provinces. The Rift Valley province alone is home to 304,000 HIV-infected adults.<sup>7</sup> The AMPATH program cares for close to 100,000 HIV-infected patients spanning Western Rift Valley and parts of Western province.

HIV infection is a devastating condition characterized by progressive damage of the cells of the immune system leading to immunosuppression and death usually from opportunistic infections and neoplasms. The most common opportunistic infection of HIV is pulmonary TB.<sup>8</sup> Tuberculosis (TB) has been declared a global public health emergency by the World Health Organization (WHO).<sup>1</sup> TB incidence has been rising all over the world, with around 9 million new cases and 2 million deaths estimated to occur each year.<sup>9</sup> In sub-Saharan Africa, due to the low standard of living, famine, and inadequate shelter with attendant overcrowding, the TB scourge has increased.<sup>4</sup> HIV infection has also contributed significantly to the resurgence of TB especially in sub-Saharan Africa.<sup>10-13</sup> Most cases of TB in patients with HIV infection are probably due to reactivation of TB infection often acquired many years before.<sup>14</sup> Pulmonary TB is the most common clinical presentation of TB accounting for 74% of all cases<sup>15-17</sup>.

Radiology remains one of the most important diagnostic modalities of TB infection. In fact, WHO recommendations for diagnosis of PTB include, 'one sputum smear positive for acid fast bacilli (AFB) and radiographic abnormalities consistent with active PTB' for sputum positive PTB and 'symptoms suggestive of PTB and three negative smears for AFB and radiographic abnormalities consistent with active PTB' for sputum-negative PTB.<sup>1</sup> Sputum negativity does not therefore exclude PTB especially when clinical symptoms and radiographic features are in support of the diagnosis. In the follow-up of PTB patients, radiology is also very valuable both in the short-term and on a long-term basis.

## **1.2 Problem Statement**

HIV is a pandemic and is a major health problem the world over with the Sub-Saharan Africa bearing the greatest brunt. In Kenya, it was declared a national disaster by the Government in 1997. Pulmonary TB is recognized as the most common opportunistic infection afflicting the immune-suppressed. It is also the commonest cause of death in this population. As a result, pulmonary TB has been declared a global public health emergency. Chest radiography forms a crucial diagnostic component of PTB as clearly outlined by WHO in its diagnostic criteria. It is affordable and widely available, even in peripheral health facilities. Radiographic features of PTB in patients with HIV have been shown to be atypical, with some recent studies revealing conflicting findings. There is no available data in our local population and yet chest x-rays are done routinely in these groups both as an aid to diagnosis and follow-up.

## **1.3 Justification**

The burden of TB globally is on a steep increase, and WHO has declared it an emergency public health problem. This rise is highest in the Sub-Saharan Africa, Kenya among them. This can be attributed to HIV infection for which PTB is the most common opportunistic infection and cause of death. HIV has been declared a national disaster in Kenya.

WHO recommends the use of chest radiographs alongside sputum staining and culture in the diagnosis of PTB. A prior study concluded that patients with HIV and an abnormal chest radiograph but no clinical features of PTB were found to have infectious PTB<sup>18</sup>. An aggressive diagnostic approach was thus recommended.

The chest x-ray findings consistent with PTB in HIV positive people have been described as atypical. However, other studies suggest that some of the key patterns seem to be changing<sup>29,37</sup>

We do not have published baseline chest radiograph findings in our setting. This study is aimed at filling this gap. It will be very useful in diagnosis of PTB. It will also inform further research to find out whether indeed these patterns are changing, how and why that is the case.

PTB is a communicable and treatable disease. Accurate and timely diagnosis is crucial. Follow-up of patients on treatment is also crucial in this regard. This therefore obviates the need to document our own accurate and current chest x-ray features in the HIV patients.

#### **1.4 Research Questions**

1. What are the chest radiograph patterns in adult patients with smear positive PTB and HIV co-infection at MTRH?
2. What is the relationship between the chest radiograph patterns and the CD 4 levels in adult patients with smear positive PTB and HIV co-infection at MTRH?

#### **1.5 Objectives**

##### **1.5.1 Main Objective**

To determine chest radiograph patterns in relation to CD 4 levels in adult patients with smear positive pulmonary TB and HIV co infection at MTRH.

##### **1.5.2 Specific Objectives**

1. To determine chest radiograph patterns in adult patients with smear positive pulmonary TB and HIV co infection at MTRH
2. To assess the relationship between chest radiograph patterns and level of CD 4 levels in adult patients with smear positive pulmonary TB and HIV co infection at MTRH



## **CHAPTER 2: LITERATURE REVIEW**

### **2.1 Introduction**

This chapter reviews materials and work done by other scholars on the study problem. It has been divided into the following sections: Relationship between TB and HIV, Chest Radiologic features of PTB and HIV positive individuals and the management of PTB.

### **2.2 Relationship between TB and HIV**

Tuberculosis and HIV infections have been shown to act together in a deadly synergy to propel the spread of the two diseases<sup>19</sup>. It is approximated that a third of the world population is infected with TB, most of which is the latent form. However with HIV co-infection, these patients are a hundred times more likely to develop the active form of the disease. This is because of the reduced level of immunity in HIV<sup>19</sup>.

Centers for Disease Control (CDC) approximates that a third of deaths of people with AIDS is directly due to TB, and that a third of new TB cases over the last five years is due to the HIV epidemic<sup>19</sup>. Other studies have also shown that AIDS is the strongest influence on the spread of TB and that TB is the most common opportunistic infection in people with HIV<sup>20</sup>.

In a West African study, a clear relationship was established between TB mortality and HIV.<sup>21</sup> In Zambia, it was found that the probability of survival for the HIV negative and HIV positive at 2 months was 95% vs 89%, at 6 months 95 vs 76%, at 12 months 91 vs 68% and at 24 months 87 vs 48%<sup>22</sup>. This clearly demonstrates that HIV hugely contributes to mortality from TB. In a different study, patients on HAART had a significantly lower mortality rate from TB/ HIV compared to HAART-naïve population.<sup>23</sup>

TB on the other hand also contributes to the progression of HIV. In one study, it was found that TB was associated with an increased risk of developing AIDS (adjusted

relative risk of 1.60, confidence interval 95%, $p=0.02$ )<sup>24</sup>. This study concluded that prolonged immune activation induced by TB leads to prolonged increased HIV replication and consequently accelerated disease progression. Another study in Uganda concluded that active TB accelerates HIV progression but the greatest effect is in early stages of HIV when there is a reserve capacity of host immune response. It further suggested that latent TB in HIV patients need to be treated.<sup>25</sup>

### **2.3 Chest Radiologic features of PTB and HIV positive individuals**

Chest radiograph patterns in PTB patients are probably determined by the presence or absence of TB and HIV co-infection and the level of immunosuppression.<sup>26</sup> Cell mediated immunity is responsible for some of the classic radiological signs like cavitations in the immunocompetent population with PTB and a normal chest radiograph in patients with severe immunosuppression.<sup>27</sup> In a study of PTB in the patients on HAART and those not on HAART, it was concluded that “HIV patients receiving HAART with PTB had a post primary pattern more frequently than those not receiving this treatment.....this is probably because of the restored cell-mediated immunity.....”<sup>26</sup>

In another study, patients with high CD4 counts (>200) were found to have similar radiological features with the HIV negative patients<sup>28</sup>. In patients with low CD4 counts, atypical pattern and disseminated disease was more frequent. Atypical pattern referred to presence of lesions outside the typical sites i.e. upper lobes and/or upper segment of the lower lobe<sup>29</sup>. Typical pattern was seen more frequently in patients with high CD4 counts and the HIV negative patients. It concluded that in high TB prevalent areas, atypical features or PTB with superficial lymph node involvement should be considered an AIDS defining disease.<sup>28</sup>

A very recent study found that cavitation(48 vs 13%) and consolidation (70 vs 42%) was seen more in those with CD4 above 200. Hilar adenopathy was more frequently seen in

patients with CD 4 < 50 compared to CD 4 51-200 (30 vs 16%)<sup>30</sup>. The strength of this study is that there was adequate sub-categorization of the CD 4 counts unlike many previous studies.

In a West African study, it was found that consolidation, apical involvement of lesions and brochopulmonary spread was more frequent in the immunocompetent patients( $P=<0.005$ )<sup>31</sup>. The same study found a significantly high frequency of pleural effusion and intrathoracic adenopathy in the HIV positive population. This study however did not categorise patients in terms of CD4 counts.

In a huge Central African study<sup>32</sup> the high CD4/immunocompetent patients had high frequency of cavitations(78vs33%), and atelectasis(24 vs 12%). Patients with low CD4 counts on the other hand had higher frequencies of adenopathy(26 vs 13%  $p=0.001$ ),pleural effusion(16 vs 6%), miliary TB(9.8 vs 5%), interstitial pattern (12 vs 7%) and consolidation(10 vs 3%). This is by far a more comprehensive and exhaustive study than most. Consolidation, being noted mostly in those with low CD 4 counts disagrees with other studies which suggest that the inverse is true.<sup>30, 33</sup>. However ,another study<sup>34</sup>, finds similar findings as far as consolidation is concerned but differs on the miliary pattern. This study finds miliary TB more prevalent in patients with CD4 > 200 (25 vs 12%). Lung infiltrates is also found to be non specific in this study(39 vs 37.5%). It shall however be noted that these studies deal with different regions and the Central African study had a far much bigger sample size(963 vs 117).

In a pooled analysis of various separate studies<sup>27</sup>, it was in agreement with other studies that adenopathy was more frequent in those with CD4<200(30 vs 7%  $p=<0.01$ ).

Cavitations was a frequent finding in patients with high CD 4 > 200 (20 vs 7%  $p=0.08$ ).However unlike other studies it found pleural effusion to be non specific to any CD4

category. This study concluded that knowledge of the degree of immunosuppression is important in evaluating chest radiograph findings in PTB/HIV population.

Closer home, two Ugandan studies concurred that cavitations and scarring were more prevalent in patients with high CD4 / HIV negative whereas adenopathy and pleural effusion were more frequent in patients with low CD 4 counts<sup>35,36</sup>. Scarring is a relatively uncommon pattern in other studies. This may be partially explained by poor health seeking behaviours in this population.

A recent Nigerian study finds cavitations more prevalent in patients with low CD 4 counts unlike all the other earlier studies. This is probably the most surprising finding so far. This study goes ahead to wonder whether in deed chest radiograph patterns in PTB patients may be changing in the advent of HIV.<sup>37</sup>

A study depicting significant variation in presentation of PTB across high resolution of CD4 strata<sup>38</sup> showed normal chest radiographs to be more frequent in CD4 <50 compared to >500 (21 vs 2%). It also found that the HIV positive and HIV negative groups showed no significant difference in chest radiograph findings of miliary and pleural effusion at CD4 >100, normal chest radiographs and scarring at CD4 >150, adenopathy at CD4 >250 and cavitation at CD 4 >300. The test for trends was  $p = <0.001$ . This study affirms the need to stratify CD4 levels optimally to pick such subtle similarities and differences between strata.<sup>38</sup>

A different study using chest CT scans actually proved that the findings were closely similar to those found in chest radiography<sup>33</sup>. It concluded that HIV positive patients had a lower prevalence of localized parenchymal disease and higher prevalence of disseminated disease at CT. This can easily be explained by the reduced cell mediated immunity in this group.

The usefulness of chest radiography was reaffirmed in a study which concluded that chest radiograph patterns in PTB/HIV was a predictor of the stage of HIV disease progression and thus a useful adjunct to clinical staging. In this study, patients with CD4 >200 had a high frequency of upper zone infiltrates with a 78% PPV. Pleural effusion was found in a wide range of CD 4 counts with a mean of 185. Patients with CD 4 <200 had high frequency of lower and mid zone infiltrates (84% PPV), normal CXR (100% PPV), adenopathy (89% PPV), and interstitial pattern (89% PPV).<sup>39</sup>

Other studies<sup>40-45</sup> simply reaffirmed the earlier known patterns that atypical features were more prevalent in people with low CD 4 counts and a typical pattern in high CD 4 counts.

In a study that sought to find out if there is an objective indicator of HIV-PTB co-infection, it concluded that absence of cavitations in these patients was consistent in those with very low CD4 counts ( $P < 0.001$ )<sup>46</sup>. It boldly concluded that lack of cavitation in PTB patients could be the objective predictor of HIV disease. This may not be entirely accurate considering other recent literature. The Nigerian study<sup>37</sup> described earlier in this section also throws the spanner in the works.

## **2.4 Management of PTB**

### **2.4.1 Diagnosis**

Definitive diagnosis of tuberculosis requires the identification of *M tuberculosis* in a culture of a diagnostic specimen<sup>50, 51</sup>. The most frequent sample used from a patient with a persistent and productive cough is sputum. Because most mycobacteria grow slowly, 3 to 6 weeks may be required for detectable growth on solid media. However, a newer, alternative method in which high-performance liquid chromatography is used to isolate and differentiate cell wall mycolic acids provides confirmation of the disease in 4 to 14 days.<sup>50</sup> Conventionally, 3 sputum samples were also used for culture diagnosis, but the use of 2 specimens, as mentioned earlier for smears, also applies for cultures.<sup>51</sup>

After medications are started, the effectiveness of the therapy is assessed by obtaining sputum samples for smears. Once again, the traditional requirements of 3 sputum smears negative for *M tuberculosis* may be unnecessary when determining if respiratory isolation can be discontinued.<sup>52</sup> A patient is considered to have achieved culture conversion when a culture is negative for the mycobacteria after a succession of cultures have been positive; culture conversion is the most important objective evaluation of response to treatment.<sup>50</sup>

#### **2.4.2 Prevention and Treatment**

The clinical management of TB is complicated by the slow growth of the pathogen, difficulty in its identification, the emergence of multidrug resistant strains, co-infection with HIV, and the need for long-term therapy. Despite the availability of effective drugs and the World Health Organization (WHO) recommendation for the use of a TB vaccine, Bacillus Calmette-Guérin (BCG), in TB endemic regions of the world, the disease incidence remains unabated.

Management entails programs aimed at control and prevention, including vaccination with BCG which is a live-attenuated vaccine derived from *M. bovis* and is used to stimulate protective immunity and prevent dissemination of MTB in an infected host. Other preventive measures include early diagnosis of latent TB using tuberculin skin tests,<sup>53</sup> contact tracing, isolation and DOTs.<sup>54</sup>

Chemotherapy is the mainstay of treatment. They are based on a principle of an initial intensive phase (which rapidly reduce the bacteria population) followed by a combination phase to destroy any remaining bacteria. Initial therapy with four drugs is normally used, and includes Isoniazid, Pyrazinamide, Rifampin and Ethambutol. A continuation phase of 4 months in uncomplicated new cases is preferred. This normally involves use of two drugs, mostly Isoniazid and Rifampicin. If a patient is HIV infected, a continuation phase of 9-12 months is recommended.<sup>55</sup>

### **2.4.3 Prognosis**

Following successful completion of chemotherapy, cure is anticipated in a majority of the patients. There is a small (5%) risk of relapse. Most recurrences occur within 5 months and usually have the same drug susceptibility. In the absence of treatment, a smear-positive TB patient will remain infectious for 2 years; in 1 year, 25% of untreated cases will die. HIV positive patients have higher mortality rates and modestly increased risk of relapse.<sup>55</sup> In patients who comply with the regimen, conventional therapy results in rapid sterilization of sputum, radiographic improvement, and low rates of relapse.

### **2.5 Conclusion**

From the foregoing, it is evident that chest radiography plays a very significant role in management of PTB. It is also obvious that HIV has complicated the diagnosis and management of TB. Chest radiograph features vary depending on the degree of immunosuppression as measured by CD 4 counts. Several studies have demonstrated variance in the chest radiograph patterns, notably cavitation, interstitial disease, miliary and consolidation patterns. Most of the studies done compared the HIV positive and the HIV negative populations without using CD 4 counts as a marker of immunosuppression. This study aims to fill the gap. This study also hopes to reduce confounders as much as practicable and by concentrating on the smear proven PTB patients reduces bias.

## **CHAPTER 3: METHODOLOGY**

### **3.1 Study Site**

The Chest Clinic at MTRH was chosen as the study site because all smear positive PTB patients with HIV co infection from the general wards and AMPATH are referred here, hence a high catchment area.

### **3.2 Study Population**

All newly diagnosed sputum positive, HIV positive adult PTB patients.

### **3.3 Study Design**

This was a cross sectional study.

### **3.4 Sampling and Recruitment**

Consecutive sampling was used. 138 adult patients with smear positive PTB and HIV co infection were assessed for eligibility. 115 of them met the inclusion criteria. Data on demographics, clinical presentation, physical examination and CD 4 count levels were recorded in the questionnaire. PA view chest radiographs were requested for those patients whose radiographs were more than two weeks old. If they were of acceptable quality, they were interpreted by two blinded radiologists with the participation of the principal investigator. In case of dissent, an opinion of a third radiologist, also blinded, was sought. This was taken as the final report. Findings were recorded in the questionnaire. 8 radiographs were of poor quality and 6 were repeated successfully. Confidentiality was ensured.

### **3.5 Eligibility Criteria**

#### **3.5.1 Inclusion Criteria**

- a. Newly diagnosed smear positive PTB patients
- b. HIV infected patients
- c. Aged 16 years and above



- d. Informed written consent given by patient or parent/guardian if below 18 years

### 3.5.2 Exclusion Criteria

- a. Patient on anti-TB treatment for more than four weeks
- b. Evidence of other confounding pulmonary or cardiac lesions
- c. Very sick patients for whom a quality PA chest x-ray is difficult
- d. First trimester pregnancy

### 3.6 Sample Size

This was done using the fisher et al. (1998) formulae equation:

$$n = \frac{Z^2_{(1-\frac{\alpha}{2})} p(1-p)}{D^2}$$

Where:

$n$  = sample size;

$Z$  = the z-value corresponding to 95% confidence (1.96);  $\alpha$  = significance level (5% ie 0.05)

$p$  = 0.39 estimated prevalence

$D$  = precision

In a report by WHO<sup>11</sup>, 39% of the TB patients had both smear positive PTB and HIV.

Using this figure in the above equation

$$n = \frac{1.96^2 \times 0.39 \times 0.61}{0.05^2} = 366$$

Adjusting for the finite population correction

$$= n / (1 + n/N)$$

Where

$n$  = sample size arrived from the 39 percent prevalence and 95% confidence interval

$N$  = 165 - Annual average number of patients recorded at MRTTH with co-infection of HIV/TB

$$= 366 \div (1 + (366/165))$$

**n=115**

### **3.7 Procedures**

The researcher took a relevant history and physical exam to look out for confounding conditions. The researcher requested and with the radiographer on duty, did a PA view chest radiograph in patients meeting the inclusion criteria, the procedure of which is shown in appendix VII. Together with the radiologists the researcher also took part in interpretation of the radiographs. For patients without CD 4 counts, the researcher also ordered and drew blood for this procedure as shown in appendix VI. The procedure for drawing blood is shown in appendix V. Other procedures are shown in the appendices.

### **3.8 Data Management**

#### **3.8.1 Data Collection**

Data was collected between October 2011 and November 2012.

Radiograph findings of TB, such as consolidation, infiltrates, cavitation, lymphadenopathy, pleural effusion, scarring, miliary pattern, pneumothorax and pneumomediastinum, interstitial pattern, hyperinflation and atelectasis were marked in the questionnaire if present in the chest radiograph. Otherwise, it was considered normal. Level of CD 4 counts were also recorded in the questionnaire. This data was then transferred to a computer database; double entry was used to ensure accuracy of the data. All patient details were kept confidential and data will only be available to the investigator and the supervisors via password protection.

#### **3.8.2 Quality Control**

All laboratory tests were done by the MTRH and AMPATH laboratories which have their internal quality controls.

All chest radiographs were interpreted independently by two radiologists, where there was consensus, the findings were documented and if not in agreement, a third radiologist was consulted and the findings adopted.

### **3.8.3 Data analysis and presentation**

Data was analyzed using STATA SE version 12. Continuous variables were summarized as mean and standard deviation if they were established to be normally distributed and as median and inter quartile range (IQR) if they were established to have a skewed (non normal) distribution. The Shapiro-Wilks test for normality and graphical tests for normality were used to assess the normality of the continuous variables. Categorical variables were summarized as frequencies and percentage.

### **3.8.4 Data dissemination**

This thesis will be published in reputable journals, presented in seminars and conferences. A copy will be given to the management of MTRH to help inform protocols for managing PTB and HIV co infections.

## **3.9 Ethical Considerations**

Approval to carry out the study was sought from the Institutional Research and Ethics Committee (IREC). Permission to use hospital records was also sought and granted by the MTRH management. All patients were informed about the purpose of the study and the procedures involved and the possible benefits and harm. Patients were informed that all study related costs would not be charged on them. Informed consent was then obtained. No incentives or inducements were used to convince patients to participate in the study. The patients received medical attention as necessary regardless of their willingness or unwillingness to participate in the study. All patient records were kept confidential by de-identifying the questionnaires and keeping them in locked cabinets. The data base was password protected. Patients were informed of their results and appropriate standard treatment given. Individual patient results were filed as part of their clinical charts to aid in their daily clinical management.

### 3.10 Study recruitment schema

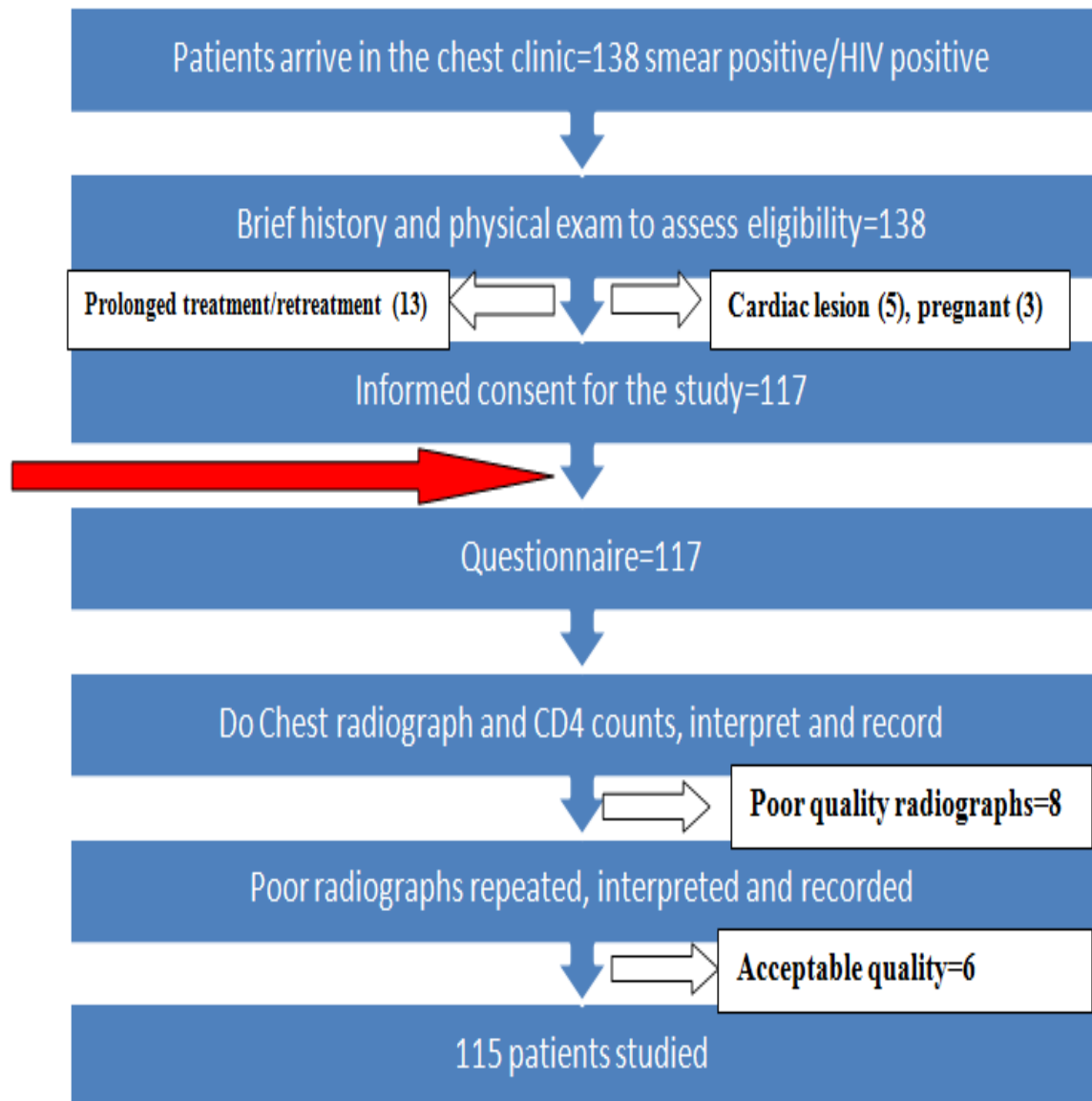


Figure 1: Recruitment schema

## CHAPTER FOUR: RESULTS

### 4.1 Introduction

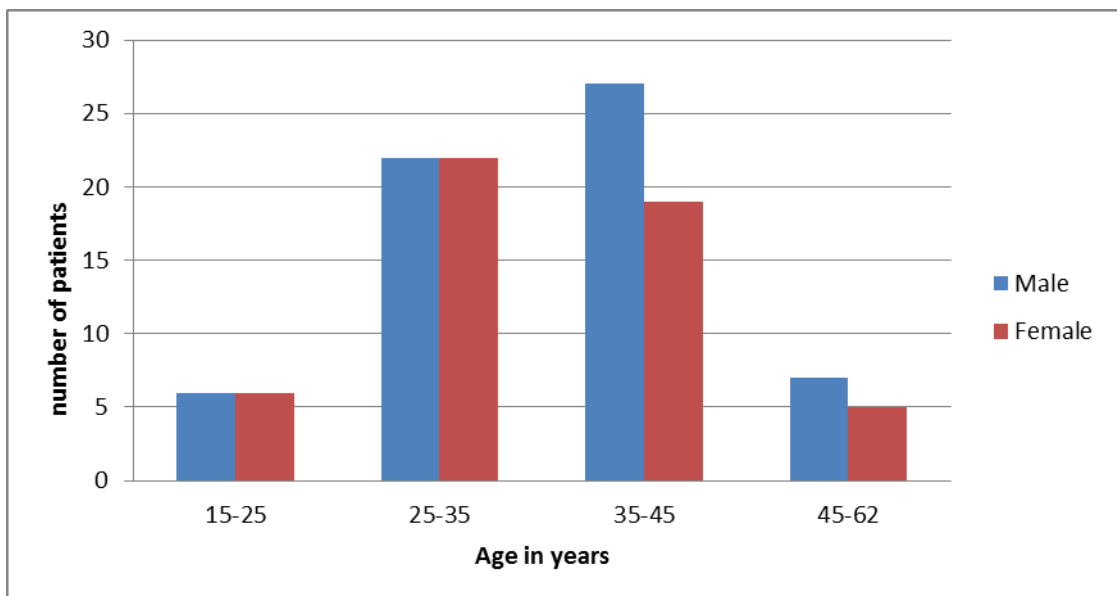
This chapter provides the detailed analysed results of radiologic patterns of chest radiographs among smear positive pulmonary tuberculosis patients co-infected with HIV.

### 4.2 Demographic data of the Participants

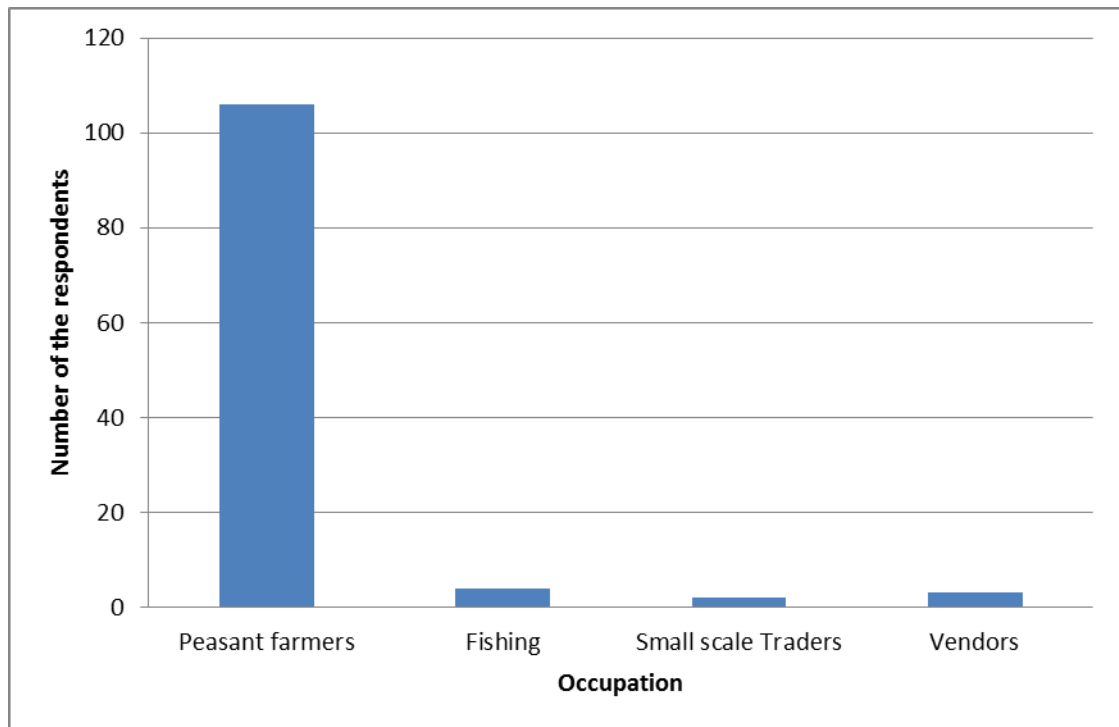
A total of 138 patients with smear positive pulmonary tuberculosis/HIV co infection were reviewed. 115 of them met the inclusion criteria. The median age was 36 years with a range of 17-62 years. The male participants comprised of 55% (63) of the participants with a male: female ratio of 1.2:1. 89% of them were peasant farmers.

This is summarized in Figure 2 and 3.

**Figure 2. Ages of the participants according to gender**



**Figure 3. Occupation of the respondents**



### **4.3 Clinical features of the participants**

The average weight of the participants was 52 kilograms. The overall median CD4 count was 151 with an Inter quartile range (IQR) of 76-283, the median SPO2 was 95 with IQR: 92-96, the median temperature was 36 with an IQR of 35.8-36.6. The median systolic blood pressure was 100 with IQR: 90-110 and the median diastolic blood pressure is 65 with IQR: 60-70. Details are as shown in tables 1.

**Table 1: Clinical characteristics of the participants**

Characteristic	Sample Size	Gender		Overall (n=115)	Test for association
		Male (n=63; 54.8%)	Female (n=52; 45.2%)		
		n(%) or Median (IQR) or Mean (SD)	n(%) or Median (IQR) or Mean (SD)	n(%) or Median (IQR) or Mean (SD)	Chi Square, Fisher's exact, Wilcoxon or T test
<b>Clinical Characteristics</b>					
Weight	115	53 (7.6)	51 (7.8)	52 (7.7)	0.179 <sup>t</sup>
Pulse	115	93 (18.3)	99 (20.1)	95 (19.3)	0.070 <sup>t</sup>
SPO2	115	94 (92-96)	95 (93-96)	95 (92-96)	0.136 <sup>w</sup>
CD4	115	134 (61-249)	200 (88-334)	151 (76-283)	0.040 <sup>w</sup>
Temperature	115	36.0 (35.8-36.6)	36 (35.6-36.7)	36 (35.8-36.6)	0.546 <sup>w</sup>
SBP	115	100 (90-110)	100 (90-110)	100 (90-110)	0.783 <sup>w</sup>
DBP	115	69 (60-70)	60 (60-70)	65 (60-70)	0.684 <sup>w</sup>
Age	115	37 (8.5)	35 (9.1)	36 (8.8)	0.177 <sup>t</sup>

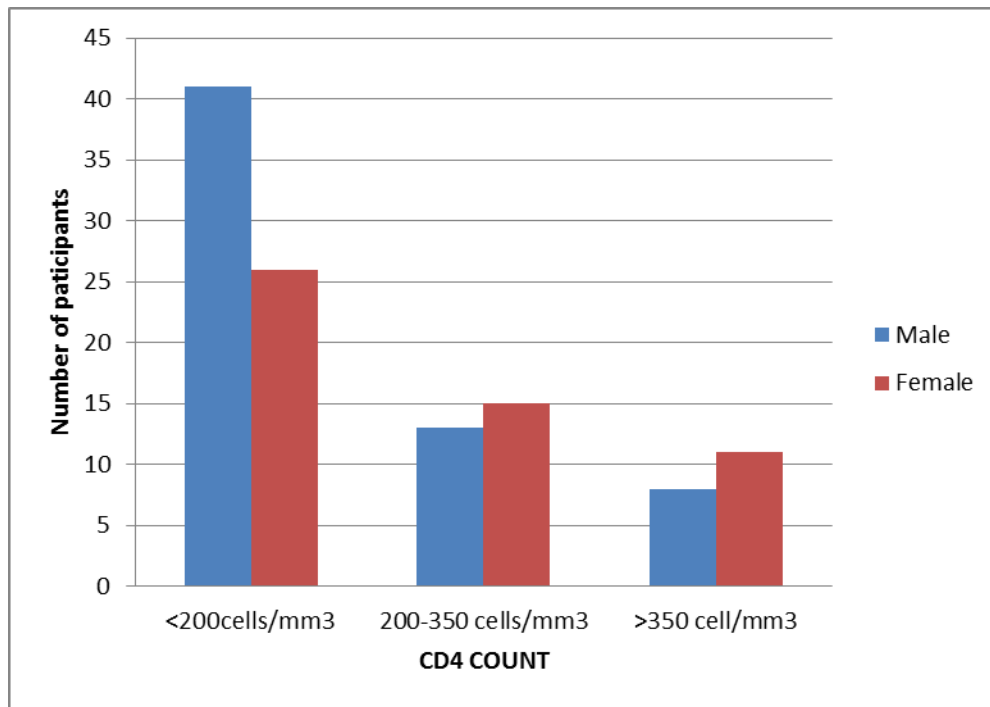
<sup>t</sup> T-test <sup>w</sup> Wilcoxon test <sup>f</sup> Fisher's exact test <sup>c</sup> Chi Square test

#### 4.4 CD4 counts of the participants

The CD4 counts among the participants were categorized as below 200, between 200 and 350 and above 350 cells/mm<sup>3</sup>

##### 4.4.1 CD 4 counts versus gender

The number of males with CD4 count less than 200 was 41 (66.1%) while females were 26 (50%). This is summarized in figure 4.

**Figure 4: CD4 count versus gender**

#### 4.4.2 CD4 Counts versus age of participants

There was no significant difference in CD4 count as per the age of the participants.

However, most participants (59%) had CD4 count less than 200 cells/mm<sup>3</sup>. This is shown in table 2.

**Table 2. CD4 Counts versus age of participants**

Cd4 (cells/mm <sup>3</sup> ) Age (yrs)	<200	200-350	>350	Total
<25	3 (4%)	5 (18%)	4 (21%)	12 (10%)
25-35	25 (37%)	9 (32%)	10 (53%)	44 (38%)
35-45	32 (47%)	10 (36%)	4 (21%)	46 (40%)
>45	8 (12%)	4 (14%)	1 (5%)	46 (13%)
Total	68 (100%)	28 (100%)	19 (100%)	115 (100%)



#### 4.5 Radiographic presentations of the participants.

The chest radiological features of the participants ranged from normal x-rays and abnormal x-rays abnormal patterns such as cavitations, pleural effusion, among others as shown in table 3 and 4.

**Table 3: frequency of radiological patterns**

<b>Radiological pattern</b>	<b>n (%)</b>
Infiltrate	69 (60%)
Cavitations	29 (25.2%)
Normal	27 (23.5%)
Interstitial	22 (19.1%)
Consolidation	16 (13.9%)
Pleural effusion	15 (13.0%)
Scarring	11 (9.5%)
Lymphadenopathy	2 (1.7%)
Pulmonary nodules	9 (7.82%)

**Table 4: Chest Radiological Presentations of Participants by gender**

Characteristic	Sample Size	Sex		Overall (n=115)	Test for association
		Male (n=63; 54.8%)	Female (n=52; 45.2%)		
		n(%)	n(%)	n(%)	Fisher's exact test
<b>Chest Radiographs</b>	115				
Abnormal		50 (79.4)	38 (73.1)	88 (76.5)	0.428
Normal		13 (20.6)	14 (26.9)	27 (23.5)	
<b>Cavitations</b>	115				
None		47 (74.6)	39 (75.0)	86 (74.8)	1.000
Right		11 (17.5)	9 (17.3)	20 (17.4)	
Left		2 (3.2)	2 (3.9)	4 (3.5)	
Bilateral		3 (4.8)	2 (3.9)	5 (4.3)	
<b>Infiltrate</b>	115				
None		26 (41.3)	20 (38.5)	46 (40.0)	0.095
Diffuse		11 (17.5)	4 (7.7)	15 (13.0)	
Left		7 (11.1)	3 (5.8)	10 (8.7)	
Right		13 (20.6)	11 (21.2)	24 (20.9)	
perihilar		6 (9.5)	14 (26.9)	20 (17.4)	
<b>Interstitial pattern</b>	115				
None		50 (79.4)	43 (82.7)	93 (80.9)	0.890
Diffuse		3 (4.8)	2 (3.9)	5 (4.4)	
Left		5 (7.9)	2 (3.9)	7 (6.1)	
Right		3 (4.8)	2 (3.9)	5 (4.4)	
perihilar		2 (3.2)	3 (5.8)	5 (4.4)	
<b>Lymphadenopathy</b>	115				
None		62 (98.4)	51 (98.1)	113 (98.3)	0.702
Left		0	1 (1.9)	1 (0.9)	
Hilar		1 (1.6)	0	1 (0.9)	
<b>Pulmonary nodules</b>	115				
None		54 (85.7)	50 (96.2)	104 (90.4)	0.108
Miliary		9 (14.3)	2 (3.9)	11 (9.6)	
<b>Consolidation</b>	115				
None		52 (82.5)	47 (90.4)	99 (86.1)	0.235
Left		2 (3.2)	0	2 (1.7)	
Right		9 (14.3)	4 (7.7)	13 (11.3)	
Bilateral		0	1 (1.9)	1 (0.9)	
<b>Scarring</b>	115				
None		57 (90.5)	47 (90.4)	104 (86.1)	0.208
Left		2 (3.2)	1 (1.9)	3 (2.6)	
Right		0	3 (5.8)	3 (2.6)	
Bilateral		4 (6.4)	1 (1.9)	5 (4.4)	
<b>Pleural Effusion</b>	115				
None		53 (84.1)	47 (90.4)	100 (87.0)	0.530
Left		3 (4.8)	1 (1.9)	4 (3.5)	
Right		6 (9.5)	4 (7.7)	10 (8.7)	
Bilateral		1(1.6)	0(0)	1(0.9)	

However, there was no significant difference among the gender on the occurrences of the chest radiological features.

#### 4.6 Association between chest radiologic findings and CD4 count

The Kruskal wallis test of similarity in the distribution of CD4 count among the levels of Cavitations, Infiltrate, Interstitial disease, Lymphadenopathy, Pulmonary nodules, Consolidation and Scarring shows that the differences from among the groups of Infiltrate, Pulmonary nodules, pleural effusion and Consolidation were statistically significant at 5% level of significance. This is shown in table 5.

**Table 5: Association of radiographic features and CD4 counts**

Characteristic	CD4 count (cells/mm <sup>3</sup> ); n(%)			Total	Chi Square or Fisher's exact test
	<200	200-350	>350		
<b>Chest Radiographs</b>					
<i>Abnormal</i>	44 (65%)	26 (93%)	18 (95%)	88 (77%)	0.001 <sup>f</sup>
<i>Normal</i>	24 (35%)	2 (7%)	1 (5%)	27 (23%)	
<b>Cavitations</b>					
<i>None</i>	54 (79%)	18 (64%)	14 (74%)	29 (25%)	0.312 <sup>f</sup>
Cavitations	14 (21%)	10 (36%)	5 (26%)	86 (75%)	
<b>Infiltrate</b>					
<i>None</i>	33 (49%)	7 (25%)	6 (32%)	46 (40%)	0.073 <sup>c</sup>
<i>Infiltrate</i>	35 (51%)	21 (75%)	13 (68%)	69 (60%)	
<b>Interstitial disease</b>					
<i>None</i>	56 (82%)	21 (75%)	16 (84%)	93 (81%)	0.714 <sup>f</sup>
Interstitial dse	12 (18%)	7 (25%)	3 (16%)	22 (19%)	
<b>Lymphadenopathy</b>					
<i>None</i>	66 (97%)	28 (100%)	19 (100%)	113 (98%)	0.084 <sup>f</sup>
Lymphadenopathy	2(3%)	0	0	2 (2%)	
<b>Pulmonary nodules</b>					
<i>None</i>	57 (84%)	28 (100%)	19 (100%)	104 (90%)	0.014 <sup>f</sup>
Miliary	11 (16%)	0	0	11 (10%)	
<b>Consolidation</b>					
<i>None</i>	66 (97%)	21 (75%)	12 (63%)	99 (86%)	<0.001 <sup>f</sup>
Consolidation	2 (3%)	7 (25%)	7 (37%)	66 (14%)	
<b>Scarring</b>					
<i>None</i>	68 (100%)	26 (93%)	10 (53%)	104 (90%)	0.0240 <sup>f</sup>
<i>scaring</i>	0	2 (7%)	9(47%)	11 (10%)	
<b>Pleural Effusion</b>					
<i>None</i>	62 (91%)	26 (93%)	12 (63%)	100 (87%)	0.006 <sup>f</sup>
<i>Pleural effusion</i>	6 (9%)	2 (7%)	7 (37%)	15 (13%)	

<sup>f</sup> is the Fisher's exact test      <sup>c</sup> is the Chi Square test

#### 4.7 Sample chest radiographs with CD4 levels

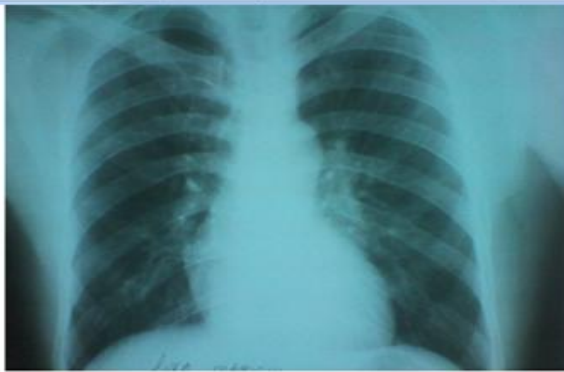


Figure 4: LM, 32 years old, male CD4 count 52 cells/mm<sup>3</sup>: normal radiograph

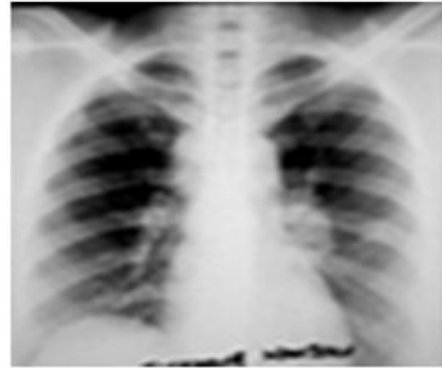


Figure 5: J.W, 35 years, CD4 265 cells/mm<sup>3</sup>.

Left hilar adenopathy



Figure 6: KY, 37 year old male, CD4 137: Miliary TB



Figure 7: KP, 41 year old female, CD4 302 cells/mm<sup>3</sup>:

bilateral pleural effusion



Figure 8: MO, 30 year old: CD4 355 cells/mm<sup>3</sup>:

Right upper lobe cavity



## CHAPTER 5: DISCUSSION

### 5.1 Introduction

This chapter is a discussion of the findings from the study and the study limitations.

### 5.2 Discussion of the findings

#### 5.2.1 Demographics

Majority of patients studied were male, comprising of 55%. This compares with other studies which have shown a male preponderance of PTB/HIV co-infection. An East African study had a 59% male preponderance<sup>29</sup> while a Nigerian study had a 58% male preponderance.<sup>37</sup> This could be attributed to the fact that men are more outgoing hence higher exposure to both HIV and TB. They are also more likely to seek medical attention late as compared to women. They also tend to have poor adherence to preventive measures like DOTS.

Mean age was 36 years with a range of 17-62 years. This compares with a study by Garcia et al where the mean age was 32 years.<sup>40</sup> Another study in East Africa had an age range of 16-45 years which is almost similar to this study.<sup>29</sup> Similarly, in Zambia the age range was 16-56 years with the majority at the 31-40 year age range.<sup>32</sup> This age group is the most active and productive both economically and socially. Majority of the participants were peasant farmers earning low income. This could contribute to the risk factors associated with spread of PTB like overcrowding, poor health seeking behaviour and poor access to proper healthcare because of affordability.<sup>55</sup>

### 5.2.2 Clinical characteristics of the participants

The average weight of the participants was 53 kg for males (SD 7.6) and 51kg for females (SD 7.8). This correlates well with the well documented constitutional symptoms like weight loss.<sup>55</sup> Females had lower average weight probably because they are generally smaller in stature than men. The median SPO2 was 95% and temperature 36°C. This largely excludes other lung pathologies like PCP and other active pneumonias. The median CD4 count for males was 134 cells/mm<sup>3</sup> and females 200 cells/mm<sup>3</sup>. This compares well with other studies which have shown that males generally have lower CD4 level than women.<sup>29,32,37</sup> This could be explained by the fact that men don't easily adhere to preventive measures as mentioned earlier.<sup>55</sup> Overall median CD4 was 151cells/mm<sup>3</sup>(76-283). In Uganda, the median CD4 was lower at 50 cells/mm<sup>3</sup> (14-150)<sup>30</sup> Studies by Asimos and Perlman et al showed 82% and 77% respectively to have CD 4 below 200.<sup>41,27</sup> Another Ugandan study showed 72% to be severely immunosuppressed<sup>35</sup> All these studies suggest that most patients with TB/HIV co-infection present with very low CD4 counts. This could be explained partially by the fact that most of these patients are peasant farmers with low income levels and poor health seeking behaviours. It also shows that immunosuppression is a risk factor for TB.

### 5.2.3 Radiological features of the participants

There was no statistically significant difference between chest radiograph patterns and gender and age of the participants. The most common radiologic finding was lung infiltrates (60%). Most of the infiltrates were in the right lung and the perihilar regions. This is in contrast to a study in Nigeria which found cavitory lesions to be more common<sup>37</sup>. In our study, cavitations contributed 25% of the radiologic findings. This two studies however agree that cavitations are commoner on the right side of the lung<sup>37</sup>. Pleural effusion (13%) and consolidation (14%) also showed right sided predilection. This could be explained by the anatomic nature of the right main bronchi<sup>55</sup>. Lymphadenopathy was noted in two patients only. This is similar to the Nigerian study which found only 3 patients with the same.<sup>37</sup> This supports the known fact that adenopathy is a rare manifestation of adult PTB. This is because most of this TB is post-primary type. Scarring (9%) and interstitial disease (19%) were evenly distributed in the right lung. The presence of scarring, though uncommon, suggested that some patients presented late to the hospital and also that these patients probably had a good immune response to enable healing by fibrosis. All the patients with lung nodules had miliary pattern (9.6%) rather than solitary nodules. 23.5% of the patients had normal chest radiographs. This compares with a Ugandan study which had shown 16% of the patients had normal radiographs.<sup>56</sup> Another study by Lado Lado et al had 33% of the respondents with normal chest radiographs.<sup>48</sup> This therefore shows that the presence of normal chest radiographs should not preclude PTB diagnosis.



#### 5.2.4 Relationship between chest radiograph findings and CD4 counts

Most of the patients with CD 4 count less than 200 cells/mm<sup>3</sup> had normal radiographs compared with those with higher CD 4 counts( $p=0.001$ ). This is in agreement with other studies.<sup>28,40,48,56</sup> In a Ugandan study, normal chest radiographs were noted in very low CD4 counts(mean CD4 13, $p=0.001$ ).<sup>56</sup> This could be due to the inability of the host to mount an immune response to cause lung parenchymal changes. It is noted in this study that the frequency of normal radiographs reduces with increasing CD4 counts. Cavitations didn't show a significant difference between the various CD4 strata. In contrast, other studies show cavitations to be more significant in higher CD4 counts. In two Ugandan studies, cavitations were noted in patients with high CD4 counts and the HIV negative patients ( $p=0.001$ ).<sup>30,35</sup> This was replicated in an Ethiopian study<sup>47</sup>. A Nigerian study however found cavitations to be significantly more in the HIV positive than the HIV negative patients<sup>37</sup>. This study didn't correlate the patterns with the CD4 levels however. Infiltrates didn't show any significant difference among the CD4 strata. This is similar to an Indian study where 39% with infiltrates had CD4 <200 and 37.5% with CD4 >200.<sup>34</sup> Consolidation was significantly more in patients with CD4 more than 350 cells/mm<sup>3</sup>,  $p=0.001$ . This correlates well with a Ugandan study,  $p=0.007$ <sup>30</sup> However a Zambian study found consolidation to be more frequent in low CD 4 counts(10 vs. 3%).<sup>32</sup> In India, this was noted more frequently in those with CD4 lower than 200(30 vs. 12%)<sup>34</sup> Miliary pattern was a significant finding in patients with CD 4 < 200( $p=0.014$ ). This is similar to an Ethiopian study ( $p=<0.05$ )<sup>47</sup> and a Zambian study(9.8 vs. 5%)<sup>32</sup> However, an Indian study found miliary pattern more common in patients with CD 4 > 200(25 vs 10%)<sup>34</sup> Pleural effusion was found to be significantly more frequent in patients with CD4 >350.( $p=0.06$ ). This contrasted with other studies whereby it was more frequent in the HIV positive population compared to the HIV negative patients.<sup>32,35,47</sup> The drawback in these studies was that the radiograph patterns were not correlated with the

CD4 levels. According to Perlman et al and Posta et al, pleural effusion was however found to be non-specific.<sup>27,39</sup> Interstitial pattern showed no significant difference in the various CD4 strata. However in other studies, it was found more in those with lower CD4 counts<sup>32,47</sup>. Posta et al showed that interstitial pattern had a 89% positive predictive value for CD 4<200.<sup>39</sup> Besen et al however found this pattern to be more common in those with HIV than those without(78 vs. 40%).<sup>45</sup> Mediastinal or hilar lymphadenopathy was seen in only two patients with CD4 < 200. This compared well with a Nigerian study where only 3 patients demonstrated this pattern<sup>37</sup> Other studies also show that this pattern is more frequent in those with lower CD4 levels.<sup>27,30,32,34,35</sup> Scarring was a notable finding in patients with higher CD4 levels>350. It tended to increase in frequency as the CD 4 level also increased. This was supported by two Ugandan studies which showed scarring to be commoner in the high CD4 category<sup>35,36</sup>

### **5.3 Study limitation**

Highly selective cohort of patients

## **CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS**

### **6.1 Conclusions**

Infiltrates are the commonest while lymphadenopathy is the least common pattern in patients with smear positive PTB/HIV co-infection.

Normal chest radiographs and miliary pattern are associated with very low CD4 counts

Consolidation, pleural effusion and scarring are associated with high CD 4 counts

### **6.2 Recommendation**

Training of health workers on chest radiograph patterns in the HIV/PTB coinfectd patients should be emphasized

Further studies need to be carried out to find out if geographical location or race have effect on chest radiograph patterns

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## **APPENDICES**

### **APPENDIX I: Consent form**

#### **A. ENGLISH:**

My name is Dr. Daniel K. Kipkemboi. I am a qualified doctor, registered by the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a Masters degree in Radiology and Imaging at Moi University. I would like to recruit you into my research which is to study the chest radiograph findings in patients with sputum positive PTB and HIV.

#### **ABOUT PTB AND HIV**

PTB is a chronic bacterial infection caused usually by *Mycobacterium tuberculosis species*. It is transmitted from an infected person by inhalation of infected droplets. A patient presents with a productive cough, sweating profusely at night, chest pain and occasionally difficulty in breathing. PTB is a leading opportunistic infection in HIV infected patients. It is a treatable disease and complications will be avoided if treatment is started early. Diagnosis consists of sputum staining and culture and chest x-ray. I will take your sputum for staining and test you for HIV, if positive in both and other lung lesion has been excluded, we will do a chest x-ray and CD4 counts. The results will be confidential and will be communicated back to you. Treatment will commence normally and will not be influenced by your participation in this study. You will not be asked to fund any test done in the course of this study. This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

If you need further clarifications please contact IREC using the address below:

The Chairman IREC,

Moi Teaching and Referral Hospital

P.O. Box 3

**Eldoret**

[Tel:33471/2/3](tel:3347123)

My Cell phone number is: 0727 549 883

**YOUR CONSENT:**

**Adults above 18 years of age**

I have been adequately informed that I am being recruited in a study to find out the chest radiograph patterns in patients with PTB and HIV. The investigator has also informed me that my participation in this study is voluntary and will not exclude me from my routine care even if I were to opt out. He has explained to me that this study is useful in the long term care of people with PTB and HIV. He has also informed me that I'll not be required to pay for the tests done for the purpose of this study. He has also assured me that the results of this study will be confidential.

Sign:.....

Name:.....

Date:.....

**YOUR CONSENT:****Patients below 18 years of age**

I have been adequately informed that my son/daughter is being recruited in a study to find out the chest radiograph patterns in patients with PTB and HIV. The investigator has also informed me that his/her participation in this study is voluntary and will not exclude him/her from routine care even if he/she were to opt out. He has explained that this study is useful in the long term care of people with PTB and HIV. He has also informed me that I'll not be required to pay for the tests done for the purpose of this study. He has also assured me that the results of this study will be confidential.

**PATIENT'S PARENT/GUARDIAN**

Sign:.....

Name:.....

Date:.....

***B. KISWAHILI***

Jina langu ni Daktari Kipkemboi K. Daniel. Mimi in daktari alyefuzu nakusajiliwa na boid ya madaktari wa Kenya (Kenya Medical Practitioners and Dentists Board). Mimi ni msomi was shahada ya juu (Masters) ya udaktari (Radiology and Imaging) katika chuo kikuu cha Moi University. Nimekuona leo kwa sababu ninafanya uchunguzi kujua matokeo ya picha ya kifua (x-ray) katika wagonjwa wenye magonjwa ya kifua kikuu (PTB) na ukimwi.

**KUHUSU MAGONJWA YA KIFUA KIKUU NA UKIMWI**

Kifua kikuu ni ugonjwa wa kifua unaosababishwa na viini viitwavyo *Mycobacterium tuberculosis*. Inaenezwa kutoka kupitia hewani. Mgonjwa aliye na kifua kikuu huwa

nakikoozi, hutoa jasho jingi usiku, huwa na uchungu kwa kifua na hushidwa kupumua. Ugonjwa huu huambukikiza sana sana wasio na kinga kamili mwilini kama wale walio na ugonjwa wa ukimwi. Ugonjwa wa kifua una tiba na madhara yake yanaweza zuiliwa ikiwa matibabu yataanzishwa mapema. Kuthibitisha ya kwanba mtu anugua ugonjwa huu, kikoozi hupimwa kutafuta viini vya *Mycobacterium tuberculosis*. Picha ya x-ray ya kifua pia hutumika. Katika uchunguzi huu, tutakupima ili tujue kama una virusi vya HIV kasha tupime kikoozi ili tuthibitisha ikiwa una viin vya *Mycobacterium tuberculosis*. Pia tutapima kiwango cha CD 4 ikiwa virusi vya HIV vitapatikana. Picha ya x-ray ya kifua pia itafanywa. Tutayaweka matokeo yako kwa njia ya kuhesimu haki yako ya kutojulishaa yeyote. Tutakujulisha kuhusu matokeo yako na maana kwa afya yako. Hatutakataa kupa matibabu yafaayo kwa magonjwa yoyote tupatayo tukikuchunguza na yatakayopatikana kwa matokeo yako. Uwe huru kuuliza maswali yoyote. Uchunguzi huu umehidhinishwa na kamati ya kusimamia machunguzi ya wasomi na haki ya wanochunguzwa (Institutional Research and Ethics Committee – IREC) katika chuo kikuu cha Moi University and Hospitali kuu ya Moi Teaching and Referral.

Iwapo unahitaji maelezo zaidi tafadhali wasiliana na IREC kwa kutumia anwani ifuatayo.

Mwenyekiti IREC

Moi Teaching and Referral Hospital

S.L.P. 3

**Eldoret**

Simu: 33471/2/3

Nambari yangu ya simu ya rununu ni: 0727 549 883

**HIDHINI YAKO:****Walio na miaka 18 na zaidi**

Nimeelezwa ipasavyo ya kwamba ninashiriki katika uchunguzi wa usomi utakayo chunguza matokeo ya picha ya kifua (x-ray) katika wagonjwa wenye magonjwa ya kifua kikuu (PTB) na ukimwi. Michunguzi pia amenieleza kuwa sitakosa matibabu yangu ya kawaida iwapo nishiriki katika uchunguzi au nisiposhiriki. Pia nimeelezwa kuwa sitahitajika kulipia chochote kinachohusiana na uchunguzi huu. Nimehakikishiwa kuwa matokeo ya uchunguzi huu ni siri.

Sahihi: .....

Jina: .....

Tarehe:.....

**HIDHINI YAKO:****Walio na miaka chini ya 18**

Nimeelezwa ipasavyo ya kwamba mwana wangu anashiriki katika uchunguzi wa usomi utakayo chunguza matokeo ya picha ya kifua katika wagonjwa wenye magonjwa ya kifua kikuu na ukimwi. Mchunguzi pia amenieleza kuwa yeye hatakosa matibabu yake ya kawaida iwapo atashiriki katika uchunguzi au asiposhiriki. Pia nimeelezwa kuwa sitahitajika kulipia chochote kinachohusiana na uchuguzi huu. Nimehakikishiwa kuwa sitahitajika kulipia chochote kinachohusiana na uchunguzi huu. Nimehakikishiwa kuwa matokeo ya uchunguzi huu ni siri.

**MZAZI AMA MLINZI:**

Sahihi:.....

Jina:.....

Tarehe:.....

**APPENDIX II: Data Collection Form****STUDY NUMBER:** .....**DEMOGRAPHICS**

Date:.....Medical Record Number: .....

Age: ..... Sex: Male  Female **HISTORY****Do you have any of these symptoms?**Chronic productive cough >2weeks Yes  No Drenching night sweats Yes  No Loss of weight Yes  No **Are you known to have any of these illness?**Lung cancer Yes  No Heart disease Yes  No Kidney disease Yes  No Have you been treated for PTB before? Yes  No **Are you a chronic smoker?** Yes  No **If female, LMP:** .....**EXAMINATION****General:**Pallor  Jaundice  Edema Dehydration  Lymphadenopathy 

Weight: .....Kg

Vital signs:

BP: .....mmHg Pulse: ...../min



Temp: .....°C

SPO<sub>2</sub>:.....%

Chest examination:

Normal

Abnormal

Heart examination:

Normal

Abnormal

Abdominal examination:

Normal

Abnormal

Nervous system examination:

Normal

Abnormal

Other findings

.....

.....

.....

.....

.....

.....

.....

.....

**TABLE 2: LABORATORY RESULTS**

TEST	RESULT	DATE
SPUTUM, ZN STAINING		
CD 4 COUNTS		

**CHEST RADIOGRAPH FINDINGS**

Cavitations            None     Right     Left     Bilateral

Infiltrate            None     Right     Left     Perihilar     Diffuse

Interstitial disease    None     Right     Left     Perihilar     Diffuse

Lymphadenopathy    None     Hilar     Right     Left     Bilateral

Pleural effusion      None     Right     Left     Bilateral

Pulmonary nodules    None     Solitary     2-5     more than 5     Miliary

Pneumothorax        None     Right     Left     Bilateral

Consolidation        None     Right     Left     Bilateral

Other findings.....

**APPENDIX III: Procedure for sputum collection and ZN Staining**

The procedure was explained to the patient and verbal consent sought, 3 sputum samples were taken on consecutive mornings. The patient was given a sterile bottle for sample collection and asked to collect the deep sputum rather than saliva. Once the samples reached the laboratory, it was applied to the slide using a loop or applicator. It was then dried and fixed, ready for staining. The numbered slides were placed on a staining rack in batches. We ensured the slides didn't touch. The slide was flooded with filtered Carbol Fuchsin and then heated slowly until steam rose. We ensured we didn't boil. Steaming was maintained for 5 minutes by using low or intermittent heat. Each slide was rinsed individually in a gentle steaming of running water until all free stain was washed away. It was then flooded with decolorizing solution for 3 minutes and rinsed thoroughly with water. It was then flooded with methylene blue for 1-2 minutes. The slide was rinsed thoroughly, and then allowed to dry. We ensured it was not blotted.

Precautions during staining included avoiding under-decolourisation with acid alcohol and avoiding thick smears as this may interfere with proper decolourisation and the counter stain may hide the bacilli. Smears once stained were not re-stained. Acid fast bacilli retained the Carbol Fuchsin and thus appeared red on microscopy.

**APPENDIX IV: Procedure for HIV Testing**

**Determine® HIV-1/2** is a rapid 15-minute test manufactured by Abbott. It is an immunochromatographic test for the qualitative detection of antibodies to HIV-1 and HIV-2. Blood sample is added to the sample pad. As the sample migrates through the conjugate pad, it reconstitutes and mixes with the selenium colloid-antigen conjugate. This mixture continues to migrate through the solid phase to the immobilized recombinant antigens and synthetic peptides at the patient window site. If antibodies to HIV-1 and/or HIV-2 are present in the sample, the antibodies bind to the antigen-selenium colloid and to the

antigen at the patient window, forming a red line at the patient window site. If antibodies to HIV-1 and/or HIV-2 are absent, the antigen-selenium colloid flows past the patient window and no red line are formed at the patient window site. To insure assay validity, a procedural control bar is incorporated in the assay device

**UNIGOLD:** Recombinant proteins representing envelope proteins of HIV-1 and HIV-2, glycoprotein gp41, gp120 (HIV-1) and glycoprotein gp36 (HIV-2) respectively are immobilised at the test region of the nitrocellulose strip. A narrow band of the nitrocellulose membrane is also sensitised as a control region. During testing two drops of serum, plasma or whole blood is applied to the sample port, followed by two drops of wash buffer and allowed to react. Antibodies specific to the recombinant HIV-1 or HIV-2 proteins will react with the colloidal gold linked antigens. The antibody gold complex moves chromatographically along the membrane to the test and control regions of the test device. A positive reaction is visualised by a pink/red band in the test region of the device. A negative reaction occurs in the absence immunoglobulin antibodies to HIV in the specimen. Consequently, no visually detectable band develops in the test region of the device. Excess conjugate forms a second pink/red band in the control region of the device. The appearance of this band indicates proper performance of the reagents in the kit.

**APPENDIX V: Procedure for drawing blood**

The procedure was explained to the patient and verbal consent sought.

Universal precautions were observed.

A tourniquet was applied at the distal site about 5cm proximal to the selected site of venepuncture. The patient makes a fist without pumping the hand. The phlebotomist put on a pair of clean gloves. The selected site was cleaned thoroughly with methylated spirit or povidone iodine starting with the center and working outward. It was then allowed to dry. The patient's arm was grasped firmly using the thumb to keep the skin taut and to anchor the vein. A sterile Vacutainer® system (**Becton, Dickinson and Company, 1**

**Becton Drive, Franklin Lakes, NJ USA 07417**) was opened and the blood collection needle inserted gently into the lumen of the vein at an angle of 15-30°, then the other end is attached to a Vacutainer® blood collection bottle. Blood flows freely into the bottle due to negative pressure.

EDTA-containing bottles were used and the sample sent for CD 4 count. After adequate blood had been collected, the tourniquet was released then the Vacutainer® needle was removed gently and an alcohol impregnated swab was applied at the site under pressure. Pressure was applied for a whole minute then the site was reassessed for continued bleed. The area was dressed with a dry gauze and tape.

#### **APPENDIX VI: Procedure for determining CD4 counts**

Blood for CD4 cell counts were taken to the lab immediately, ideally within 24 hours. Blood samples were stored at room temperature and analyzed within 48 hours of collection.

Vacutainer®bottles were loaded onto a BD FACSCalibur™ flow cytometer (**BD Biosciences, 2350 Qume Drive, San Jose, California, USA, 95131**). This is a flow cytometer that quantities absolute CD4 and %CD4 counts based on the use of monoclonal antibodies against the CD4 molecules. Stained cells pass under a laser beam which generates a light scatter and a fluorescence pattern. The amount and intensity of scattered light is proportional to the characteristics being measured. This is converted to electricity and the machine reports this in counts and scatter plots.

The samples in Vacutainer® bottles were transferred to BD TruCount® tubes and processed. They were then loaded onto the flow cytometer. The system printed out the results on paper. Quality control checks were run daily.

**APPENDIX VII: Procedure for doing a Chest Radiograph**

A posterior-anterior (PA) view was done. Appropriate radiation protection measures were adhered to. Gonad protection using lead apron and adequate lead shields for pregnant women were used. The patient was erect whenever possible. To avoid blur and get better quality images, the radiographs were taken during arrested inspiration with the scapulae moved off the lung fields. Rotation was avoided during positioning. The x-ray beam was centered at the fourth thoracic vertebra. To minimize cardiac magnification, a focus-film distance of 180 cm was used. For a posterior-anterior view, the patient faced the cassette. The elbows were fixed, the backs of the hands placed on the hips and the elbows pushed forwards. The arms were folded over the head and the axilla was placed against the cassette. The elbows were raised; otherwise the soft tissues and the humerus may obscure the lung apices. The film was then developed in the dark room.

