PREVALENCE OF POST-TUBERCULOSIS AIRFLOW OBSTRUCTION 
IN PATIENTS WHO HAVE COMPLETED PULMONARY TUBERCULOSIS 
TREATMENT AT TWO INFECTIOUS DISEASES HOSPITALS IN ZIMBABWE 

BY 

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ABBREVIATIONS

ATS    American thoracic society

ATT    Anti-tuberculosis Treatment

BRIDH Beatrice Road Infectious Diseases Hospital

COPD  Chronic Obstructive Pulmonary Disease

CXR    Chest X ray

ECM    Extra cellular matrix

FEF    Forced Expiratory Flow

FEV₁   Forced Expiratory Volume in one second

FVC    Forced Vital Capacity

GOLD Global Initiative for Chronic Obstructive Lung Disease

JREC Joint Parirenyatwa Hospital and College of Health Sciences Research Ethics Committee

LAM    Lipoarabinomannan

LTBI  Latent Tuberculosis Infection

MMP Matrix Metalloproteinase

ORs  Odds Ratios

PFTs Pulmonary Functions Tests

PTB Pulmonary Tuberculosis
PLATINO Large Population Based Multicenter Study done in Latin America

RS  Radiographic Score

TB  Tuberculosis

TIMP Tissue Inhibitor of Metalloproteinase

WHO World Health Organization
DEFINITION OF TERMS

**Post-tuberculosis** - after completing 6 months of TB treatment.

**Sputum negative PTB**- person who presents with symptoms and/ signs suggestive of pulmonary TB, in particular unexplained productive cough for 2 weeks or more with chest x-ray findings suggestive of TB.

**Chronic Obstructive Pulmonary Disease**- a disease characterized by progressive airflow limitation that is not fully reversible.
ABSTRACT

Tuberculosis (TB) is a major cause of death worldwide. About two thirds of patients develop impaired pulmonary function after completion of pulmonary TB treatment. It seems a high proportion of TB deaths are due to post-TB chronic airflow obstruction but data is lacking to support this assertion.

Research question- What is the prevalence of post-tuberculosis airflow obstruction in patients who have completed pulmonary tuberculosis treatment at Wilkins and Beatrice Road Infectious Diseases Hospital (BRIDH)?

Primary objective-

To determine the prevalence of post-tuberculosis airflow obstruction in patients who have completed pulmonary tuberculosis treatment at Wilkins and BRIDH hospitals.

Secondary objectives-

1  To identify factors that may influence lung function outcomes in post-TB patients.
2  To identify the pattern of spirometry values among post-TB patients.

Design, Setting and Participants

The study was a cross-sectional study at Wilkins and BRIDH hospitals in patients who had completed 6 months of anti-TB treatment.

Sample size- Three hundred and twenty-seven patients.

Methods

Spirometry was done in patients who had completed 6 months of anti-TB treatment. Participants were recruited from Wilkins and BRIDH hospitals after an informed consent. Eligible were adults aged 18-65 years who have completed 6 months of anti-TB treatment. Those with a history of smoking, occupational exposure, asthma, COPD, interstitial lung disease and bronchiectasis were excluded.

Results

The prevalence of post-tuberculosis airflow obstruction was 65.7%. Restriction probable was found in 14.4% and normal spirometry in 19.9% of the participants. Female sex (p=0.020) and recurrent episodes of TB (p=0.026) were associated with development of post-TB airflow obstruction.

Conclusion

There is a high prevalence of post-tuberculosis airflow obstruction, with moderate obstruction according to the GOLD criteria being most prominent. Recurrent episodes of TB and female sex were associated with development of post-TB airflow obstruction.
DEDICATION

WEBIE I THANK YOU
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CHAPTER 1

1.1 INTRODUCTION

Tuberculosis (TB) is one of the oldest diseases known to affect human beings. *Mycobacterium tuberculosis* causes TB. The lungs are usually affected, although in around thirty-three percent (33%) of TB cases infection may occur in other organs.

Tuberculosis is a major cause of death worldwide. More than five million new cases of tuberculosis were reported to the World Health Organization (WHO) in 2005 and more than 90% of cases were reported from developing countries. In 2010 there were an estimated 8.8 million incident cases and 1.45 million deaths from TB worldwide, 1.1 million deaths were HIV infected. An estimated 14 million people worldwide are infected with active tuberculosis.

TB is a disease of poverty mainly affecting young adults in their most productive years. In sub Saharan Africa the poorest people have the highest prevalence of TB and a high proportion of patients report with well advanced pulmonary TB. TB treatment is also commonly delayed by 4 to 8 weeks in studies in Ghana and Senegal because of lack of health care facilities, limited resources and lack of transportation.\(^1\) These factors may allow TB to cause more damage.

About two thirds of patients develop impaired pulmonary function after completing TB treatment and obstructive defect has been found to be the most common\(^2\). It is possible that a high proportion of TB patients develop post-TB airflow obstruction which manifests as Chronic Obstructive Pulmonary Disease (COPD) but data are lacking to support this assertion.

Pulmonary TB can involve the airways, leading to mucosal edema, hypertrophy and hyperplasia of mucous glands, increased mucous hyper secretion and smooth muscle hypertrophy. This affects the caliber of the airways, increases their thickness and decreases airflow. Through the mechanism of cicatricial fibrosis there is also a reduction of total lung capacity.\(^3\)
It is now becoming clear that TB, like tobacco smoke, is also a significant risk factor for COPD. However the impact of pulmonary tuberculosis on the prevalence of COPD has often been neglected.4

1.2 Background information

COPD is a leading cause of morbidity and mortality worldwide. Tobacco smoking is established as a major risk factor, but emerging evidence suggests that other risk factors are important especially in developing countries. These include biomass fuel, occupational exposure to dusts and gases, history of pulmonary tuberculosis, chronic asthma, chronic respiratory tract infections during childhood, outdoor air pollution and poor socioeconomic status.5

Post-tuberculosis airflow obstruction has been described in medical literature as early as 1950s and 1960s by several authors. Martin and Hallett reported that “it is increasingly evident that a diffuse obstructive pulmonary syndrome is often associated with tuberculosis”.6 Chronic airflow obstruction as a complication of pulmonary TB has been re-studied recently in many regions of the globe. In the executive summary of the 2006 update of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines the role of tuberculosis as a cause of chronic airflow obstruction was discussed.7 According to this, chronic bronchitis or bronchiolitis and emphysema can occur as complications of pulmonary tuberculosis.

The current definition of COPD according to the GOLD criteria takes into account history of smoking8. In this study the terminology “airflow obstruction” has been used instead of COPD. The diagnosis of COPD recommended by GOLD is based on the degree of airflow limitation assessed by spirometry.
Table 1. Classification of COPD severity by spirometry using post bronchodilator FEV₁

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>FEV₁/FVC&lt;0.70</th>
<th>FEV₁&lt;80% predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>mild</td>
<td>FEV₁/FVC&lt;0.70</td>
<td>FEV₁≥80% predicted</td>
</tr>
<tr>
<td>Stage II</td>
<td>moderate</td>
<td>FEV₁/FVC&lt;0.70</td>
<td>50%≤FEV₁&lt;80% predicted</td>
</tr>
<tr>
<td>Stage III</td>
<td>severe</td>
<td>FEV₁/FVC&lt;0.70</td>
<td>30%≤FEV₁&lt;50% predicted</td>
</tr>
<tr>
<td>Stage IV</td>
<td>very severe</td>
<td>FEV₁/FVC&lt;0.70</td>
<td>FEV₁&lt;30% predicted or FEV₁&lt;50% predicted plus chronic respiratory failure</td>
</tr>
</tbody>
</table>

Considering the high incidence of tuberculosis, especially in developing countries and the success of therapy, the numbers of living tuberculosis survivors are increasing. Further evaluation of patients after TB is not routinely recommended. Current tuberculosis treatment guidelines suggest that performing a chest radiograph at the completion of therapy may be useful, but is not essential. Additional evaluation after tuberculosis has been cured is currently recommended only for those patients who have suggestions of disease recurrence.

Although Pulmonary Tuberculosis (PTB) has long been known to result in chronic respiratory symptoms and functional impairment, there has not been much research done presumably because of declining incidence of TB in industrialized countries and the success of treatment from the 1960s onwards. Even in developing countries with high TB burdens the focus of TB control programs has been on case identification and treatment completion aimed at interruption of the infectious cycle with little interest in post treatment sequelae.
1.3 Statement of the problem

The incidence of tuberculosis per 100 000 people in Zimbabwe was last reported at 633 in 2010 according to a World Bank report published in 2012\(^\text{12}\). Among African nations Zimbabwe is one of those most heavily affected by tuberculosis. The 2007 Global Tuberculosis Control report from WHO ranks Zimbabwe among 22 countries worldwide with the highest TB burden.

In a nationwide survey in South Africa of 13 826 adults, results suggested that in a TB endemic area the strongest predictor of COPD was history of pulmonary tuberculosis. Furthermore the risk of COPD was more strongly associated with tuberculosis than with tobacco smoking or exposure to smoke from biomass fuel.\(^\text{13}\)

There is paucity of data in Zimbabwe on tuberculosis sequelae and post-TB airflow obstruction. In a TB endemic area such as Zimbabwe, risk factors for pulmonary function impairment after TB treatment need to be identified.
2.1 LITERATURE REVIEW

Pathophysiology of post-TB airflow obstruction

Immunological mechanisms have been postulated as a cause of post-tuberculosis airflow limitation.\textsuperscript{14} TB leads to pulmonary damage by increasing the activity of matrix metalloproteinases (MMP). Matrix metalloproteinases are proteolytic enzymes that have a number of physiological functions including remodeling of the extracellular matrix, facilitating cell migration, cleaving of cytokines and activating defensins. Excess MMP activity may however lead to tissue destruction\textsuperscript{15}.

The development and subsequent disease progression following TB results in characteristic destructive parenchymal lung changes. There is destruction of collagen and elastin which give structural support to the lung.\textsuperscript{15} MMP 9 release is stimulated by the antigenic wall component of \textit{Mycobacterium tuberculosis}, lipoarabinomannan (LAM), and genetic expression of MMP-1 and MMP-9 is upregulated. This leads to collagen breakdown in the extra cellular matrix (ECM). Interleukin-8 and other cytokines are also stimulated which leads to further damage.\textsuperscript{15}

The serum of tuberculosis patients was found to have MMP-9 levels which were three times higher than in controls in a study by Hrabec et al\textsuperscript{16}. Patients with advanced disease were also found to have more elevated levels compared to those with limited disease.\textsuperscript{16} Granulomas of patients with active TB had increased expression of MMP-1 and MMP-7 compared with controls in a study by Elkington et al. The airway epithelial cells adjacent to these granulomas also had increased MMP secretion.\textsuperscript{17} There was also unregulated MMP1 activity because of suppression the specific inhibitor of MMP-1, (tissue inhibitor of metalloproteinase 1 (TIMP-1)), which can lead to destruction of the ECM\textsuperscript{17}. TNF-alpha has also been shown to stimulate MMP secretion.
from granulomas cultured from patients with active tuberculosis and it also plays a role in the formation of tuberculosis granulomas.\textsuperscript{18}

Structural changes in the lung and re-modelling of the pulmonary ECM seen in both TB and COPD is associated with expression of certain MMPs.\textsuperscript{11} After anti-tuberculosis treatment the enhanced levels of Th-1 come down and a proportion of patients develop Th-2 mediated airflow obstruction.\textsuperscript{14}

The histopathological findings from tuberculosis include the formation of caseous granulomas and tissue liquefaction. From these changes residual lesions remain in many patients resulting in pulmonary sequelae that are characterized by impairment in the bronchial and parenchymal structure. The structural changes include broncho-vascular distortions, bronchiectasis, emphysema and fibrosis.

**Association between Tuberculosis and Chronic Obstructive Pulmonary Disease**

Post-tuberculosis pulmonary impairment has emerged as a distinct clinical entity that is almost indistinguishable from other forms. There has recently been increased interest in pulmonary tuberculosis as a cause of chronic airflow obstruction.\textsuperscript{11}

A few clinical studies have been designed to examine the association between PTB and chronic respiratory impairment. However these clinical studies have been relatively small.\textsuperscript{11}

An early retrospective study by Wilcox P A and Ferguson D in 1968 of 71 patients previously treated for PTB found an excess prevalence of obstruction compared to controls. This was associated with greater radiological abnormality at diagnosis and amount of sputum produced at the time of assessment.\textsuperscript{19}
In another study 76 patients with severe active pulmonary TB were prospectively studied over a 6 month period to confirm that treatment improves lung function despite the development of residual fibrosis. Improvement in lung function occurred in 54% of patients, but residual airflow limitation or a restrictive pattern was evident in 28% and 24% of patients respectively. The results of this study demonstrated that although antimicrobial chemotherapy for pulmonary tuberculosis is associated with improved lung function, there is residual impairment in a large proportion of patients.\textsuperscript{20}

South African gold miners were retrospectively studied comparing those who were treated for PTB and those who were not. They had all had Pulmonary Function Tests (PFTs) between January 1995 and August 1996 which were repeated between April and June 2000. There was a mean excess loss of 40.3mls/yr in FEV\textsubscript{1} and 42.7ml/yr in FVC in those who developed TB during the follow up period, after controlling for age, height, baseline lung function, silicosis, years of employment, smoking and other respiratory diagnosis. Later clinical presentation or more severe pulmonary tuberculosis were associated with greater lung function loss.\textsuperscript{21}

In a study by De Valliere S and Barker R. D, 33 patients were treated for an average of 20.6 months for multidrug resistant pulmonary TB, 31 (97%) had abnormal spirometry at completion of treatment. Restriction alone and combined obstructive/restrictive deficits predominated.\textsuperscript{22}

In contrast to these clinical studies, a number of epidemiological studies conducted over the past decade or so, on the association between mainly occupational and environmental risk factors and respiratory disease have included a measure of past TB. The purpose of collecting this information was mainly to control for past TB as a potential confounder rather than interest in TB per se.\textsuperscript{11} These studies however contributed to our understanding between PTB and chronic respiratory outcomes, including symptoms and lung function loss.
Table 2

Association between *tuberculosis* and lung function deficit/COPD in South African studies

<table>
<thead>
<tr>
<th>Study author, year, reference</th>
<th>Type of population (n)</th>
<th>TB definition (sample frequency)</th>
<th>Confounders/ covariates controlled</th>
<th>Outcome</th>
<th>Association/ lung function loss OR(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population Jithoo, 2006</td>
<td>Community study (847)</td>
<td>Past TB (15%)</td>
<td>Smoking, age, sex, education, occupational exposure, BMI, smoky domestic fuel, asthma</td>
<td>COPD (GOLD stages I and II COPD (GOLD stages III and IV)</td>
<td>2.6(1.5-4.6) 8.9(4.2-18.9)</td>
</tr>
<tr>
<td>Occupational Cowie, 1998</td>
<td>Gold miners (cohort 242)</td>
<td>Confirmed TB cases over 4.5 years (22.3%)</td>
<td>Smoking, age, silicosis, mining duration, baseline FEV₁</td>
<td>Average annual FEV₁ loss</td>
<td>29mls per year</td>
</tr>
<tr>
<td>Hnzido et al</td>
<td>Gold miners (27 660)</td>
<td>Recorded TB cases</td>
<td>Age, height, duration since TB, pneumoconiosis, HIV infection</td>
<td>Average FEV₁, FVC excess loss (for 1,2 and 3+ episodes of TB)</td>
<td>FEV₁ 1:153ml 2:326ml 3+:410ml FVC 1:96ml 2:286ml 3+:345ml</td>
</tr>
<tr>
<td>Naidoo et al, 2005</td>
<td>Coal miners Past TB (3.0%)</td>
<td>Smoking, age, height, employment status, dust exposure</td>
<td>Average FEV₁, FVC excess loss</td>
<td>FEV₁ 20.8% of predicted FVC 13.5% of predicted</td>
<td></td>
</tr>
<tr>
<td>Adams 2007</td>
<td>Fish processing workers (643) Past TB treatment (13%)</td>
<td>Smoking, age, sex, atopy</td>
<td>COPD (GOLD Stages II-IV)</td>
<td>4.47 (1.54-13.01) 0.81 (0.44-1.50)</td>
<td></td>
</tr>
<tr>
<td>Baatjies et al., 2009 Baatjies et al., unpublished</td>
<td>Bakery workers (517) Past TB (7%)</td>
<td>Smoking, age, atopy</td>
<td>COPD (GOLD Stages II-IV)</td>
<td>8.2 (1.3-52.0) 2.3(1.0-5.3)</td>
<td></td>
</tr>
</tbody>
</table>
In a large population based multicenter study in Latin America (PLATINO) which was carried out in 5 Latin American cities and included 5,571 subjects aged > 40 years, subjects performed pre and post bronchodilator spirometry. They were asked whether they had been diagnosed with pulmonary tuberculosis by a physician.\(^8\)

The results of this study showed that the overall prevalence of airflow obstruction (Forced Expiratory Volume in one second (FEV\(_1\))/Forced Vital Capacity (FVC) < 0.7) post bronchodilator was 30,7% among those with a history of tuberculosis compared with 13,9% among those without a history of TB\(^8\).

The findings from this study also suggest that the limitation to airflow caused by TB is independent of smoking which is in accordance with previous studies.\(^{30}\)

Jotam G Pasipanodya et al compared pulmonary function in a case control study of patients with tuberculosis who had completed at least 20 weeks of therapy and patients with Latent Tuberculosis Infection (LTBI) in a study done in Texas, United States of America. Pulmonary impairment was present in 59% of tuberculosis subjects and 20% of LTBI control subjects. FVC, FEV\(_1\), FVC/FEV\(_1\) ratio and the mid expiratory phase of forced expiratory flow were significantly lower in the treated pulmonary tuberculosis than in the comparison group. After adjusting for risk, survivors of tuberculosis were 5.4 times more likely to have abnormal pulmonary function tests than were LTBI patients. (p>0.001: 95% confidence interval 2.98-9.68).\(^{31}\)
In a study done in Pakistan which included 47 adults previously treated for pulmonary tuberculosis and presenting subsequently with chronic exertional dyspnea for which no alternate cause was found, pre and post bronchodilator FVC, FEV₁ and FEV₁/FVC were recorded in each case using simple spirometry. Results showed that 55.3% were found to have an obstructive ventilator defect of different degrees. Severe/ stage III in 69.2%, moderate/ stage II in 23.0% and mild/stage I in 5.9%. 29.7% were found to have a restrictive pattern and 14.8% revealed a mixed obstructive and restrictive pattern.²²

SK Verma et al conducted a prospective study in India aimed to find the prevalence of airway obstruction in post-pulmonary tuberculosis patients. 92 patients who had taken a full course of anti-tuberculosis treatment were selected for the study. 36 (39.1%) patients had obstructive airway disease by spirometry criteria of which 7 (7.6%) had reversible phenomena and 29 (31.5%) had irreversible phenomena. 37 (40.2%) had restrictive pathology and a normal spirometry was seen in 9 (9.7%) patients.¹⁴

**Relationship between number of TB episodes and severity of airflow obstruction**

The association between TB and airflow obstruction appears to be dose dependent. Hnzido showed that lung damage is directly associated with the number of episodes of TB among patients suffering from silicosis.²⁵ A total of 27 660 black South African gold miners who had reliable pulmonary function tests from January 1991 to August 1996 were retrospectively followed for the incidence of pulmonary tuberculosis to 1970. The lung function measurements in 1995 to1996 were related to the number of previous episodes of TB. The estimated average chronic deficit in Forced Expiratory Volume in one second FEV₁ after one, two and three or more episodes of TB was 153ml, 326ml and 410ml respectively. The corresponding deficits in Forced Vital Capacity (FVC) were 96ml, 286ml and 345ml. The percentage of subjects with
chronic airflow impairment FEV₁<80 was 18.4% in those with one episode, 27.1% in those with two and 35.2% in those with three or more episodes of tuberculosis.²⁵

Twenty seven patients who had completed TB treatment within 6 months (group I) and those who had taken longer duration of treatment because of failure of initial treatment due to multidrug resistant TB (group II) were evaluated by D Naso et al by spirometry. Group II, of multidrug resistant TB had severe combined respiratory disorder as the most prevalent disorder.³

**Synergy of TB and other COPD risk factors**

There is a deleterious and synergistic interaction between TB and other COPD risk factors. These include smoking, exposure to biomass fuel, occupational exposure to dusts and gases, chronic asthma, chronic respiratory tract infections during childhood, outdoor air pollution and poor socioeconomic status.⁴

In the past few years systematic reviews and meta-analysis have synthesized a large body of evidence on Tobacco and TB which showed that smokers are more likely to develop TB than non-smokers⁴.

Tobacco smoke remains the main risk factor for COPD.³³ Other risk factors including occupational, household and environmental exposures have been also shown to play an important role.³⁴,³⁵ Chronic respiratory tract infections particularly in childhood have been regarded as a risk factor for COPD³⁶. HIV infection is also increasingly being recognized as a cause of premature emphysema.³⁷

About 3 billion people worldwide use solid fuels for cooking.³⁸ Case control studies have implicated indoor biomass fuel burning to be a risk factor for COPD, odds ratios (OR) ranging from 1.35 to 6.61.³⁹ In developing countries females are particularly at risk of developing chronic airflow obstruction from biomass exposure.
Lung function tests in post-TB airflow obstruction

Post-TB impairment can manifest as reversible or irreversible obstructive airflow obstruction, mixed defects or as pure restrictive defects. Lee and Chang compared lung function in patients with chronic airflow limitation due to tuberculosis destroyed lung and COPD patients and concluded that Forced Vital capacity (FVC) and post bronchodilator forced expiratory volume in 1 second (FEV₁) of post tuberculosis patients were lower compared with those of COPD patients.⁴⁰

A similar case control study by Pasipanodya et al comparing pulmonary function in pulmonary tuberculosis patients and latent tuberculosis patients found that FVC, FEV₁, FEV₁/FVC ratio and mid Forced Expiratory Flow (FEF 25-75) were significantly lower in treated pulmonary tuberculosis patients than in the comparison group.³¹

PLATINO study found that FEV₁ is reduced compared to FVC in most cases⁸. However another previous study by Vargha G had found after 15 years of follow up of 40 patients that there was a higher yearly decline in FVC compared to FEV₁.⁴¹

Correlation between post tuberculosis airflow obstruction and chest x-ray abnormalities

Increased lung function loss with advanced radiological disease was established in early literature.⁶ The association of lung function loss with radiological change was confirmed by Ross et al²¹ in a study done in South African gold miners where patients with greater radiological infiltrations at diagnosis were found to be associated with development of greater residual lung impairment and lung function loss.

Studies from India indicate that healed TB with or without significant chest x-ray abnormality (up to 48% of healed TB) have COPD based on spirometry criteria. The longer the duration post completion of anti-tuberculosis treatment (ATT) the greater is the chance of developing
spirometry positive COPD. Relative risk of 20% 5 years post anti-TB treatment increases to 41% at 10 years post anti-tuberculosis treatment (ATT).\textsuperscript{42}

In a study in Korea by Kim SJ, Suk MH et al, even minimal scar change on chest radiograph without destroyed lung was associated with chronic airflow limitation.\textsuperscript{43} This was true in all subjects regardless of previous treatment history for pulmonary TB. The prevalence of COPD increased from 3.7\% to 5.0\% by including participants with radiographically minimal previous TB lesions or past history of TB treatment.\textsuperscript{43}

A study done in northern Taiwan reviewed chest radiographs according to extent of infiltration using radiographic scores before and after anti-tuberculosis treatment. Each lung was divided into 3 areas and each area rated on a scale of 0 to 3 for extent of infiltration. The risk of pulmonary function deterioration was greater in patients with extensive disease before treatment and less radiographic improvement after treatment.\textsuperscript{44}

In a study done in the Johannesburg area of Gauteng South Africa the most significant factor influencing post-TB treatment lung function status as measured by FEV1 (% predicted), was the pretreatment and post treatment radiographic score, which act as a marker of the extent of pulmonary parenchymal involvement in tuberculosis.\textsuperscript{20}

A scoring system for the radiographs previously reported by Snider\textsuperscript{45} was used for the initial and final assessment. Each lung was divided into thirds and each third was rated on a four point scale of 0 to 3 for the extent of infiltration giving a maximum radiographic score of 18.

*Table 2. Radiographic scoring system of lung infiltration for pulmonary TB\textsuperscript{20}*

<table>
<thead>
<tr>
<th>Score</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No infiltrate</td>
</tr>
<tr>
<td>1</td>
<td>1/3 or less of the zone</td>
</tr>
<tr>
<td>2</td>
<td>Infiltrate involving more than 1/3 but less than 2/3 of the zone</td>
</tr>
<tr>
<td>3</td>
<td>Infiltrate involving more than 2/3 of the zone</td>
</tr>
</tbody>
</table>
Yasuda J et al investigated pulmonary hemodynamics and chest x-ray findings to explore significance of obstructive ventilatory impairment in patients with pulmonary tuberculosis sequelae. They described every case with 5 items of chest x-ray findings and the extent of each finding they had defined. The findings were emphysematous change, fibrosis, bronchiectasis and/cavity, atelectasis and pleural thickening. Emphysematous change on chest x-ray was more likely to have airway obstruction than any other finding.46

In a study done in Saudi Arabia chest x-rays were divided into mild, moderate or severe with regards to residual changes and compared with previous chest x-rays. A significantly higher rate of abnormal spirometry was observed in patients with advanced lung damage on chest radiography (advanced 38.5% vs mild 10%).47

2.2 Justification for the study

The above findings call attention to the fact that treatment of a patient with pulmonary tuberculosis must not be restricted to bacteriological healing of the disease.

Recognizing the residual breathing dysfunction and assessing its severity would rationalize its management and could minimize the frequency of unnecessary treatment given to patients on the presumption of active or reactivated TB.32

This study will determine the burden of post-tuberculosis airflow impairment and identify risk factors for pulmonary function deterioration after completion of pulmonary TB treatment. This will be important for prognostics, management and prediction scores for those who may be at risk. This study may also serve as a baseline for future studies on the management of post-TB airflow obstruction.
2.3 Research question

What is the prevalence of post-tuberculosis airflow obstruction in patients who have completed pulmonary tuberculosis treatment at Wilkins and BRIDH Hospitals?

2.4 STUDY OBJECTIVES

2.4.1 Primary objective

1. To determine the prevalence of post-tuberculosis airflow obstruction in patients who have completed TB treatment at Wilkins and BRIDH Hospitals.

2.4.2 Secondary objectives

1. To identify factors that may influence lung function outcome in post TB patients.

2. To identify the pattern of spirometry values among post TB patients.
CHAPTER 3

3 RESEARCH METHODOLOGY

3.1 Study design

The study was a cross-sectional study at Wilkins and Beatrice Road Infectious Diseases hospitals.

3.2 Study setting

Wilkins and BRIDH Hospitals

3.3 Study participants

These were out-patients who had completed 6 months of TB treatment at Wilkins or BRIDH Hospitals, both sputum positive and sputum negative cases. No TB culture was done for sputum negative patients but some had positive gene Xpert results. These patients were only considered as having completed TB treatment if they were now sputum negative for those who were initially sputum positive or if they had clinical and radiological improvement for those who were sputum negative. They had chest x-rays before and after TB treatment.

3.4 Inclusion criteria

• Adults aged 18-65 years

• History of PTB -sputum positive or a sputum negative patient with symptoms, signs and radiological findings suggestive of pulmonary TB.

• Completed 6 months of anti-tuberculosis treatment.
3.5 **Exclusion criteria**

- History of current or previous smoking
- History of occupational exposure to dust or chemicals
- Diagnosed cases of asthma or COPD, interstitial lung disease, bronchiectasis
- Co-morbid illnesses such as ischaemic heart disease, heart failure, severe anaemia
- Spirometry contraindicated such as recent eye or upper abdominal surgery.

3.6 **Sample size calculation**

Sample size was calculated assuming a prevalence of airflow obstruction of 30.7% in patients who would have completed TB treatment, at 95% confidence interval and a degree of precision of 5% using Dobson’s formula. A minimum sample size of

\[ n = \frac{Z^2 \cdot p(1-p)}{d^2} \]

\[ = \frac{1.96^2 \times 0.307 \times 0.693}{0.05^2} \]

\[ = 327 \]

The minimum sample size calculated was 327 patients.

3.7 **Sampling methods**

Participants were selected from Wilkins and BRIDH Hospitals. The 1st eligible and consented patients and each subsequent, eligible and consented patient attending the clinic were recruited until the desired number was achieved.
3.8 Study procedures

- Recruitment was done between 24 January 2014 and 6 June 2014.
- Patients meeting the criteria were interviewed after completing the consent forms and data recorded in pre-designed forms.
- Spirometry was done without any premedication such as short acting bronchodilator.
- A portable battery operated spirometer (Easy-One NDD Medical technologies) was used. There was no need for calibration.
- The technique was first explained to the patients and actual measurements were done after they became familiar with the correct technique. Patients were asked to blow out for 6 seconds which is according to the American Thoracic Society (ATS) criteria.
- A minimum of three attempts were recorded and only considered if the variation between two best readings was <5%. If not the attempts were repeated till the variation between the two best readings was <5%. The spirometer automatically calculated the variations and indicated if there was need for a next attempt.
- Spirometric values were recorded as FVC, FEV₁ and FEV₁/FVC.
- Patients’ chest x-rays before starting TB treatment and after completing TB treatment were compared by the principal investigator only because of financial constraints. No validated radiological scoring system was used to compare the chest x-rays because different radiological presentations which have no validated scoring system were compared, rather than the extent of infiltration.
3.9 **Study outcomes**

3.9.1 **Primary outcomes**

- Prevalence of post-TB airflow obstruction

3.9.2 **Secondary outcomes**

- Pattern of spirometry values among post TB patients
- Factors that influence lung function outcome in post-TB patients

3.10 **Data management and analysis**

Data was entered in Microsoft excel then exported to stata version 13 for cleaning and analysis. Frequencies and percentages were generated for categorical data. For continuous data the means and standard deviations or median and inter quartile ranges were also reported. The t-test was used to compare continuous data by looking at 2 categories. Chi square test was used to test for association between categorical variables. Logistic regression was done to assess factors associated with post-TB airflow obstruction.
3.11 Ethical considerations

- A written informed consent was obtained from each patient before recruitment into the study (see appendix II).

- There were no risks for participants.

- The names of participants did not appear on any form or result sheet. Instead participants were given a study number which was used as a means of identification.

- The results were provided to the patient and the attending doctors at Wilkins or BRIDH hospital.

- Permission to carry out the study was approved by City Health Ethics Committee and Joint Parirenyatwa Hospital and College of Health Sciences Research Ethics Committee (JREC).
CHAPTER 4

RESULTS

A total of 472 TB patients were interviewed, 97 were excluded because of a history of smoking, 33 were excluded because of a history of asthma or occupational exposure and 15 declined to participate. A total of 327 patients were recruited from Wilkins and BRIDH hospital and the targeted number of patients was 327. The majority of the patients 55.4% were male. Males were significantly older (mean age=39.0 years, sd=10.7 years) than their female counterparts (mean age=35.6 years, sd=9.8 years), p=0.003. The patients were generally lean with a mean BMI of 21.7 (sd 4.1). Most of them were from high density areas (81%)

Table 4: Demographic Characteristics of study participants

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>Frequency, n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>146(44.7)</td>
</tr>
<tr>
<td>Male</td>
<td>181(55.4)</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
</tr>
<tr>
<td>High density</td>
<td>265(81.0)</td>
</tr>
<tr>
<td>Low density</td>
<td>62(19.0)</td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
</tr>
<tr>
<td>18-35</td>
<td>143(43.7)</td>
</tr>
<tr>
<td>36-50</td>
<td>145(44.3)</td>
</tr>
<tr>
<td>51-65</td>
<td>39(11.9)</td>
</tr>
<tr>
<td>Weight, mean(sd)kg</td>
<td>61.1(11.8)</td>
</tr>
<tr>
<td>Height, mean(sd)m</td>
<td>1.68(0.09)</td>
</tr>
<tr>
<td>BMI, mean(sd)</td>
<td>21.7(4.1)</td>
</tr>
</tbody>
</table>
### Table 5.

Clinical characteristics of the study participants

*n=327*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV status</td>
<td></td>
</tr>
<tr>
<td>Negative %</td>
<td>82(25,1)</td>
</tr>
<tr>
<td>Positive %</td>
<td>245(74,9)</td>
</tr>
<tr>
<td>CD4 count</td>
<td></td>
</tr>
<tr>
<td>&lt;200</td>
<td>45(18.4)</td>
</tr>
<tr>
<td>&gt;200</td>
<td>34(13.9)</td>
</tr>
<tr>
<td>Unknown</td>
<td>166(67.8)</td>
</tr>
<tr>
<td>Sputum status</td>
<td></td>
</tr>
<tr>
<td>Sputum positive %</td>
<td>91(27.8)</td>
</tr>
<tr>
<td>Sputum negative %</td>
<td>236(72.2)</td>
</tr>
<tr>
<td>Number of TB episodes</td>
<td></td>
</tr>
<tr>
<td>1 episode %</td>
<td>263(80.4)</td>
</tr>
<tr>
<td>&gt;1 episodes %</td>
<td>64(19.6)</td>
</tr>
<tr>
<td>FVC% median (IQR)</td>
<td>89(Q₁=67, Q₃=113)</td>
</tr>
<tr>
<td>FEV₁% median (IQR)</td>
<td>58(Q₁=42, Q₃=81)</td>
</tr>
</tbody>
</table>

Most patients were HIV positive (74.9%) but the majority of them did not know their CD4 count (67.8%). 27.8% of patients were sputum positive and the rest were sputum negative. 19.6% of patients had more than 1 episode of TB.
There was a greater reduction in FEV\(_1\) %predicted (median 58, interquartile range Q\(_1\)=42 Q\(_3\)=81) than FVC% predicted (median 89 Q\(_1\)=67 Q\(_3\)=113).

The prevalence of post-TB airflow obstruction was 65.7%, with 14.4% of patients having restriction probable and 19.9% normal spirometry. There was no way to capture mixed picture from the spirometry results.

**Figure 1: Distribution of patients according to pattern of spirometry results**
Regarding the patients who had obstructive defect on spirometry, moderate obstruction (39%) was the most common stage of COPD severity according to the GOLD criteria. 27% had severe obstruction, 21% had very severe obstruction and 13% had mild obstruction.
Table 6: Association between patients’ characteristics and post-TB airflow obstruction

<table>
<thead>
<tr>
<th>characteristic</th>
<th>Spirometry results n (%)</th>
<th>Chi² p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>normal</td>
<td>Obstruction</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>46(25.4)</td>
<td>110(60.8)</td>
</tr>
<tr>
<td>Female</td>
<td>19(13.0)</td>
<td>105(72.0)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-35</td>
<td>30(21.0)</td>
<td>93(65.0)</td>
</tr>
<tr>
<td>36-50</td>
<td>29(20.0)</td>
<td>95(65.5)</td>
</tr>
<tr>
<td>51-65</td>
<td>6(15.4)</td>
<td>27(69.2)</td>
</tr>
<tr>
<td>Residential area</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High density</td>
<td>52(19.6)</td>
<td>176(66.4)</td>
</tr>
<tr>
<td>Low density</td>
<td>13(21.7)</td>
<td>39(62.2)</td>
</tr>
<tr>
<td>HIV status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>14(17.1)</td>
<td>59(72.0)</td>
</tr>
<tr>
<td>Positive</td>
<td>51(20.8)</td>
<td>156(63.7)</td>
</tr>
<tr>
<td>Sputum status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>49(20.8)</td>
<td>150(63.6)</td>
</tr>
<tr>
<td>Positive</td>
<td>16(17.6)</td>
<td>65(71.4)</td>
</tr>
<tr>
<td>number of TB episodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>one</td>
<td>60(22.8)</td>
<td>167(63.5)</td>
</tr>
<tr>
<td>&gt;one</td>
<td>5(7.8)</td>
<td>48(75.0)</td>
</tr>
</tbody>
</table>
Female sex (p=0.020) and recurrent TB episodes (p=0.026) were associated with development of post TB-airflow obstruction.

**Table 7: Association between chest x-ray abnormalities and post-TB airflow obstruction**

n=327

<table>
<thead>
<tr>
<th>Spirometry result</th>
<th>Chest x-ray findings</th>
<th>Cavities</th>
<th>consolidation</th>
<th>Pleural effusion</th>
<th>Miliary mottling</th>
<th>Reticulonodular infiltrates</th>
<th>No CXR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal spirometry</td>
<td></td>
<td>6(27.3)</td>
<td>18(27.3)</td>
<td>11(19.6)</td>
<td>6(40.0)</td>
<td>12(15.0)</td>
<td>12(13.6)</td>
</tr>
<tr>
<td>Obstruction</td>
<td></td>
<td>12(54.6)</td>
<td>41(62.1)</td>
<td>35(62.5)</td>
<td>8(53.3)</td>
<td>58(72.5)</td>
<td>61(69.3)</td>
</tr>
<tr>
<td>Restriction probable</td>
<td></td>
<td>4(18.2)</td>
<td>7(10.6)</td>
<td>10(17.9)</td>
<td>1(6.7)</td>
<td>10(12.5)</td>
<td>15(17.05)</td>
</tr>
</tbody>
</table>

There was no association between chest x-ray findings and post-TB airflow obstruction (p=0.254.)
Table 8: Univariate and multivariate analysis of factors associated with post TB airflow obstruction

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Univariate logistic regression</th>
<th>Multivariate logistic regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Obstruction on spirometry</td>
<td>OR(95% CI)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>110</td>
<td>71</td>
</tr>
<tr>
<td>Female</td>
<td>105</td>
<td>41</td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-35</td>
<td>93</td>
<td>50</td>
</tr>
<tr>
<td>36-50</td>
<td>95</td>
<td>50</td>
</tr>
<tr>
<td>51+</td>
<td>27</td>
<td>12</td>
</tr>
<tr>
<td>HIV status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>59</td>
<td>23</td>
</tr>
<tr>
<td>Positive</td>
<td>156</td>
<td>89</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low density</td>
<td>39</td>
<td>23</td>
</tr>
<tr>
<td>High density</td>
<td>176</td>
<td>89</td>
</tr>
<tr>
<td>CD4 count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;200</td>
<td>21</td>
<td>24</td>
</tr>
<tr>
<td>≥200</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>Sputum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>150</td>
<td>86</td>
</tr>
<tr>
<td>Positive</td>
<td>65</td>
<td>26</td>
</tr>
<tr>
<td>No. of TB episodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One</td>
<td>167</td>
<td>96</td>
</tr>
<tr>
<td>One +</td>
<td>48</td>
<td>16</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No chest x-ray</td>
<td>61</td>
<td>27</td>
</tr>
<tr>
<td>Cavitations</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Consolidation</td>
<td>41</td>
<td>25</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>35</td>
<td>21</td>
</tr>
<tr>
<td>Miliary mottling</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Reticulonodular infiltrates</td>
<td>58</td>
<td>22</td>
</tr>
</tbody>
</table>
On univariate logistic regression female sex (OR 1.65; 95% CI 1.03-2.64, p=0.035) and CD4 count≥200 (OR 2.74; 95% CI 1.07-7.07, p=0.036) were associated with post-TB airflow obstruction. On multivariate logistic regression only female gender (OR 1.78; 95% CI 1.10-2.88, p=0.019) was associated with post-TB airflow obstruction. HIV negative patients (OR 0.68; 95%CI 0.40-1.18, p=0.173), sputum positive patients (OR1.43; 95%CI 0.85-2.43, p=1.180) and recurrent TB episodes (OR 1.72; 95%CI 0.93-3.20, p=0.084) were more likely to develop post-TB airflow obstruction but the difference did not reach statistical significance on logistic regression.
CHAPTER 5

DISCUSSION

5.1 Prevalence of post TB COPD

The results of this study showed that the prevalence of post-tuberculosis airflow obstruction was 65.7% which is in accordance with previous studies. Reports from previous studies have shown prevalences ranging from 30.7-93.1%. 8,14,48,31,49,19,50 Although most of the previous studies included occupational cohorts22,21,23,24 which had high prevalences of lung disease or were population based8,51 the results from this study which was clinically based have found comparable results.

The distribution of patients according to severity of airflow obstruction showed 13% had mild obstruction, 39% had moderate obstruction, 27% had severe obstruction and 21% had very severe obstruction. An earlier study done in Pakistan by Baig et al showed majority of patients 69.2% had severe obstruction, 23% moderate obstruction and 5.9% mild obstruction32. The difference in the severity might be accounted for by the fact that in the earlier study, they studied a predominantly symptomatic population, presenting with chronic exertional dyspnea for which no alternate cause was found while patients from this study were asymptomatic.

In a study by Hnzido the loss of lung function was found to be highest within six months of the diagnosis of tuberculosis and stabilized after twelve months when the lung function loss was considered chronic25.

This study having been conducted in urban infectious diseases hospitals, is likely to show a lower prevalence than in the rural areas where patients are more likely to present with more advanced disease because of lower socioeconomic status, which includes poor transportation facilities, malnutrition and exposure to biomass fuel.
5.2 Pattern of spirometry values among post-TB patients

Spirometry results showed 65.7% obstructive defect, 14.4% restriction probable and 19.9% normal spirometry. An earlier study by S. K Verma showed 39% obstructive defect, 40% restrictive defect and 9.7% normal spirometry.\textsuperscript{14} However this previous study had a small sample size of 92 patients. Spirometry is not accurate at predicting pulmonary restriction and in this study the term ‘restriction probable’ was used. Patients with this pattern should usually be referred for additional PFTs to confirm the diagnosis by doing Total Lung Capacity (TLC) by lung volume measurements.\textsuperscript{52}

The results of this study show that the association of post TB airflow obstruction with FEV\textsubscript{1} values (FEV\textsubscript{1} % predicted, median 58 Q1=42 Q\textsubscript{3} =81) was stronger than for FVC (FVC% predicted, median 89 Q\textsubscript{1} =67 Q\textsubscript{3} =113). This resulted in a reduction in the FEV\textsubscript{1}/FVC ratio, characterized by an obstructive pattern. This is in accordance with previous studies which have shown a stronger association of FEV\textsubscript{1} than FVC values resulting in an obstructive pattern.\textsuperscript{8} In the present study post bronchodilator spirometry was not done which could have overestimated the proportion of patients with obstruction attributable to post-TB airflow obstruction. However even studies which have used post bronchodilator spirometry also found a significant association between TB and airflow obstruction.\textsuperscript{8}

5.3 Factors associated with post-TB airflow obstruction

Recurrent TB episodes were associated with an increased risk of developing post TB COPD (OR-0.026) which is in accordance with previous studies\textsuperscript{22,25}. An earlier study by Hnizdo et al showed that lung damage is directly associated with the number of episodes of TB among
patients suffering from silicosis. The proportion of sputum positive patients in the recurrent TB episodes in this study was 40.6% which supports that recurrent TB episodes are a significant predictor of development of airflow obstruction.

Gender differences have been documented in previous studies on the risk of developing COPD, with females presenting at a younger age with predominantly bronchial obstruction and males presenting with predominantly emphysematous change. In this present study females were more likely to develop post-TB airflow obstruction than males (OR 1.78; 95%CI 1.10-2.88, p=0.019). Results from a study done in Zimbabwe, Harare high density suburbs showed that male sex was a significant risk factor for developing pulmonary TB (aOR 3.1; 95%CI 1.6-6.3) but did not compare males and females in terms of development of post-tuberculosis sequelae.

There was no association between age and post-TB airflow obstruction (p=0.962) though FEV\textsubscript{1} and FVC are expected to decline with age. The fixed FEV\textsubscript{1}/FVC<70 which was used in this study has also been shown to over diagnose both the presence and severity of COPD in the elderly according to previous studies. However on logistic regression patients above 50 years were more likely to develop post-TB airflow obstruction than those below 35 years but the difference did not reach statistical significance (OR 1.21; 95% CI 0.56-2.59 p=0.624).

There was no association between sputum status and development of post TB COPD (p=0.376). This is in contrast with a previous studies by Kuei-Pin Chung et al and J Ross et al which have shown smear positive disease to be an important predictor of pulmonary function deterioration after the completion of pulmonary TB treatment. However in this present study sputum positive patients were more likely to develop post-TB airflow obstruction than sputum negative patients (OR 1.43; 95%CI 0.85-2.43 p=0.180) but the difference did not reach statistical significance.

Initials ___________
HIV has been shown to have an independent effect on chronic airflow limitation\textsuperscript{11} and to cause premature emphysema\textsuperscript{55,56}. The synergistic effect of HIV infection and pulmonary TB would be expected to result in significant airflow obstruction. In this study there was no association between HIV status and development of post-TB airflow obstruction. Low CD4 counts also did not increase the risk of development of post-TB airflow obstruction, but very few patients had CD4 count results, only 33.4\%. An earlier study by Hnizdo had also demonstrated that loss of lung function due to TB was not biased by HIV status as HIV positive and HIV negative patients had similar losses.\textsuperscript{25}

There was no association between chest x-ray findings and the development of post-TB airflow obstruction. Most earlier studies had not looked at the different x-ray findings but had indicated that large areas of lung infiltration were associated with development of post TB-airflow obstruction\textsuperscript{21,42,43,44}. However Yasuda J et al looked at emphysematous change, fibrosis, bronchiectasis and/cavity, atelectasis and pleural thickening, and emphysematous change was found to more likely result in airflow obstruction than any other finding.\textsuperscript{46} The chest x-ray findings evaluated by Yasuda J et al were however different from those evaluated in this present study which included cavities, consolidation, pleural effusion, military mottling and reticulo-nodular infiltrates.
5.4 Study limitations

- Airflow obstruction present, but not perceived by the patient before the diagnosis of TB was difficult to differentiate from post-tuberculosis airflow obstruction because spirometry was not performed before the patient developed PTB.
- Patients with smear negative TB were also included in the study who may have been wrongly diagnosed as TB.
- Post bronchodilator spirometry was not done which could have increased the proportion of patients with obstruction attributable to post-TB airflow obstruction.
- The chest x-rays were not interpreted by a radiologist which could have affected the interpretation.

5.5 CONCLUSION

From this study, there is a high prevalence of post-TB airflow obstruction with moderate obstruction according to the GOLD criteria being the most prominent. Recurrent episodes of TB and female sex were associated with development of post-TB airflow obstruction.

5.6 RECOMMENDATIONS

- Post-TB patients should be followed up by spirometry to detect if they have residual lung dysfunction to avoid their retreatment as recurrent TB.
- Patients with recurrent TB episodes should have more regular follow up since they are at greater risk for development of post-TB airflow obstruction.
- There is need to perform treatment trials to see if bronchodilators improve spirometry parameters (FEV₁ and FVC) in post-TB airflow obstruction.
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7. APPENDICES

7.1 DATA COLLECTION SHEET

1. Registration
   a) Date
   b) Patient's ID

2. Demographics
   a) Sex
      1. male  2. female
   b) Age
   c) Residential area

3. Clinical Data
   a) HIV status
      1. Positive  2. Negative
   b) If HIV positive
      1. Baseline CD4 count
      2. Current CD4 count
   c) Date of commencement of TB treatment
   d) Date of completion of TB treatment
   e) How was the diagnosis of TB made
      i. Sputum positive  ii. Chest X-ray  iii. Smear negative
   f) History of previous TB treatment
      1. Yes  2. No
      Dates
   g) Other clinical conditions
      (specify)
PULMONARY FUNCTION TESTS

Patient’s ID ………………………………………………………………………………………………………

Height (cm)…………………………. Weight (kg)………………………….

History……………………………………………………………………………………………………

…………………………………………………………………………………………………………

………

Position……………………………………………………………………………………………………

SPIROMETRY VALUES IN LITRES

<table>
<thead>
<tr>
<th>ACTUAL READING</th>
<th>PREDICTED VALUES</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>FVC</td>
<td></td>
</tr>
<tr>
<td>FEV-1</td>
<td>FEV-1</td>
<td></td>
</tr>
<tr>
<td>FEV-1/FVC%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
PROTOCOL TITLE:

Prevalence of post tuberculosis (TB) Chronic Obstructive Pulmonary Disease in patients who have completed TB treatment at two infectious diseases hospitals in Zimbabwe.

NAME OF RESEARCHER: DR TATENDA MEMORY NYAGURA

PHONE: 0772 514 133

PROJECT DESCRIPTION:

Spirometry will be performed on patients who have completed pulmonary tuberculosis treatment. The patient will be asked to take a deep breath, then blow into a machine (spirometry)

YOUR RIGHTS

Before you decide whether or not to volunteer for this study, you must understand its purpose, how it may help you, the risks to you, and what is expected of you. This process is called informed consent.

PURPOSE OF RESEARCH STUDY

To determine the prevalence of post tuberculosis chronic obstructive pulmonary disease at Beatrice Road Infectious Diseases Hospitals (BRIDH) and Wilkins Hospitals. This study will provide information that will justify screening for residual lung dysfunction following treatment for pulmonary tuberculosis and rationalize its management.
PROCEDURES INVOLVED IN THE STUDY

If you participate you will be asked to:

a) Give demographic and clinical information; and
b) Have spirometry done.

DISCOMFORTS AND RISKS

There are no risks for participants. However there may be slight discomfort. Minimal exertion is required during the procedure.

POTENTIAL BENEFITS

Spirometry will be done free of charge and patients with residual lung dysfunction are referred for further management.

STUDY WITHDRAWAL

You may choose not to enter the study or withdraw from the study at any time without loss of benefits entitled to you.

CONFIDENTIALITY OF RECORDS

The names of participants will not appear on any form or result sheet. Instead participants will be given a study number which will be used as a means of identification.

PROBLEMS/QUESTIONS

Please ask questions about this research or consent now. If you have any question in future please ask Dr Tatenda Memory Nyagura.
AUTHORIZATION

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I know being in this study is voluntary. I choose to be in this study: I know I can stop being in the study and I will not lose any benefits entitled to me. I will get a copy of this consent form. (Initial all the previous pages of the consent form).

___________________________________________________________
Participant’s Signature                                      Date

___________________________________________________________
Participant’s Name (Printed)

___________________________________________________________
Researcher’s Signature                                      Date

___________________________________________________________
Witness’ Signature                                           Date

Initials ___________
7.3 INFORMED CONSENT FORM - SHONA

MUSORO WEONGORORO:

Kuongorora uwandu hwevanhu vanosara vane dambudziko rekuzarirwa kana vapedza kurapwa chirwere cheRurindi (Tuberculosis (TB)) pazvipatara zviviri zvezvirwere zvinotapuriranwa muZimbabwe.

MUONGORI: DR TATENDA MEMORY NYAGURA

RUNHARE: 0772 514 133

TSANANGUDZO YETSVAKIRIDZO INO:

Varwere vanenge vapedza kurapwa chirwere cheRurindi(TB) vachaongororwa mafemero avo (Spirometry). Vachakumbirwa kuti vafemere mukati vobva vafuridza mumuchina (spirometry)

KODZERO YAKO

Usati wabvuma kubatsira mutsvakiridzo ino zvakakosha kuti utange wanzwisisa maererano nechinangwa cheongororo ino, uye kuti ingakubatsira sei uyezve kuti iwe unotarisirwa kuitei mutsvakiridzo ino

CHINANGWA CHETSVAKIRIDZO INO

Tsvakiridzo ino ndeye kuongorora uwandu hwevanhu vanosara vaine dambudziko rekuzarirwa kana vapedza kurapwa chirwere cheRurindi(TB) paWilkins nepaBeatrice Road Infectious Diseases Hospitals (BRIDH). Tarisiro ndeyekuti zvichabuda mutsvakiridzo ino zvichabatsira kuti tigare takatarisira dambudziko iri uye tizogone kubatsira vanenge vanaro nemazvo.

Initials __________
MAITIRWO ACHAITWA ONGORORO INO

Mukabvuma kupinda mutsvakiridzo ino munotarisirwa zvinotevera:

a) Kupa rondedzero maringe neutano hwenyu; uye

b) Kuongororwa mafemero enyu kuti akamira sei (Spirometry).

NJODZI DZAMUNOGONA KUSANGANA NADZO

Hapana njodzi inotarisirwa patsvakiridzo ino, asi muchakumbirwa kuti mushandise simba renyu zvishoma pamuchaongororwa kufema.

BATSIRO

Muchaongororwa mafemero enyu pachena uye kana pane zvinenge zvawanikwa zvisina kumira zvakana pakufema kwenyu muchatumirwa kuna vana chiremba vanogona kukubatsirai.

KUSADA KUENDERERA MBERI NEONGORORO

Makasununguka kuregedza kuenderera mberi neongororo ino uye hamutarisirwe kuripiswa nemhaka yekusarudza kusaenderera mberi uye zvose zvamunenge matenderana kuti muchawana apo panenge patanga ongororo munozviwana zvisineyi nekuti maregedza pachidanho chipi cheongororo.

KUCHENGETEDZWA KWEUMBOO HWAPIHWA

Zita renyu uye zvose zvamuchabvunzwa zvingaita kuti vamwe vanhu vagone kufungidzira kana kuziva kuti ndimi makabatsira mutsvakiridzo ino zvichachengetedzwa muchivande.
MIBVUNZO KANA ZVICHEMO

Makasununguka kuti mubvunzurudze chero chipi maererano neongororo ino kubvazvino kana panguva ipi zvayo inotevera. Muno kurudzirwa kuendesa mibvunzo iyi kana zvichemo kuna Chiremba muzvare Tatenda Memory Nyagura.

MIBVUMO


________________________                           _________________

Siginecha yemupi weumbowo                         Zuva

________________________

Zita ramupi weumbowo

________________________                           _________________

Siginecha ya Muongorori                           Zuva

________________________                           _________________

Siginecha yemurevereri                        Zuva

Initials ___________
Initials ___________