LUNG FUNCTION ABNORMALITIES BEFORE AND AFTER TREATMENT OF PULMONARY TUBERCULOSIS IN SELECTED HEALTH FACILITIES IN DAR ES SALAAM

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Department of Internal Medicine

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By

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A Dissertation submitted in Partial Fulfillment of the Requirement for the Degree of Masters of Medicine in Internal Medicine

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CERTIFICATION

The undersigned certifies that, they have read and hereby recommend for examination by Muhimbili University of Health and Allied Sciences a dissertation entitled ***Lung Function Abnormalities Before and After Treatment for Pulmonary Tuberculosis in Selected Health Facilities in Dar Es Salaam,*** in (partial) fulfillment of requirements for the degree of Master of medicine (Internal Medicine) of Muhimbili University of Health and Allied Sciences.

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Prof. Tumaini Nagu

(Supervisor)

Date: _____

_____

Dr. Grace Shayo

(Co- Supervisor)

Date: _____

DECLARATION AND COPYRIGHT

I, **Dr. Reinhard E. Lema**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature:…… **Date:……..**

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DEDICATION

This work is dedicated to my supervisors Prof. Tumaini Nagu and Dr. Grace Shayo.

ABSTRACT

Background: Tuberculosis (TB) causes the highest number of deaths worldwide as a single infection. Tanzania, reports more than 80,000 TB cases every year. However, in Tanzania post TB treatment lung disease has not been fully explored. This study aimed to document abnormalities in lung function at initiation and at the end of anti TB therapy and explore the associated factors among patients treated for first ever Pulmonary Tuberculosis in one of the five (5) selected TB clinics in Dar es Salaam.

Methodology: A prospective longitudinal study was conducted in 5 tuberculosis (TB) clinics, in Dar es Salaam between August 2020 to May 2021. Newly diagnosed pulmonary TB (PTB) patients aged 15 years or above, were recruited upon written consent or accent where applicable. Patients were evaluated using spirometry at recruitment and at treatment completion. The outcome of interest was proportions of abnormal lung function; obstructive, restrictive and mixed lung function defects at recruitment and at TB treatment completion. Chi-square χ^2 test was used to compare the differences in proportions of lung function abnormalities. Paired t test was used to assess the change in lung functions and Log binomial regression model was used to determine factors associated with abnormal lung functions at treatment completion. All patients were treated as per national TB treatment guidelines with Rifampicin (R), Isoniazid (H), Pyrazinamide (Z) and Ethambutol (E).

Results: A total of 332 patients with PTB were recruited. Overall 64.1% (n=213) of patients showed some form of abnormal lung function at treatment initiation. At treatment completion, abnormal lung function was observed among 47.3% (n=142). The median FEV1 (IQR) at the end of TB treatment was significantly higher, (2.33L ± 0.26) compared to the FEV1 at the start of treatment which was (2.18L ± 1.16) P= 0.001. Similarly, the median FVC (IQR) at the end of TB treatment had significantly increased 3.05L ± 0.31 compared to at the initiation of TB treatment (2.82L ± 1.5) P= 0.010. Being underweight, (RR: 1.49, 95% 1.13 - 1.95 CI; P<0.004), male sex (RR: 1.22, 95% CI 1.19 - 2.23 CI; P=0.004), cavitation (RR: 1.90, 95% CI 1.29 – 2.78, P = 0.02) and lung parenchymal fibrosis on chest X ray were RR: 2.16, 95% CI 1.32 – 3.53, P 0.001 were significantly associated with increased risk for abnormal lung functions at treatment completion.

Conclusion: Six months anti-tuberculosis chemotherapy was associated with improvement in lung functions in a number of patients. However, about 1 out of 2 of our patients treated for tuberculosis had residual abnormality in lung function at the end of tuberculosis treatment. There is need for further studies to find additional agents that will enhance the effect of anti-tuberculosis chemotherapy in improving lung health. Secondly, patients treated for tuberculosis need longer follow up beyond the period of treatment. The appropriate length of follow up is a subject for further research.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

AFB	Acid Fast Bacilli
AMO	Assistant Medical Officer
ATS	American Thoracic Society
BMI	Body Mass Index
COPD	Chronic Obstructive Pulmonary Disease
DM	Diabetes Mellitus
DST	Drug Susceptibility Testing
EPTB	Extra Pulmonary Tuberculosis
ERS	European Respiratory Society
FEV_1	Forced Expiratory Volume in one second
FVC	Forced Vital Capacity
HIV	Human Immunodeficiency Virus
LFT	Lung Function Test
LLN	Lower Limit of Normal
MUHAS	Muhimbili University of Health and Allied Sciences
MTB	*Mycobacterium tuberculosis*
MDR	Multi Drug Resistant TB
NTLP	National Tuberculosis and Leprosy Program
NLHEP	National Lung |Health Education Program
PTB	Pulmonary Tuberculosis
TB	Tuberculosis
TRRH	Temeke Regional Referral Hospital
WHO	World Health Organization
ZN	Ziehl Neelsen

DEFINITION OF TERMS

Bacteriologically confirmed Tuberculosis (TB**):** A TB case from whom a biological specimen is positive for TB through acid Fast Bacilli (AFB) smear microscopy, *M.tb* culture, or TB molecular test (LPA, Gene Xpert® MTB/RIF) (1).

Pulmonary Tuberculosis (PTB): TB involving the lung parenchyma (1).

Forced Vital Capacity (FVC): The volume of air that can be forcibly exhaled after fully inflating the lungs (2).

Timed Forced Expiratory Volume (FEV_t): The volume of air exhaled at a specified time after beginning the forced vital capacity maneuver. E.g. FEV_1 is the forced expiratory volume in 1 second (2).

OPERATIONAL DEFINITIONS

TB case definition for this study is based on the National TB and Leprosy Program (NTLP) guideline of Tanzania, which is newly diagnosed PTB patient who is bacteriologically confirmed by sputum microscopy or GeneXpert (1)**.**

An Obstructive ventilatory defect was defined as ratio of Forced Expiratory Volume in 1 second (FEV1) to Forced Vital Capacity (FVC) below the 5th percentile of the predicted value, or when FEV1/FVC ratio and FEV_1 are both below the lower limit of normal (3,4).

A Restrictive ventilatory defect is defined as FVC below the lower limit of normal (LLN) with a FEV_1/FVC ratio above the LLN (3,4).

A Mixed ventilatory defect was defined as FEV_1/FVC ratio below 5^{th} percentile and FVC below the LLN (3,4).

Lower Limit of Normal (LLN) was defined as the age and height specific predicted 5^{th} percentile for the individual (3–5).

An abnormal lung function in this study was regarded as any of the following ventilatory defects; obstructive, restrictive and mixed.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Tuberculosis (TB) is commonly caused by *Mycobacterium tuberculosis.* TB infection most often affects the lungs and only affects other organs in a third of cases. Transmission usually takes place through airborne spread of droplet nuclei expectorated by infectious pulmonary tuberculosis (PTB) patients (6).

TB is classified as pulmonary when it is confined to the lungs or extra pulmonary when it involves other organs apart from the lungs or both (6). Common symptoms of PTB include persistent cough for 2 weeks or more, associated with production of sputum and sometimes blood in sputum (hemoptysis). Other symptoms include systemic symptoms such as fever, night sweats and unexplained weight loss of at least ten percent of body weight (6).

1.1.1 Diagnosis of PTB

The World Health Organization (WHO) has approved several diagnostic tests for TB.

i. **Sputum smear microscopy for Acid Fast Bacilli**. A single sputum smear has a sensitivity of approximately 60% and specificity of 98%. There is a wide variation however depending on disease advancement (6). A second sputum smear sample increases the mean yield sensitivity by 9% (7). One spot sputum sample and a second early morning sputum sample is required for AFB microscopy (8).

ii. **Mycobacterial culture** facilitates definitive diagnosis, includes isolation and identification of *M. tuberculosis* from clinical specimen. Available culture media include the solid egg based Löwenstein-Jensen (LJ) or liquid media system, BACTEC Mycobacteria Growth Indicator Tube (MGIT) (6).

iii. **Molecular techniques** include Gene Xpert and Line Probe Assay. The Gene Xpert MTB/RIF assay simultaneously detect TB and Rifampicin resistance in < 2 hours (6). It has a sensitivity of 89% compared to culture and a specificity of 99% (9,10).

iv. **Radiological diagnosis:** Chest X-ray is the primary tool for detecting PTB. Has high sensitivity but poor specificity (6). Computed Tomography scans are important for detection of radiographically occult disease (11). Magnetic Resonance Imaging provides a better evaluation of mediastinal nodes, reduces radiation exposure (11). Positron Emission Tomography scan has 80% sensitivity and 75% specificity (12).

1.1.2 Pathogenesis of Lung Function Impairment in PTB

Pathogenesis of lung function impairment involves a complex inter-play of the host's immune system response to the mycobacterium invasion, genetic and environmental factors such as smoking. Invading mycobacteria gain access to the alveoli where they are phagocytized by non-activated resident macrophages or dendritic cells (DCs). Presentation of the mycobacteria antigen by neutrophils to macrophages/dendritic cells and their secretion of IL-12 stimulates the CD4+ and CD8+ lymphocytes, natural killer cells and B cells to release various cytokines. T-lymphocytes secrete Interferon-gamma (IFN-γ) which in turn activates macrophages and potentiate their intracellular killing effects (6,13). In addition, interleukin -2, 4, 5, 6, 10, 12, 13, 17 and Tumor Necrosis Factor-alpha (TNF-α) are released by various inflammatory cells (13,14). (TNF α) potentiates effective granulomas and neutrophil aggregation at the Ghon focus. Activated macrophages aggregate around the tubercle bacilli (granuloma formation) (13). Granulomas try to confine the mycobacterium and prevent spread however other theories propose that it is MTB's strategy to evade host immunity (13,14). Healing may occur with fibrosis and calcifications of the lesions in the lung parenchyma or/and lymph nodes (Ghon complex) (13,14).

A weak macrophage activating response results in delayed hypersensitivity reaction that leads to extensive tissue destruction. Liquefactive necrosis causes granuloma destruction causing cavitation (6,13,14).

Matrix metalloproteinase (MMPs), a group of proteases in the epithelial cells may be activated by mycobacterial protein. This causes further destruction of the extracellular matrix of the lung. Inflammatory cytokines such as Tumor Necrosis Factor -alpha, Interleukin-6, 8 and 12 contribute to formation of cavities, fibrosis and bronchial wall

thickening in active TB patients (13,14). Eventually remodeling caused by PTB causes irreversible bronchial and parenchymal structural changes that continue to persist even after PTB is cured (15). These cytokines are implicated for short term as well as long term lung parenchymal damage.

1.1.3 Lung Function Tests in the Post PTB Infection and treatment

Pulmonary TB causes severe lung function abnormality, which may improve to some extent with effective TB chemotherapy. There is however persistence in pulmonary function abnormality even after treatment completion (16–18). Post TB treatment patients continue to suffer from the architectural damage of the lungs and airway ending up with obstructive, restrictive or mixed lung function abnormalities (19).

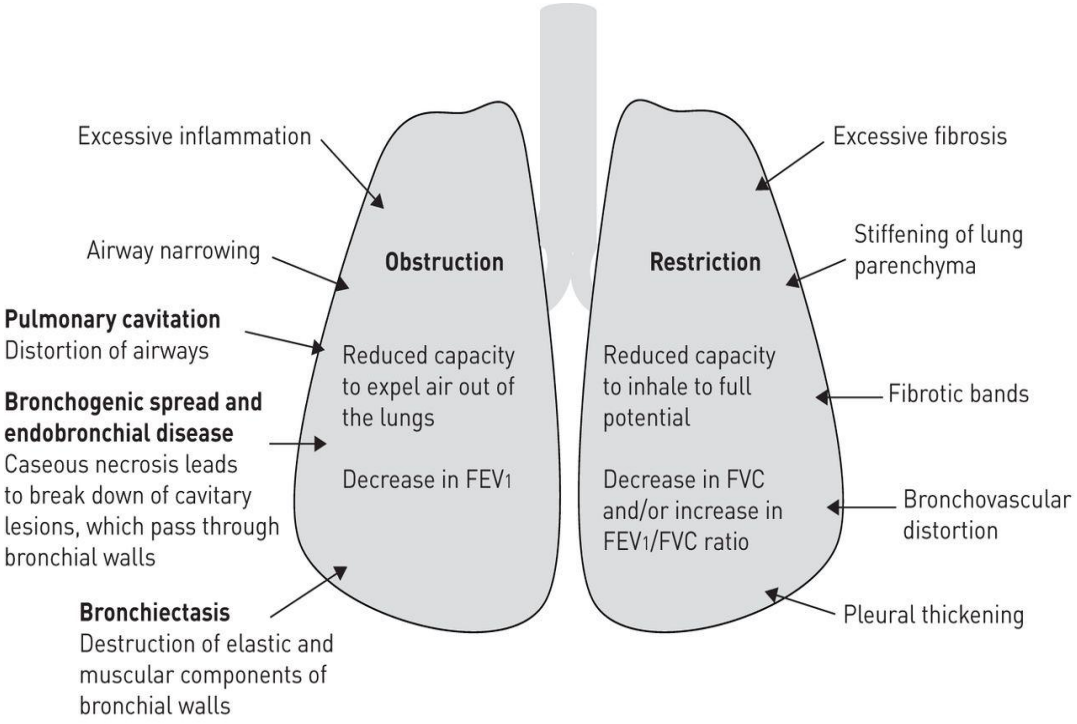

Figure 1: Mechanisms and radiographic features associated with airflow obstruction and restrictive defects in patients with TB history.

Diagram adopted from; *Tuberculosis and lung damage, from epidemiology to pathophysiology* (14)

1.1.4 Treatment of PTB

The Tanzania TB treatment guideline as adopted from World Health Organization (WHO) recommends for drug sensitive TB patients to receive first line anti tubercular treatment. An initial phase of two months of a fixed dose combination of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol (1) followed by a continuation phase consisting of a fixed dose combination of Isoniazid and Rifampicin given for 4 months (1). Multidrug Resistant TB (MDR-TB) have resistance to both Rifampicin and Isoniazid. In Tanzania they are treated for a minimum of 20 months (1). WHO has recently endorsed Bedaquilline and Delamanid for shorter duration treatment of MDR-TB. With this new molecules treatment time is shortened to between 9 to 12 months (1,20). Uncontrolled Interleukin-6 production in PTB has been associated with irreversible lung tissue damage. Adjunct therapies from host cytokines including IL-6 are potential host directed therapies for PTB (13,14).

1.2 Literature Review

1.2.1 Burden of Tuberculosis

Tuberculosis (TB) is the top cause of death from an infectious origin worldwide(6). Globally, TB contributed to 1.2 million deaths among HIV-negative people in the year 2018 with 251 000 more deaths among HIV positive people. In the same year the global incidence of TB was 10 million which is equivalent to 132 cases per 100 000 population. Africa is the second globally with an incidence of 231 per 100 000 population (21).

Tanzania being among the 30 high TB burdened countries in the world has an incidence rate of 253 per 100 000 population, the leading country being Lesotho (611 per 100 000 population) followed by the Philippines (554 per 100 000 population) (21). According to WHO estimates, PTB accounts for 79% of all TB cases in Tanzania. Mortality due TB is estimated to be 40 per 100 000 population in HIV negative patients and 29 per 100 000 population in HIV positive patients (21).

TB incidence in Tanzania reported by the National TB and Leprosy Program by 2018 was 253 per 100,000 of population. 48% of all forms of TB cases notified were bacteriologically confirmed and 79% were pulmonary. 28% were HIV positive and 98% were initiated with anti-retroviral therapy (1).

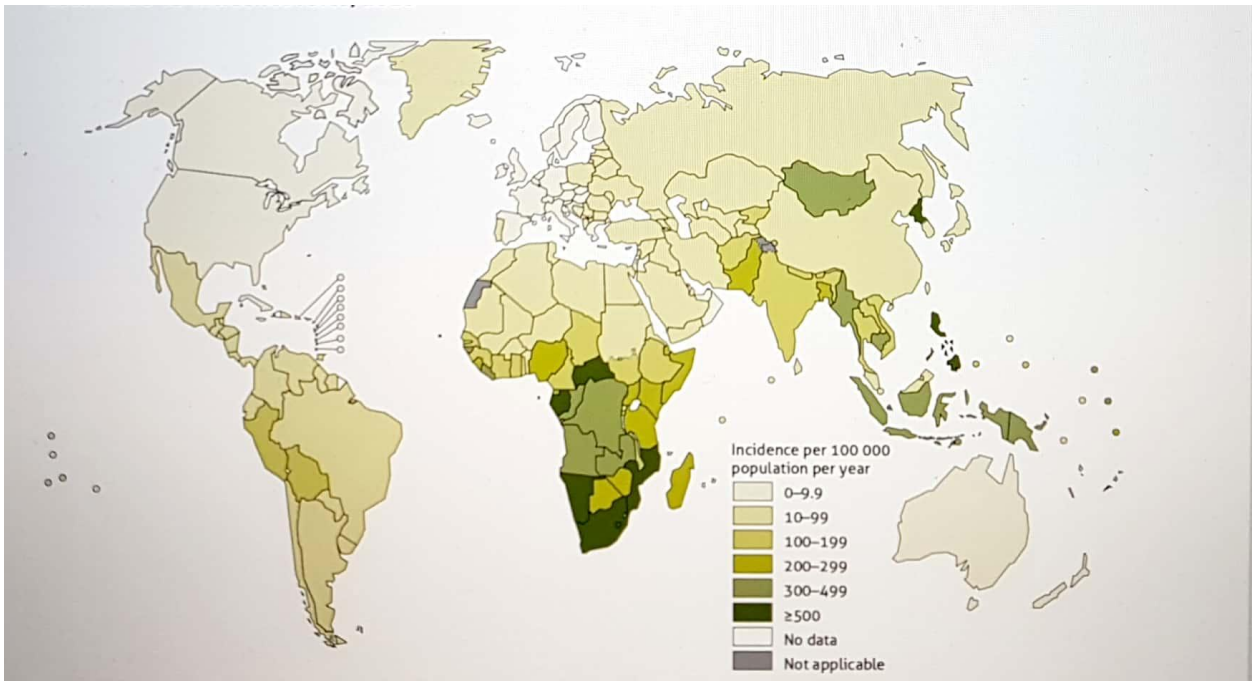

Figure 2: Global estimated TB incidence rates.

WHO global burden of TB report, 2019 (21)**.**

1.2.3 Inflammation and lung disease following treatment for tuberculosis

Following the host immune response to *Mycobacterium tuberculosis* invasion (14), patients with PTB eventually suffer from bronchial and lung parenchymal structural changes(15). Prior to PTB chemotherapy, studies have demonstrated baseline impairment of lung functions (16,17). Patients with PTB have lower mean FEV_1 at the beginning of treatment compared to the normal population (17). In caring for PTB patients, assessment of lung function abnormality at the beginning of treatment is important. This is because it will eventually influence the post treatment lung function status (18).

Several studies have shown abnormality in FEV1 at the onset of treatment which improves with treatment with TB chemotherapy (16,22). A prospective nested case control study was done on 40 patients newly diagnosed with PTB in Serbia (Southeastern Europe) by Milan *et al*. The study showed a significant improvement in the lung functions (Forced Vital Capacity) after following up the patients for six months of treatment (23). Maguire et al

and Anna et al echoed similar trends in two different studies in Indonesia (16,17). Despite improvement in lung functions following treatment, some studies have shown the opposite, particularly towards the end of six months of treatment. This has been attributed to the reparative processes of the lung architecture (22). Despite the adequate PTB chemotherapy and improvement in lung function that comes during and after treatment, patients will still have moderate to severe pulmonary function abnormality (16–18). This underscores the fact that TB related morbidity does not stop after 6 months of treatment.

1.2.4 Patterns of Lung Function Impairment following tuberculosis treatment

Patients post PTB treatment succumbs to the consequence of architectural lung damage. This manifests through the abnormalities of lung function. Common patterns of lung function abnormality include obstructive, restrictive or mixed patterns (19).

Various studies have shown the obstructive pattern to be more prevalent irrespective of the duration of post treatment completion mainly presenting with Bronchiectasis (24,25). However, literature suggest that the abnormality is more prevalent among smoking compared to non-smoking patients with PTB (19,24–26).

Restrictive patterns are also common among patients with PTB (24,26). A study done in India by Akshay *et al* showed a higher prevalence of restrictive patterns with a prevalence of 52% compared to 24% obstructive patterns, the remaining patients had normal lung functions. This study was conducted among adult patients 1 year following successful treatment for PTB. In this study, the restrictive patterns were more in the females and in diabetic patients (27). This is however different from the findings of a study by Manji *et al* in Tanzania in which the males had a higher prevalence of restrictive patterns (26). The mixed pattern of lung function abnormality is a coexistence of both obstructive and restrictive patterns and has been documented in patients with PTB even in Tanzania (26).

1.2.5 Tuberculosis (TB) sequela and complications

Post PTB treatment patients may have large residual cavities in their lungs. These cavities may be invaded by *Aspergillus fumigatus*, and the patient will suffer from Aspergillosis. The patient may present with hemoptysis, persistent fatigue and weight loss due to aspergillosis (6,24).

Pulmonary fibrosis and bronchiectasis are among common complications. The patients may present with symptoms of cough, hemoptysis and dyspnea (25,28). TB associated pulmonary hypertension may present with an un-explained shortness of breath and desaturation with mild exercise (28,29). It is hence of paramount importance to enquire of the history of PTB in all patients with pulmonary hypertension. Post TB chronic obstructive pulmonary disease has been documented by many studies (23–25). Patients may present with dyspnea, cough, weight loss, chest pain and wheezes. Following recurrent bacterial or viral pneumonia, patients post PTB may also present with fever (23–25).

1.2.6 Factors associated with abnormalities in lung functions

A retrospective cohort study involving 41 patients with PTB in Korea by Ko *et al* showed a higher median decline in annualized FEV_1 in patients with advanced TB (involving 2 or more lobes) compared to localized TB (involving 1 or less). This highlights that the extent of disease is an important factor in decline of pulmonary functions. Similar trends have been reported by Chung *et al* in Taiwan, Fiogbe *et al* in Benin and in one South African study (15,18,30,31).

Development of airflow obstruction is associated with longer duration of illness prior to treatment (23,31). These findings are somehow similar to the ones reported by Bertrand in Cameroon (32). In a Russian study by Mikhail et al, risk factors for reduced pulmonary function included a past history of recurrent TB among others (19). This was in keeping with a study by Manji et al in Tanzania who also reported recurrent TB to be a risk factor (26).

Mikhail et al also found that age over 50 years was associated with a higher risk of abnormal lung functions (19). This was slightly different from Manji et al who reported associated age to be above 40 years (26).

According to Manji et al, male sex was associated with abnormal lung functions (26). In contrast to Manji et al, a study in Benin reported female sex to be associated with lung function abnormality (31). Manji et al also found that being HIV positive was associated with increased risk of abnormal lung function (26). This is different from the study in Benin in which being HIV positive was not associated with abnormal lung function (31).

TB is seen to cause chronic impairment of lung function. Severity of TB parenchymal damage as well as worsening in functional capacity increases with each TB episode (33). A past history of PTB in a study in Sudan was strongly associated with chronic airflow obstruction (34). Cytokines play a key role in pathogenesis of PTB and have shown to be a potential avenue for host directed therapy against PTB (13,35). Deficiencies and low levels of IFNγ have been associated with increased lung tissue necrosis (35). Elevated levels of IL-1, IL-6, TNF-α, along with other inflammatory cytokines at PTB treatment baseline have been associated with increased severity in lung tissue damage (36). Hence higher levels of inflammatory makers seem to be related to abnormal lung functions due to increased lung tissue damage.

Unfortunately due to irreversible lung destruction and remodeling caused by TB, cure does not necessarily mean full pulmonary functional recovery (27,37). Despite the 90% treatment success rate, 74% of post TB patients in Tanzania were reported to continue to suffer from residual lung function abnormality at treatment completion (26). Patients fare well in terms of microbiological response after cure, nevertheless their lung function health is uncertain and has not been fully investigated. Factors amenable to intervention that may influence these potential long term consequences are not known (16,37). The morbidity due to TB may be underestimated if residual pulmonary disability after TB treatment is not assessed. Hence it is essential to assess and document the trend and patterns of pulmonary functions at the beginning and the end of treatment (15,17).

1.3 Statement of the Problem

Tanzania is among the TB heavily burdened countries in the world (38). In 2019 Tanzania notified 74,692 TB cases of all forms, however 79% of the cases were pulmonary tuberculosis (21).

Tanzania national guidelines for treatment of tuberculosis requires routine follow up with microbiological tests (smear microscopy) to ensure microbiological cure and hence treatment success (1). Microbiological cure for TB among new and relapse cases in Tanzania is good and stands 90% (38). The guideline does not specify requirement for risk stratification or any need of follow up of patients beyond six months of TB treatment. However, there are no systematic data to show the short- and long-term outcomes of lung function among patients treated for tuberculosis. This limits institution of appropriate interventions should there be need.

There are growing concerns in recent literature that microbiological cure is not adequate to address the short- and long-term consequences of PTB in terms of lung health (17, 19). In Tanzania post TB lung health has not been fully explored. Despite the magnitude of TB in Tanzania where more than 80,000 patients with tuberculosis are notified every year, the extent of lung function changes and disease pattern before and following a successful PTB treatment is yet to be fully examined. Furthermore, there are no routine follow up of patients beyond the TB treatment duration (1). Consequently, this has led to a number of patients living with chronic lung disease without structured care and follow up. Post TB disease sequelae may be associated with several diseases presenting with obstructive lung function (e.g. COPD, Bronchiectasis) or restrictive (e.g. TB pleurisy, fibrosis) or vascular e.g. pulmonary hypertension. These diseases if not identified and treated early may result in greater morbidity, increased costs to patients, their families as well as to the health care system; poor quality of life and death. Late presentation may necessitate interventions such as partial or complete lung resection (23–25,28,29,39). This study therefore addresses in part the gap by assessing the pattern and changes in lung functions among patients with PTB before and after treatment in selected hospitals in Dar es Salaam.

1.4 Rationale of the Study

Individuals recovering from TB are at higher risk of long-term mortality and morbidity than the general population (21,40). These are from chronic complications such as bronchiectasis, severe lung fibrosis and pulmonary hypertension.

Absence of information on the extent of the abnormality of lung function in Tanzania makes it difficult to justify the need for additional interventions for TB patients. In addition, lack of full exploration of the patterns of lung function abnormalities as well as factors associated with the abnormalities affecting patients post TB treatment leaves a vacuum as to which interventions will further improve lung health of patients treated for TB during and/or beyond the treatment duration. Knowing the extent of changes in lung functions as well as the associated factors for the abnormal lung function post TB treatment may provide an opportunity to plan for and implement appropriate intervention for the patients to avoid/reduce lung sequel due to TB disease. This study therefore provides information that will be useful in advocating for routine care beyond the period of TB chemotherapy. It will also form basis for guidance to physicians to think beyond microbiological cure and particularly lung function beyond to reduce morbidity, mortality as well as improve the quality of life in this group of patients.

1.5 Conceptual Framework

The conceptual framework below shows how various risk factors influence the patterns and extent of lung parenchymal remodeling following a diagnosis of PTB. Eventually these changes on the lungs are measured and interpreted by a spirometer.

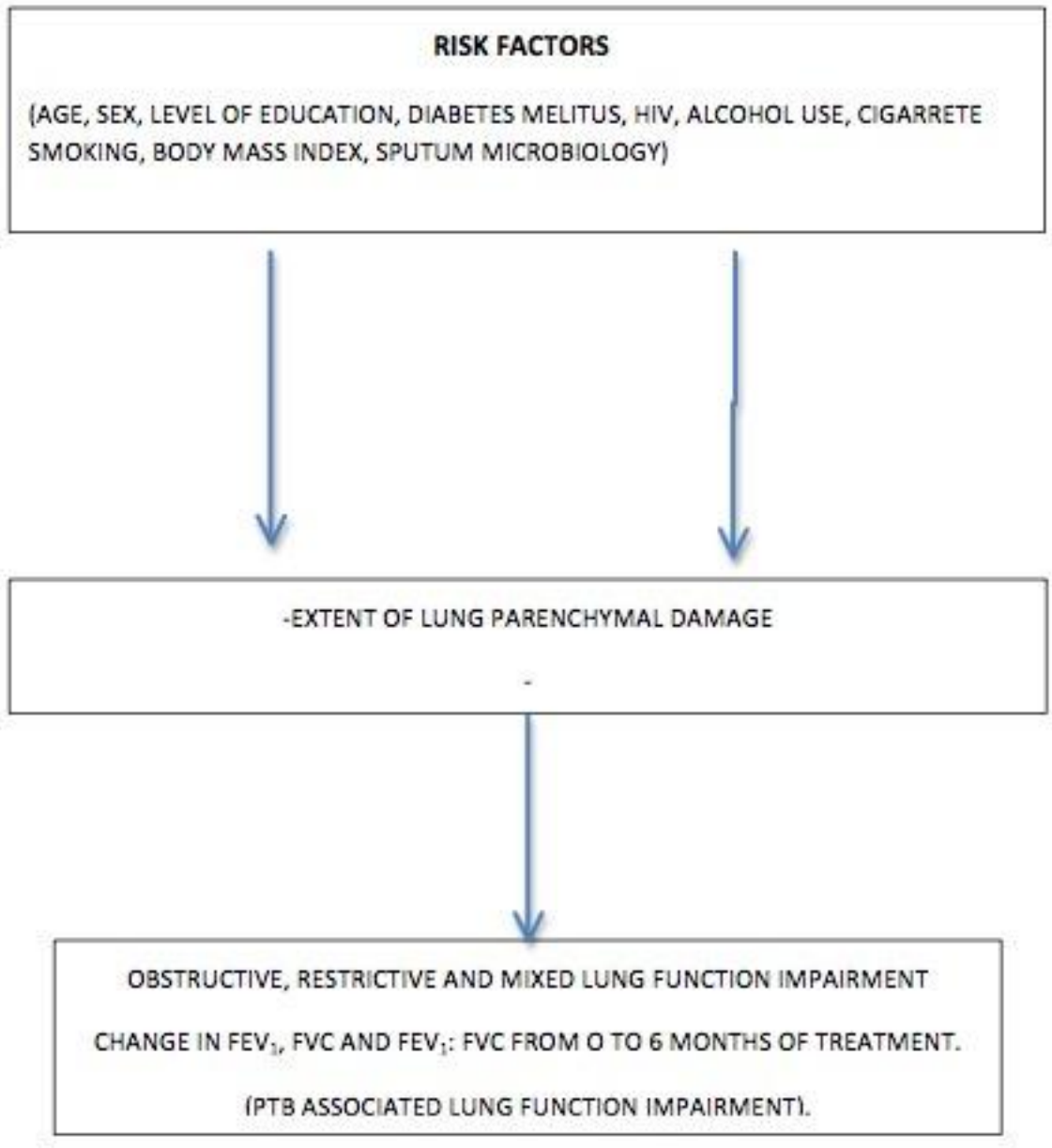

Figure 3: Conceptual framework

1.6 Research Questions

1. What are the patterns of lung function abnormalities among patients treated for PTB at selected TB clinics in Dar es Salaam.

2. What is the mean change in lung function ($FEV_{1,}$ FVC and FEV_1: FVC) from treatment initiation to treatment completion among patients treated for PTB at selected TB clinics in Dar es Salaam.

3. What are the factors associated with lung function impairment among patients treated for PTB at selected TB clinics in Dar es Salaam.

1.7 Objectives of the Study

1.7.1 Broad Objective

To examine the lung function abnormalities before and after treatment of Pulmonary Tuberculosis at selected TB clinics in in Dar es Salaam.

1.7.2 Specific Objectives

1. To describe the patterns of obstructive, restrictive and mixed lung function impairments before treatment initiation and at treatment completion among patients treated for pulmonary tuberculosis in selected TB clinics in Dar es Salaam.
2. To determine the mean FEV1, FVC and FEV_1: FVC at baseline and at treatment completion among patients treated for pulmonary tuberculosis in selected TB clinics in Dar es Salaam.
3. To determine factors associated with lung function abnormality among patients treated for pulmonary tuberculosis in selected TB clinics in Dar es Salaam.

CHAPTER TWO

2.0 RESEARCH METHODOLOGY

2.1 Study Design

We employed a prospective longitudinal single arm cohort study among newly diagnosed tuberculosis patients.

2.2 Study Area

The study was conducted in TB Clinics in Temeke Regional Referral Hospital (TRRH), Mbagala Rangi Tatu Hospital, Mbagala Kizuiani Dispensary, Amana Regional Referral Hospital and Mwananyamala Regional Referral Hospital in Dar es Salaam. All the selected study health facilities are state owned.

Temeke municipality leads in the burden of TB in Dar es Salaam. TRRH has a bed capacity of approximately 200 patients. Its TB clinic serves patients from a number of units including Mtoni, Mgulani, Changombe, Tandika, Sandali and Temeke. Clinic patient turnover is 2400 to 3000 patients per month. Most of the patients are government sponsored patients; private patients are about 50 to 60 per month. An average of 3 to 4 patients are usually newly diagnosed smear positive patients in a day. The TB clinic has 3 TB clinical coordinators, which are Advanced Medical Officers (AMO) and two Nurse Officers. Services in the TB clinics are available throughout the weekdays from 8am in the morning with the exception of weekends. Services offered include vital signs, weight and height measurement, Anti-TB medications, Sputum for AFB and Sputum for Gene Xpert. A chest X-ray is usually done at the patients' expense in patients with clinical suspicion of pulmonary tuberculosis with sputum negative results.

Mbagala Rangi Tatu is a hospital with the following catchment areas; Toangoma, Mianzini, Kibonde Maji, Mbagala Kuu, Mbagala Charambe and Kiburugwa. Some patients come from Mkuranga, which is in a different municipality. Clinic patient turnover is 3000 to 4500 patients per month. Most of the patients are public patients; private patents are approximately 10 to 15 per month. An average of 5 to 10 patients newly diagnosed smear

positive patients in a day. The TB clinic has 2 TB clinical coordinators (Clinical Officers) and 2 Nurses. Services in the TB clinics are available throughout the weekdays and on Saturday from 8am in the morning with the exception of Sunday. Services offered include vital signs, weight and height measurement, Anti-TB medications, Sputum for AFB and Sputum for Gene Xpert. A chest X-ray is only done at the patients' expense in patients with clinical suspicion of pulmonary tuberculosis in the setting of negative sputum smear results.

Mbagala Kizuiani dispensary TB clinic serves patients from a number of wards including, Vikindu, Mbande, Chamazi, Toangoma, Kongowe and Kisemvule. Clinic patient turnover is 35 to 45 patients per month. All of the patients attended are public patients. An average of 6 patients are usually newly diagnosed smear positive patients in a week. The TB clinic has one TB clinical coordinator (Clinical Officer) and 1 Nurse. Services in the TB clinics are available throughout the weekdays from 8am in the morning with the exception of weekends. Services offered include vital signs, weight and height measurement, Anti-TB medications and Sputum for AFB.

Mwananyamala Regional Referral hospital TB clinic serves patients around Kinondoni district. Patients are served every day from Monday to Friday with the exception of weekends. Clinic patient turnover is 400 to 500 patients per month. Almost all patients are public patients. It receives an average of 3 patients newly diagnosed PTB (Sputum smear positive) during clinic days. Amana Regional Referral Hospital TB clinic serves patients around Ilala district. Patients are served every day from Monday to Friday with the exception of weekends. Clinic patient turnover is 400 to 500 patients per month. Almost all patients are public patients. It also receives an average of three sputum positive, newly diagnosed PTB patients on a clinic day. Services offered in both clinics include vital signs, weight and height measurement, Anti-TB medications, Sputum for AFB and Sputum for Gene Xpert.

2.3 Study Duration

This study was conducted from August 2020 to May 2021.

2.4 Study Population

The study population was all bacteriologically confirmed new patients diagnosed with pulmonary tuberculosis (PTB), aged 15 years or above that were started on anti TB therapy at one of the participating study clinics. We considered 15 years age to maximise population coverage as per Tanzania NTLP guidelines (41), this is also similar to other local population studies (5).

2.5 Sample Size Estimation

The sample size required for this study was calculated by using the formula described by Kish and Lesley.

$$n = \frac{Z^2P(100-P)}{\varepsilon^2}$$

Whereby:

- n = minimum sample size required
- Z = standard normal deviation set at 1.96 (corresponding to confidence level of 95%)
- P = prevalence of abnormal lung functions at end TB treatment = 74% (Manji et al-Tanzania)
- ε = marginal error to be used of 5.0%

$n= 1.96^2X74(100-74)/5^2$

n= 295 patients.

Non-response rate (loss to follow up and mortality in the course of treatment) of 10% basing on the 2018 National Tuberculosis and Leprosy Program data was considered(41).

Adjusted sample size = n x 1/R, where R is the response rate, which is 90% in this study (100% – 10%). Adjusted sample size comes to 330 subjects. In this study 332 patients were recruited.

2.6 Inclusion And Exclusion Criteria

2.6.1 Inclusion Criteria

1. All newly diagnosed bacteriologically confirmed PTB patients
2. Patients aged 15 years and above.
3. Patients who have consented to participate.

2.6.2 Exclusion Criteria

1. Participants with any skeletal or neurological condition impairing lung function testing.
2. Participants with known pre-existing diseases such as COPD, Asthma.
3. Patients with previous history of TB.

2.7 Sampling Technique And Study Procedures

2.7.1 Consenting and recruitment

All patients with positive sputum smear for AFB or Gene X-pert were invited to participate in the study voluntarily. All study participants were requested to provide consent for participation upon fulfilling the inclusion and exclusion criteria. Those aged 15 - 17 years (less than 18 years) needed guardians to provide consent and they provided assent. Participants to the study were recruited consecutively until the desired sample size was attained.

2.7.2 Patient History

Pertinent history of the patients participating in the study was obtained with the aid of a structured interviewer-based questionnaire (Clinical Research Form). This included the patient's socio-demographic data, presenting clinical features presented with PTB including a past medical history and assessment of associated risk factors.

2.7.3 Physical Examination

This was done with the aid of the structured form. Participants body height, weight, chest auscultation findings, presence of cervical lymphadenopathy, presence of Bacilli Calmette Guerin (BCG) scar were assessed and recorded.

2.7.4 Anthropometric measurement

Patients' height was measured in a standing position without shoes using a height measuring rod and recorded to the nearest 0.5 centimeters.

Weight was measured in standing position without shoes and with light clothing using a SECCA weighing scale. Readings were recorded to the nearest 0.5 kilograms (Kg). Body Mass Index (BMI) was calculated by taking the patient's weight in kilograms divided by height in meters squared (m^2). BMI were categorized according to WHO as follows: normal 18.5 kg/m^2 to 24.9kg/m^2, under-weight if below 18.5 kg/m2, overweight if BMI ≥25kg/M^2 - 29.99 Kg/M^2 and Obesity if BMI ≥ 30kg/M^2.

2.7.5 Laboratory Investigations

2.7.5.1 Fasting blood glucose

- A drop of capillary fingertip blood was obtained from each study participant by using a needle pricker. Fasting blood glucose measurement was done using the ACCU- check glucometer after the interview and was recorded in mmol/L. Diabetes was defined as fasting blood glucose levels (FBG) ≥ 7mmol/L (42).

2.7.5.2 Sputum for Gene- Xpert

A) Sputum collection

- Ensuring that no one was standing in front of the patient, the patient was instructed to cough deeply and expectorate sputum amounting 3-5mls into the sputum container. One sputum sample was collected per patient.
- The patient was instructed to avoid contaminating the outside of the container with sputum. If the outside of the container was contaminated the container was discarded and a fresh sputum container was provided.

B) GeneXpert

The collected sputum sample was labeled stored in a safe box and immediately taken for Gene Xpert at the laboratory within the health facility. Gene Xpert is a molecular test that combines detection of TB and rifampicin resistance. Results were reported as MTB detected or MTB not detected. Rifampicin resistance for MTB was reported as not detected, detected or intermediate.

2.7.5.3 Sputum for Acid Fast Bacilli (AFB) Testing.

Sputum for AFB is at month 2 of treatment and at month 5.

Sputum collection procedure is similar to the one explained for Gene Xpert above.

The sputum samples were examined for AFB using Ziehl-Neelsen (ZN) technique. Carbolfuchsin was used to stain the sputum specimen on a glass slide. The slide is then heated for 1 minute to fix the stain; acid alcohol is then applied to decolorize the Carbolfuchsin. Methylene blue (counter stain) is finally added and the slide observed under a bright field microscope. The AFB appear as red rods using the ZN technique after retaining the color of Carbolfuchsin reagent.

No AFB seen in at least 100 fields was reported as negative for AFB, 1-9 AFB per 100 fields was reported as scanty, 10-99 AFB per 100 fields was reported as 1+, 1-10 AFB per field in at least 50 fields was reported as 2+ and more than 10 AFB per field in at least 20 fields was reported as 3+.

2.7.5.4 HIV testing

HIV testing was done according to Tanzania HIV treatment guidelines(43). Pre- testing counseling was done for all consenting participants followed by post- testing counseling. SD Bioline HIV 1/2 was done and if negative the patient was recorded as having no HIV infection but if positive then this was followed with a confirmatory Uni-Gold HIV test, if positive then the patient was recorded as having HIV infection. If negative, then the patient had to undergo another rapid test from the beginning using a different sample. If the result was consistently inconclusive the patient was counseled that he/she might be undergoing a period of acute HIV infection and asked to come again after 2 weeks for another repeat HIV test. If the results were still inconclusive then the participant was referred to a higher health facility or sample taken and referred to another laboratory for DNA PCR testing.

The information on the clinic registers and patient's treatment cards was obtained and noted on the patients Clinical Research Form. This includes results for sputum for AFB, sputum for Gene Xpert and HIV serology status.

2.8 Spirometry

All patients underwent baseline sprirometry at diagnosis of TB before treatment initiation. Spirometry was done by using MIR Spirodoc spirometer model: 2001/72950/2009, manufactured by Medical International Research (MIR) in Italy. This is a portable user-friendly machine that complies with the 2019 American Thoracic Society and European Respiratory Society spirometry standards. The Spirometer consists of a replaceable mouthpiece (Spirette) that was replaced after each test (44). A pulmonologist at MUHAS trained the researchers on proper use of the spirometer prior to data collection.

Spirometry was done in a quiet environment, in a well-ventilated room that was separated from the waiting room where other patients were. Spirometry was done with the patient in standing position, erect with shoulders slightly back and chin slightly elevated. The operator (researcher) instructed and demonstrated the test to the patient in Swahili or English language.

The operator demonstrated the positioning of the mouth piece, correct posture, deep inspiration until completely full, then rapid expiration with maximum effort until completely empty (44,45).

After the patient had understood the instructions, he/she was guided into performing the maneuvers. Instructions were repeated as necessary with demonstration. A minimum of three maneuvers was done so as to obtain the best readings. If three attempts failed to produce acceptable readings, the patient was allowed to make further attempts but not exceeding eight attempts. The machine automatically grades each test according to the U.S.A National Lung Health Education Program in conformity to the ATS/ERS standards. Acceptable curves were those with grades A to C. The Spirometer selects automatically the attempt with the largest sum of FVC and FEV_1 as the best attempt to give the observed FVC, FEV_1 and FEV_1 /FVC ratio values for each patient. Only acceptable spirometry results were analyzed. All patients underwent a second spirometry from the 1st week of month 6 of treatment when they came for refill of anti-tubercular drugs.

From a local study (5) Spirometry reference equations were obtained. These reference equations enabled us to calculate the predicted (FEV_1, FVC and FEV_1/FVC). FEV6 was used as an acceptable surrogate of FVC test(46,47). In this study, the computation of the predicted lung function values was done automatically by the Spirodoc MIR Spirometer machine. This is in accordance to the reference equations obtained by *Knudsen et al* (5).

Table 1: Categorization of pulmonary functions in the study

	FEV1/FVC%	FVC predicted
Normal	> 70%	> 80%
Obstructive	< 70%	> 80%
Restrictive	> 70%	< 80%
Mixed	< 70%	< 80%

Source: American Thoracic Society. Standardized Pulmonary Function Report; 2017(48)***. American Academy of family physicians. Stepwise interpretation of lung functions; 2014***(49)***.***

2.9 Chest X-Ray

Poster anterior chest X- rays (CXR) were done for all patients only at TB diagnosis. The X-ray images/films were reviewed and interpreted by the principal investigator and independently by a radiologist. Any difference was settled by discussions for consensus. Interpretation of Chest X-ray was according to validated tool by Ann Ralf et al (50) for patients with pulmonary TB. The tool assigns a numerical score (0 - 100%) based on the extent of the abnormalities on X ray. Each hemi thorax on the X ray was divided into 10 equal areas each carrying 10% and estimation of the extent of damage was done. An average score of both hemi-thoraces was calculated to estimate the extent of damage of lung parenchyma on X ray. In addition, a score of 40 is added whenever a cavity was found regardless of the size or amount. Therefore, the total minimum score was 0 and maximum score 140

2.10 Study Outcomes

The study outcome of interest was the proportions of abnormal lung function, defined as obstructive, restrictive and mixed at recruitment and at PTB treatment completion.

2.11 Study Variables

2.11.1 Dependent Variables

The following variables were the dependent variables:

1. FEV_1 in liters at treatment initiation and at treatment completion
2. FVC in liters at treatment initiation and treatment completion
3. FEV_1: FVC at treatment initiation and treatment completion
4. Proportion of patients with Obstructive lung dysfunction at treatment initiation and at treatment completion.
5. Proportion of patients with restrictive lung dysfunction at treatment initiation and at treatment completion
6. Proportion of patients with mixed (obstructive and restrictive) lung dysfunction at treatment initiation and at treatment completion

2.11.2 Independent Variables

1. Age as a continuous variable, categorized as ≤30 years, 31-50 years and ≥51 years
2. Sex as a categorical variable, categorized as male or female
3. Level of education as a categorical variable, categorized as no education, primary, secondary and college/university
4. Smoking as a categorical variable, categorized as never, current and past
5. Alcohol use as a categorical variable, categorized as never, current and past
6. HIV status as a categorical variable, categorized as positive or negative
7. Diabetes Mellitus (DM) as a binary variable. Diabetes was defined as FBG≥7mmol/L(42) or being on treatment for DM.

8. Body Mass Index (BMI) as a continuous variable was categorized as normal (18.5 kg/m^2 to 24.9kg/m^2), under-weight (< 18.5 kg/m2) and overweight/obesity (≥25kg/m^2)
9. Sputum microbiology as a categorical variable, categorized as AFB+, AFB++, AFB+++, Scanty and GeneXpert positive.
10. Extent of lung damage on chest X-ray at PTB diagnosis as a continuous variable. This was defined as the proportion of total lung affected recorded in percentage (50).

2.12 Data Management and Analysis

Data was collected and entered using Kobo Tool box for medical sciences data. Data was transferred into STATA version 20 statistical software for analysis. The outcome variables (continuous variables) including; observed FEV_1, observed FVC and observed FEV_1/FVC at treatment initiation and completion (after 6 month) were summarized as means (sd) and medians (IQR). Non parametric paired t test (Wilcoxon rank signed test) was used to compare the change in lung volumes between treatment anti-TB initiation and treatment completion. Categorical variables including the socio-demographic, clinical characteristics, radiographic characteristics and patterns of abnormal lung functions (obstructive, restrictive and mixed) were summarized as proportions and compared using Chi-square χ^2 test.

Log binomial regression model was used to determine factors associated with abnormal lung functions at the end of treatment for PTB. All independent variables were analyzed in a univariate model to determine their risk ratio (RR), 95% CI and p-value. All variables that were statistically significant with a p- value of <0.2 at univariate analysis were entered in a multivariate model where a p value <0.05 was considered statistically significant.

2.13 Ethical Clearance

Ethical approval for conducting this research was obtained from the MUHAS senate for research and publications as the institutional research ethical committee. Permission to conduct the study was obtained from District Medial Officer of Temeke Municipality and Temeke, Mwananyamala and Amana regional referral hospitals. Consent/assents were obtained from all participants prior to data collection. Written consent was obtained from all study participants aged 18 and above. Parents/guardians of minors (<18 years) provided a written consent on behalf of the children after the minors gave their assent to participate in the study. Privacy and confidentiality were observed during all procedures. Confidentiality of patient's information was maintained throughout study. This was strict use of patient identification numbers and data was not shared with any third parties. Case record forms were stored in locked cabinets only accessible to the researchers. All clinical data of relevance to the management of patients were shared with the attending clinicians and referral to chest physicians was advised.

2.14 Data Dissemination

Findings of this study will be shared at MUHAS scientific conference July 2021. A copy of error free dissertation will be made available at the MUHAS library as well as MUHAS electronic repository. A manuscript will be prepared for publication in peer reviewed medical journals.

CHAPTER THREE

3.0 RESULTS

During the study duration, a total of 332 patients with pulmonary tuberculosis were recruited. A total of 32 patients had only one spirometry reading, so the remaining 300 patients completed both spirometry examinations. Reasons for non-response were; defaulting, death, moving out of the city and loss to follow up as shown in the consort diagram (figure 4).

In the social demographic characteristics described (Table 2), majority of the study participants were young 89% were 50 years or below. The highest proportions of the patients were in the age category of 31-50 years 157 (47.3%). About two thirds of the study participants were males 214 (64.5%), 195 (58.7%) had completed primary education, 266 (80.1%) were residents of Temeke. More than two thirds of the study participants were never smokers 228 (68.7%) while about 33 (9.9%) were current smokers and 71 (21.4%) had smoked in the past.

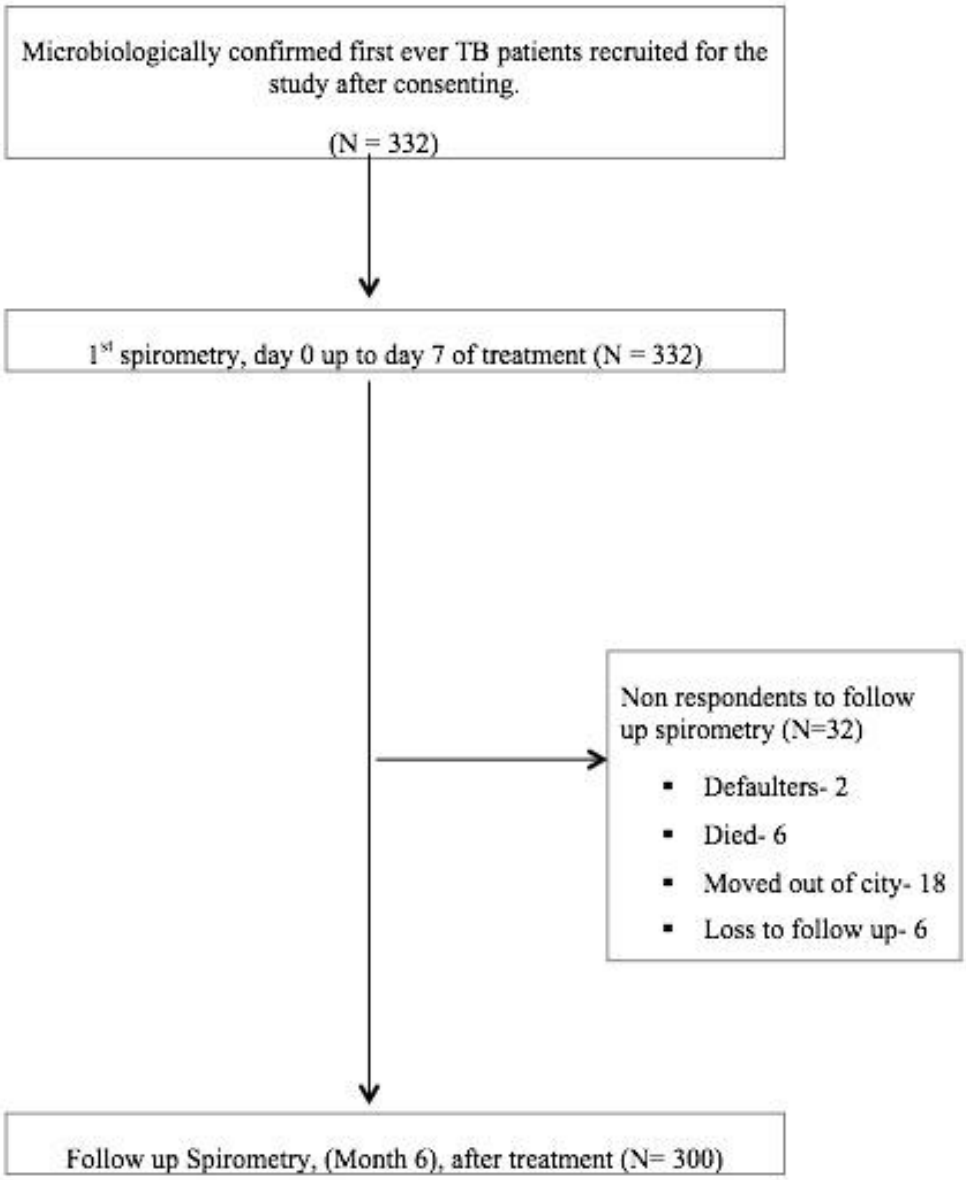

Figure 4: Consort flow diagram of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam

Table 2: Baseline socio-demographic and behavior characteristics of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam N=332

Variables and Categories	Frequency (n)	Percentage (%)
Age (years)		
≤30	139	41.9
31-50	157	47.3
≥51	36	10.8
Sex		
Female	118	35.5
Male	214	64.5
Marital status		
Single	151	45.5
Married/Cohabiting	140	42.2
Divorced/Widowed	41	12.4
Education		
No education	20	6
Primary	195	58.7
Secondary	98	29.5
College/University	19	5.7
Occupation		
Agriculture	20	6
Petty Trade	178	53.6
Industrial	10	3
Office	15	4.5
Others	109	32.8
Residence		
Temeke	266	80.1
Ilala	25	7.5
Kinondoni	41	12.4
Cigarette smoking		
Current	33	9.9
Past	71	21.4
Never	228	68.7
Alcohol consumption		
Current	47	14.2
Past	107	32.2
Never	178	53.6

Clinical characteristics of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam N=332

Table 3 summarizes the clinical characteristics of the study participants. 309 (93.1%) presented with history of cough for more than 2 weeks or more, about 50 (15.1%) had history of hemoptysis and most presented with 2 or more week's history of fever 234 (70.5%). Approximately half of the patients had drenching night sweats 185 (55.7%), while 99 (29.8%) had history of unintentional weight loss.

Almost half of the patient had normal BMI 162 (48.8%) while 138 (41.6%) were underweight. More than two thirds of the patients had a BCG scar 285 (85.8%), had normal fasting blood glucose levels 308 (92.8%) and no family history of diabetes 308 (92.8%). Majority of study patients 266 (80.1%) had diagnosis through gene X-pert 266 (80.1%) only 15 (4.5%) had sputum AFB +++. About 73 (22%) patients were HIV positive, most of the patients were HIV negative 259 (78%).

Table 3: Clinical characteristics of patients with Pulmonary Tuberculosis at the initiation of anti-tuberculosis chemotherapy in selected health facilities in Dar es Salaam N=332

Variables	Frequency (n)	Percentage (%)
Cough ≥ 2 weeks		
Yes	309	93.1
No	23	6.9
Hemoptysis		
Yes	50	15.1
No	282	84.9
Fever≥ 2 weeks		
Yes	234	70.5
No	98	29.5
Drenching night sweat		
Yes	185	55.7
No	147	44.3
Noticeable Weight loss		
Yes	99	29.8
No	233	70.2
Chest examination findings		
Normal	276	83.1
Abnormal	56	16.9
BMI		
Under weight	138	41.6
Normal	162	48.8
Overweight/obesity	32	9.6
Cervical lymph nodes		
Present	8	2.4
Absent	324	97.6
BCG scar		
Present	285	85.8
Absent	47	14.2
Diabetes Mellitus		
Yes	24	7.2
No	308	92.8
Family history of Diabetes		
Yes	30	9
No	302	91

Sputum microbiology		
Scanty	16	4.8
AFB +	26	7.8
AFB ++	9	2.7
AFB +++	15	4.5
Gene Xpert Positive	266	80.1
HIV status		
Positive	73	22
Negative	259	78

*Crackles/ bronchial breath sounds/ Rhonchi

3.1 Prevalence and patterns of lung function abnormalities of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam at treatment initiation N=332

The overall prevalence of lung function abnormality at baseline was 213 (64.1%). Most of the abnormality was due to restriction 120 (36.1%), followed by obstructive 62 (18.7%) and lastly mixed 31 (9.3%). About one third of the patients had normal lung functions 119 (35.8%). (Figure 5)

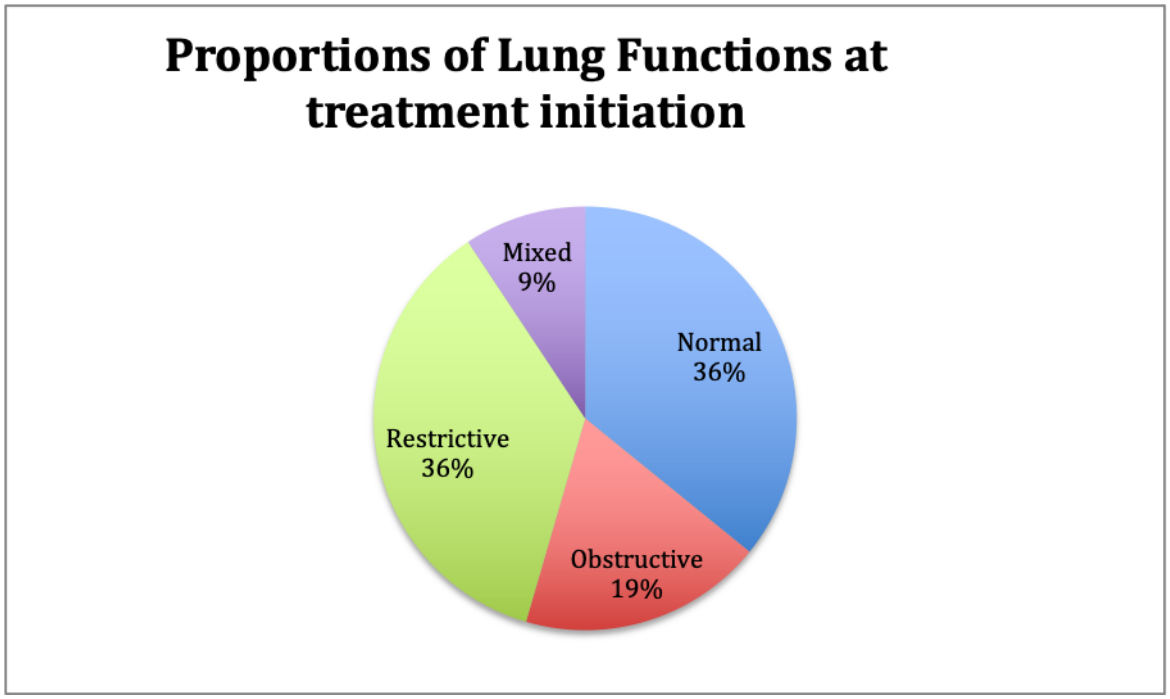

Figure 5: Prevalence and patterns of lung function abnormalities among patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam at treatment initiation N=332

3.2 Prevalence and patterns of lung function abnormalities of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam at treatment completion N=300

The overall prevalence of abnormal lung function at treatment completion was 142 (47.3%). Restrictive pattern was most common 100 (33.3%) followed by obstructive pattern 27 (9%) and lastly mixed pattern 15 (5%). More than half of the patients had normal lung functions 158 (52.7%). (Figure 6)

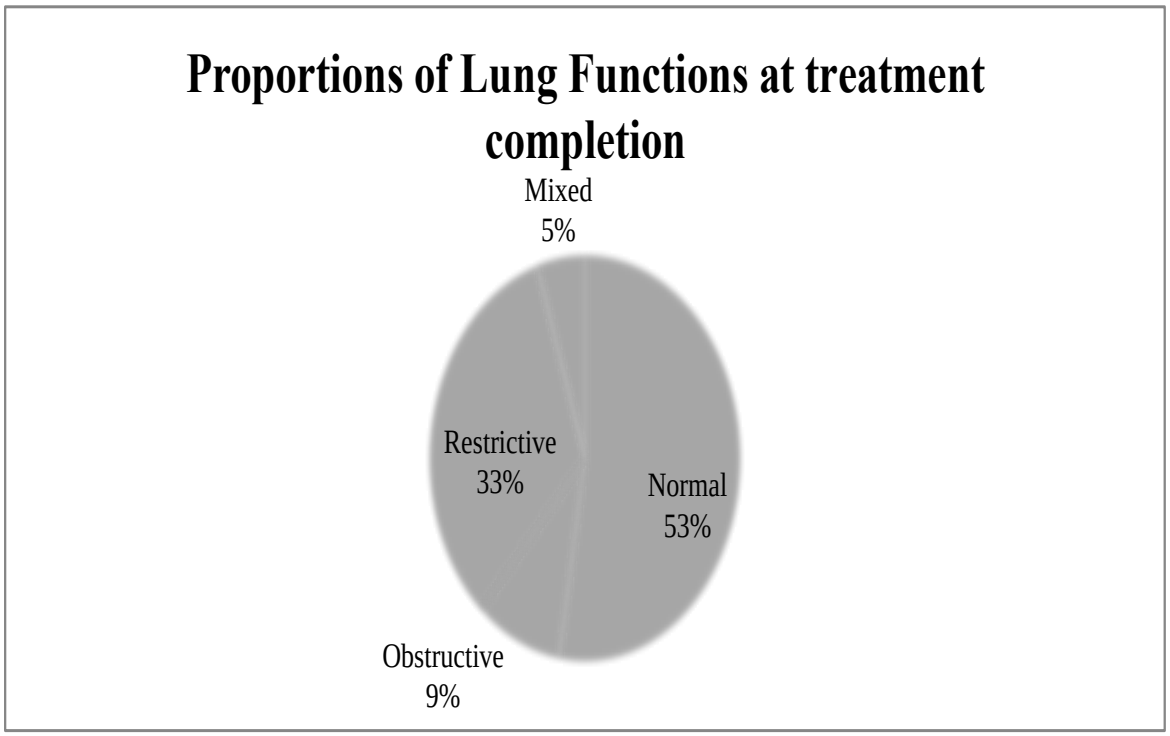

Figure 6: Prevalence and patterns of lung function abnormalities of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam at treatment completion N=300

3.3 Change in lung functions of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam following anti tubercular treatment.

As shown in table 4 below, the mean and median FEV1, FVC and FEV1/FVC were similar therefore we used means to summarize the changes in lung volumes before and after treatment for TB.

There was a significant increase in the median change in FEV1 ($p = 0.001$) and FVC ($p = 0.010$) at the end of TB treatment. However, there was no statistical significance in the change in FEV1: FVC $P= 0.058$. (Table 4)

Table 4: Distribution of mean and median lung volumes of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam following anti tubercular treatment

Variable	Observations (n)	Mean (SD)	Median (IQR)	P value
FEV1 (L)				
At start of TB treatment	300	2.20(0.84)	2.18 (1.16)	
At end of TB treatment	300	2.33(0.55)	2.33 (0.26)	**0.001***
FVC (L)				
At start of TB treatment	300	2.91(1.18)	2.82 (1.50)	
At end of TB treatment	300	3.05(0.77)	3.05 (0.31)	**0.010***
FEV1/FVC				
At start of TB treatment	300	80.51(46.21)	80.65 (23.30)	
At end of TB treatment	300	77.04(10.56)	76.40 (4.30)	0.058*

***Wilcoxon signed rank test**

3.4 Chest radiographic characteristics of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam.

All the patients (N=332) underwent posterior-anterior (PA) chest radiographs at the beginning of treatment. The most prevalent radiographic abnormality was lung consolidation 259 (78.1%) followed by nodules 47 (14.2%), pleural effusion 44 (13.3%) and cavitation 40 (12.1%). Other radiographic abnormalities included; fibrosis 14 (4.2%), tracheal deviation (due to fibrosis) 7 (2.1%), mediastinal shift 6 (1.8%) and lung collapse 11 (3.3%) (Figure 7)

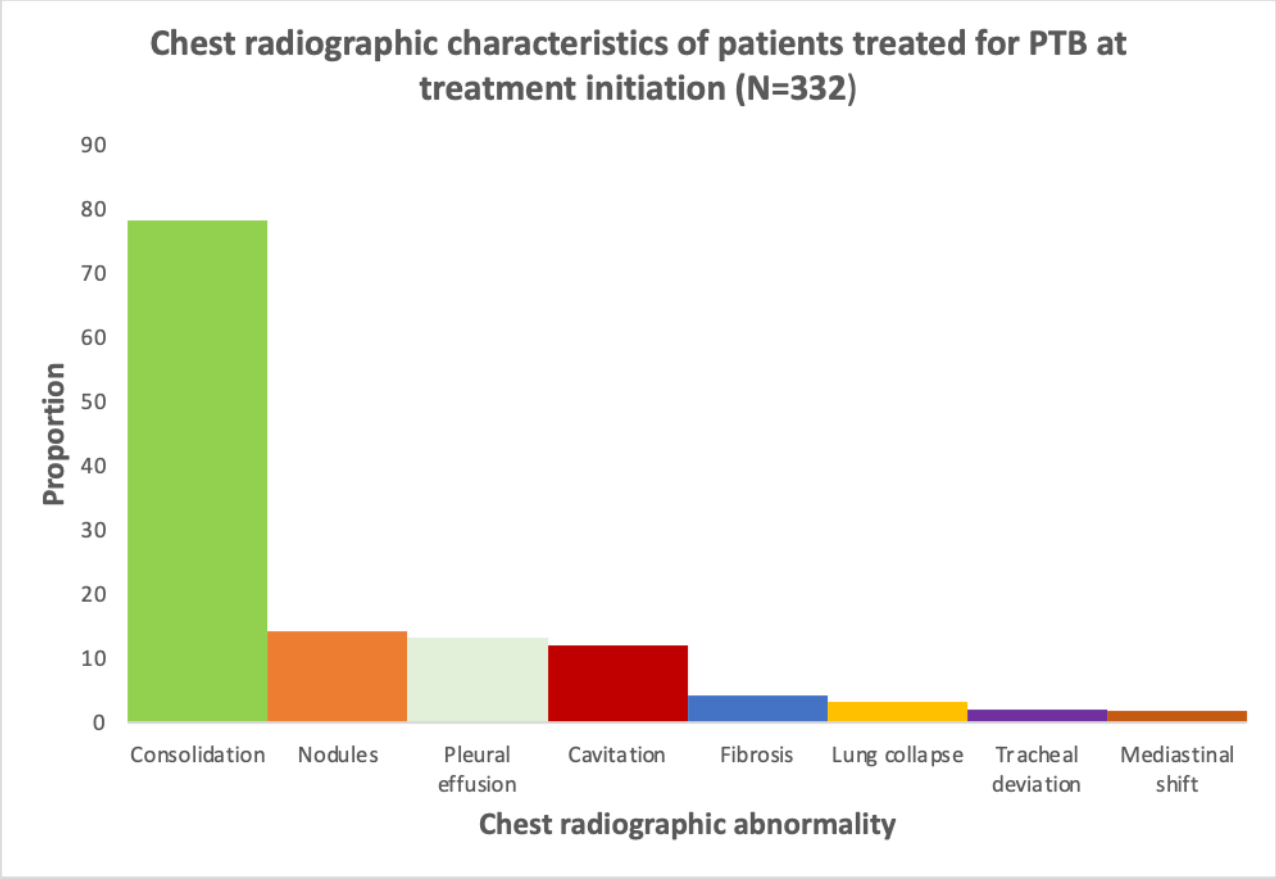

Figure 7: Chest radiographic abnormalities seen among patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam (N=332)

3.5 Lung functions by radiographic characteristics of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam at treatment initiation

The median chest x-ray score at the diagnosis (Ralph et al scoring tool) was 50%. Median chest x-ray score was not significantly associated with abnormal lung functions. Patients who had fibrosis at treatment initiation were more likely to present with obstructive or mixed compared to those with no fibrosis (p = 0.046).

Table 5: Lung functions Lung functions by radiographic characteristics of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam at treatment initiation N=332

		Lung Functions				P Value
		Normal	**Obstructive**	**Restrictive**	**Mixed**	
Median Chest X-ray Score (IQR)		33.4(26.7)	58.8(56.6)	45(50.1)	66.7(66.6)	0.236
CXR Abnormality	**Total 332**	**Normal n (%)**	**Obstructive n (%)**	**Restrictive n (%)**	**Mixed n (%)**	**P Value**
Cavitation						
Yes	40	11(27.5)	12(30)	12(30)	5(12.5)	0.149
No	292	108(36.9)	50(17.1)	108(36.9)	26(8.9)	
Fibrosis						
Yes	14	4(28.6)	4(28.6)	4(28.6)	2(14.3)	**0.046**
No	318	115(36.2)	58(18.2)	116(36.5)	29(9.1)	
Consolidation						
Yes	259	83 (32.0)	53(20.5)	99(38.2)	24(9.3)	**0.040**
No	73	36 (49.3)	9(12.3)	21(28.8)	7(9.6)	
Nodules						
Yes	47	8(17.0)	11(23.4)	20(42.6)	8(17.0)	**0.013**
No	285	111(38.9)	51(17.9)	100(35.1)	23(8.1)	
Pleural Effusion						
Yes	44	13(29.5)	5(11.4)	21(47.7)	5(11.4)	0.249
No	288	106(36.8)	57(19.8)	99(34.4)	26(9.0)	

Proportion of patients with obstructive and restrictive lung function abnormalities were significantly higher among those with consolidation compared to those without consolidation P = 0.04. Likewise, patients who had nodules on chest X ray were more likely to present with significantly higher proportions of abnormal lung functions P = 0.013. (Table 5)

3.7 Factors associated with abnormal lung functions of patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam at treatment completion N=300

In the multivariate log binomial regression being underweight (aRR 1.49 95% CI 1.13, 1.95 P=0.004), male sex (aRR 1.22 95% CI 1.19, 2.23 P=0.004), Cavitation on CXR at diagnosis (aRR 1.65 95% CI 1.08, 2.51 P=0.020) and lung parenchymal fibrosis on CXR at diagnosis (aRR 2.21 95% CI 1.37, 3.54 P=0.001) were found to be independently associated with abnormal lung function at treatment completion. (Table 6)

Table 6: Factors associated with abnormal lung functions in patients treated for Pulmonary Tuberculosis in selected health facilities in Dar es Salaam at treatment completion N=300

	Univariate analysis			**Multivariate analysis**		
Variable	**cRR**	**95% C.I.**	**P**	**aRR**	**95% C.I.**	**P**
Age groups						
≤30	1			1		
31-50	0.76	(0.58 – 1.00)	**0.053**	0.83	(0.61 – 1.14)	0.258
≥51	1.11	(0.78 – 1.59)	0.560	1.28	(0.87 – 1.89)	0.216
Sex						
Female	1			1		
Male	1.56	(1.16 – 2.11)	**0.003**	1.22	(1.19 – 2.23)	**0.004**
Education						
College/University education	1.65	(0.81 – 3.37)	**0.165**	2.28	(0.79 – 6.56)	0.126
No Formal education	1			1		
Primary school education	1.17	(0.63 – 2.18)	0.616	0.91	(0.49 – 2.07)	0.824
Secondary school education	1.28	(0.68 – 2.43)	0.444	1.17	(0.48 – 2.87)	0.731
Smoking						
Current	0.78	(0.47 – 1.29)	0.344			
Past	1.12	(0.85 – 1.49)	0.417			
Never	1					
Alcohol Use						
Current	0.89	(0.60 – 1.34)	0.595			
Past	1.05	(0.80 – 1.38)	0.720			
Never	1					
HIV						

No	1					
Yes	0.91	(0.66 – 1.25)	0.559			
BMI (Kg/m^2)						
Normal	1			1		
Underweight	1.51	(1.16 – 1.97)	**0.002**	1.49	(1.13 – 1.95)	**0.004**
Overweight/obesity	1.27	(0.81 – 1.98)	0.301	1.33	(0.86 – 2.06)	0.203
Sputum microbiology						
+	1			1		
++	0.64	(0.17 – 2.43)	0.514			
+++	0.77	(0.29 – 2.08)	0.606			
Gene x-pert positive/Scanty	0.79	(0.45 – 1.38)	0.408			
Diabetes Mellitus						
No	1					
Yes	0.87	(0.51 – 1.48)	0.603			
Cavitation						
No	1			1		
Yes	1.90	(1.29 – 2.78)	**0.001**	1.65	(1.08 – 2.51)	**0.020**
Fibrosis						
No	1			1		
Yes	2.16	(1.32 – 3.53)	**0.002**	2.21	(1.37 – 3.54)	**0.001**
Consolidation						
No	1			1		
Yes	0.92	(0.35 – 2.41)	0.868	0.97	(0.38 – 2.48)	0.948
Nodules						
No	1			1		
Yes	1.68	(1.14 – 2.48)	**0.008**	1.39	(0.90 – 2.15)	0.137
Pleural Effusion						
No	1			1		
Yes	1.28	(0.81 – 2.01)	0.293	1.00	(0.58 – 1.73)	0.986

Key: cRR: Crude Risk Ratio, aRR: Adjusted Risk Ratio, 1: Reference group, C.I: Confidence Interval, BMI: Body Mass Index, FBG: Fasting Blood Glucose, DM: Diabetes Mellitus

CHAPTER FOUR

4.0 DISCUSSION

In this longitudinal study among patients treated for pulmonary tuberculosis, we have the following main findings; first; about 2 out of 3 patients with for pulmonary tuberculosis have abnormal lung function at the time of treatment initiation. Second, at the end of treatment for PTB, about one out of two among those treated for PTB had abnormal lung function. Abnormality was evident in one out of two patients at the end of treatment. Third restrictive pattern was the predominant lung function abnormality both at the beginning and at the end of TB treatment. Four; there was a statistically significant increase in median FEV_1 and FVC at the end of TB chemotherapy in comparison to initiation of treatment. Five; underweight, male sex, cavitation and fibrosis on chest x-ray taken at treatment initiation were independently associated with increased risk of abnormal lung functions at treatment completion.

Our study found the overall prevalence of abnormal lung function at treatment initiation to be 64.1%. This has also been observed in other parts of the world, both African and non-African populations. In India (22) and Indonesia (16) the prevalence of abnormal lung functions at PTB treatment initiation was found to be lower compared to the present study. This might have been affected by small sample sizes employed in these studies or race. More recent studies have found higher prevalence of abnormal lung functions at intensive phase of PTB treatment 83.4% (51) or at completion of intensive phase 78% (52). Restrictive pattern of lung function abnormality at treatment initiation have been predominantly observed in most studies (23,51,52). This was also observed in the present study where the prevalence of restrictive pattern was 36% followed by obstructive pattern 18.7% and finally the mixed pattern (9%) . This may be due to both fibrosis associated with TB as well as pleurisy causing pain that may ultimately reduce inspiratory effort.

The present study found the overall prevalence of abnormal lung function at treatment completion to be 47.3%. Similar findings have also been demonstrated in other parts of the world, including India 47% (53) and 11.9% (22), Russia 47.7% (19), Indonesia 27% (17) and 24.6% (16). In Africa, studies have shown even higher prevalence's, probably due to

high burden of TB in this region of the world. A study in South Africa (18) found 52% prevalence of abnormal lung functions after 6 months of anti-tuberculosis medications. Similar studies in Nigeria and Mozambique found 72.1% and 68.9% prevalence of abnormal lung function post treatment respectively (52,54). In Tanzania, *Manji et al* found 74% prevalence of abnormal lung functions among patients post PTB treatment (26). This is higher than the present study.

The predominant patterns of lung function abnormality reported in majority of the studies is the restrictive pattern (27,52,54–57). These findings are similar to our study in which, restrictive patterns were found to lead by 33.3% followed by obstructive 9% and finally mixed 5%. However, there are some studies that have shown predominance of obstructive pattern of lung function abnormality post PTB treatment (19,23,24,26). A restrictive pattern may be associated with extensive TB lesions on chest X ray, these include consolidation, pleural effusion cavitation and fibrosis (56). In the present study, obstructive patterns were less, especially at treatment completion. This can be attributed to clearance of the endo-bronchial secretions by TB chemotherapy. Moreover, it can be because our study did not include patients with prior history of PTB. Obstructive patterns have been associated with previous history of PTB (58). In addition, Some studies have demonstrated obstructive patterns of lung function abnormality to be more prevalent among smokers compared to nonsmoking patients with PTB (19,24,26). In the present study, majority of the patients had never smoked cigarettes (68.7%). This might also explain why we observed less of obstructive patterns of lung function abnormality.

Our results show that there was a decrease in the proportion of patients with abnormal lung function at the end of treatment, from 64.1% at treatment initiation to 47.3% at treatment completion. Furthermore there is significant improvement in the median FEV1 from 2.18L IQR 1.16 to 2.33L IQR 0.26 (p=0.001) and FVC from 2.82L IQR 1.50 to 3.05L IQR 0.31 (p=0.010). Similar findings have also been reported in other studies. *Plit et al* in South Africa also showed improvement in lung functions following treatment completion(18). A recent prospective cohort study by *Khosa et al* in Mozambique demonstrated that the proportion of patients with abnormal lung function decreased at the end of treatment 68.9% compared to initiation of anti TB therapy 78% (52). *Milan et al* in southeastern Europe

found a significant improvement in the mean FVC at the end of 6 months with anti TB treatment (23). *Maguire et al* in Indonesia also found a decrease in the proportion of patients with lung function impairment from 39% to 24.6% after 6 months of treatment with anti TB chemotherapy (16). Furthermore, their study showed an increase in the proportion of predicted values of FEV_1 and FVC at the end of treatment. In the same region, *Anna et al* in another study showed a change in the mean predicted FEV_1 from 63% at baseline to 71% after 6 months of treatment (17). It suffices to acknowledge that even if there is improvement in lung functions, majority of TB patients still have abnormal lung function. This is well explained by our results in line with *Patil et al* in India who found that values for pulmonary function tests were still lower in some patients even after completion of 6 months of treatment with anti-tuberculosis chemotherapy (22). Important of note is that, the present study and most studies found significant improvement of lung functions with timely use of anti-tubercular chemotherapy. Furthermore, there is yet some residual lung function abnormality despite significant improvement in lung functions in half of the patients treated for pulmonary TB.

Notably in the present study we observed improvement/normalization of lung functions with anti-tubercular chemotherapy. Findings in the present study can be compared by the prevalence of lung function abnormality found by *Monica et al* in a recent case control study in Tanzania. *Monica et al* study found the prevalence of abnormal lung function to be 48.7% at the beginning of treatment among newly diagnosed adult PTB controls (59). This is lower compared to the present study. *Manji et al* in Dar es Salaam found the prevalence of abnormal lung function to be 74% towards the end of TB chemotherapy (26). The difference in prevalence of abnormal lung functions in the present study might have lowered because of the collective milestone that Tanzania as a country has made to combat TB.

Age group between 21-60 years, heavy smoking have been associated with increased risk of lung function abnormality in TB (26,55,60). In our study, this was not the case as non was significantly associated with lung function abnormality

Our study found that male sex was an independent predictor of abnormal lung function at the end of treatment p=0.004. *Manji et al* in Tanzania demonstrated similar findings (26) .Other studies found female sex was an independent predictor of abnormal functions (31,52). In this study 64.5% of patients were males. In our settings, other factors associated with abnormal lung functions such, as smoking and exposure to industrial toxins are more prevalent among males (61).

Being HIV positive or negative has not been shown in this study to be significantly associated with impaired lung function, despite being observed in other studies (26). In our study, two out of ten PTB patients had HIV infection. This number might be small to detect any changes. People Living with HIV (PLHIV) are more likely to present with extra pulmonary PTB (62). Furthermore, lung parenchymal disease observed in PTB patients is mainly a result of host immune response, which may be dampened in the setting of HIV infection thus they may present with less parenchymal abnormality and consequently less likely to present with abnormal lung function (62,63).

Our study found that being underweight at treatment completion was independently associated with 49% increased risk of abnormal lung functions. *Khosa et al* demonstrated similar findings in a follow up study in Mozambique (52). This highlights a potential avenue for intervention in the care of patients post PTB. Probably maintaining adequate body weight during and after the period of TB chemotherapy is pertinent to improved lung functions and reduction in lung function abnormalities. The present study also found that being overweight/obese at treatment completion was not significantly associated with increased risk of abnormal lung function. Although obesity is likely to be associated with obstructive pattern due to obstructive apnea, the proportion of obesity in our patients was almost negligible 9.6% (64).

Several studies have demonstrated the association between the extents of lung damage on chest X-ray with lung function abnormality (27,30,31,65,66). In the present study, fibrosis on chest x-ray was associated with restrictive lung function abnormality at treatment initiation and treatment completion. Furthermore, a higher median chest x-ray score was associated with abnormal lung functions at treatment initiation but not at treatment

completion. In our study, cavitation's and fibrosis on chest x ray were independently associated with increased risk of abnormal lung functions at the end TB treatment p=0.020 and p=0.001 respectively.

4.1 Strengths of Study

To the best of our knowledge, this is the first study to document abnormalities of lung functions before and after treatment for pulmonary tuberculosis. It was a multi-center study including five TB clinics located in three districts of Dar es Salaam, which increases the strength to generalize these findings for similar patients in Dar es Salaam. The study is informative as it gives an account of the evolution, chronicity and magnitude of abnormal lung functions and various associated factors. This study emphasizes to the clinicians the importance of continued monitoring of lung health post TB treatment.

This study also highlights potential avenues for intervention to prevent or reduce post TB lung disease

4.2 Limitations of the Study

1. We were unable to access baseline CD4 count which rendered difficult to examine the impact of severe immunosuppression on PTB and lung functions
2. The pleurisy due to pneumonia may limit inspiratory effort and hence lead to erroneous interpretation of pulmonary function which may be interpreted as restriction.
3. We did not perform bronchodilator reversibility testing to exclude un diagnosed asthma or COPD

CHAPTER FIVE

5.0 CONCLUSION

Two out of three patient starting treatments for pulmonary tuberculosis have abnormal lung function. Importantly, although lung function improves with anti-tuberculosis treatment, one out of two patients treated for PTB have residual lung function abnormalities at the end of their treatment predominantly presenting as restrictive pattern. Underweight, male sex, cavitation and fibrosis on chest x-ray taken at treatment initiation were found to be significantly associated with abnormal lung functions at the end of treatment for PTB.

5.1 RECOMMENDATIONS

Based on our findings we recommend the following:

- Further research is needed to document the patterns of lung abnormalities beyond six months of PTB treatment.
- There is need to engage TB program to establish and optimize guidelines for follow up of patients beyond TB chemotherapy period.
- We need further research to identify potential adjuvant therapies in addition to anti-TB chemotherapy, which will be employed rather early with the aim of improving lung health.

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APPENDIX

Appendix 1: Informed Consent Form - English Version

Consent to participate in the Study titled "Lung function abnormalities before and after treatment of Pulmonary Tuberculosis in selected health facilities in Dar es Salaam".

ID No……..

Dear Sir/Madam,

Introduction: My Name is Dr. Reinhard Lema a resident doctor in the department of Internal Medicine at Muhimbili University of Health and Allied Sciences (MUHAS). I am conducting a research study on change in lung functions among adults treated for Pulmonary Tuberculosis in Dar es Salaam. I kindly invite you to take part in this research study.

Purpose of the Study: I am conducting this study because Tanzania has a high burden of Pulmonary Tuberculosis. The disease causes irreversible lung destruction hence impaired lung functions and chronic lung diseases in 74% of patients despite successful cure. This study is useful as it evaluates the changes in the lung functions and magnitude of associated chronic lung diseases in PTB patients in our setting. Information generated from this study will aid improvement of long term respiratory medical care in PTB patients in Tanzania.

How to Participate: If you are willing to participate in this study, you will have to sign this consent form as an agreement for participation. I will then conduct a short interview on you to obtain the history of your disease followed by physical examination. Some investigations will be done on you as part of the interview, a pinprick to obtain a drop of capillary blood for random blood glucose checking. A venous blood sample will also be collected once from one of your hands for inflammatory markers testing. I will refer you to the hospital X-ray unit for a chest X-ray if you haven't done one during this illness. Finally I will measure your lung function using a Spirometer.

Spirometry is a physiological test that measures the maximal volume of air that an individual can inspire and expire with maximal effort. While standing you will be required to fully inspire air into your lungs and then fully expire with your mouth fixed on the mouthpiece of the spirometer. A minimum of three maneuvers will be done to obtain the measure of your lung functions. All the information gathered from the interview and investigations results will be recorded in a clinical research form. The whole interview is expected to take approximately 1 hour. Random Blood Glucose and Spirometry results will be shared with you at the end of the interview.

Confidentiality: Information obtained from this study will be kept confidential. Serial numbers instead of your name will be used in this study. If the results are published or presented, individual names will not be used. Electronically stored data will be password protected, clinical research forms will be locked in safety cabinet at the study office, which is not at the clinic.

Costs: You will not be required to pay any amount for your participation in this study. Nor will you receive any payment.

Voluntary participation and the right to withdraw from the study: Your participation is voluntary and you have the right to withdraw from participating in this study at any time. Whatever your decision may be, it will have no effect in any way to your rights to care and treatment.

Risks/Adverse effects: Spirometry may cause occasional minor discomfort and simple, self-limited arrhythmias especially in patients with cardiac diseases. There is potential risk of infection transmission by direct contact with surfaces such as mouthpiece and handheld spirometer. Indirect transmission by aerosol droplets generated into the air by patient blowing into the equipment. I have taken precaution to minimize this risk by adhering to the infection prevention and control guidelines.

Questions: If you have questions during the course of the study, concerning your rights as a participant, you may contact Prof. Tumaini Nagu, Supervisor for this study, MUHAS, P.O. Box 65001, Dar es Salaam, Tanzania.

Mobile phone: +255 743 265 265. E mail: jtjoyce20@gmail.com

Dr. Bruno Sunguya, Director of Research and Publication (DRC) of MUHAS, P.O. Box 65001, Dar es Salaam, Tanzania. Tel. 022-2152489. Email: drp.muhas.ac.tz.

Participant's Statement I agree to take part in this study on change in lung functions among adults treated for Pulmonary Tuberculosis in Dar es Salaam.

The nature and purpose of the study have been fully explained to me.

Signature of patient----------

Signature of the Investigator----------

Date ----------

Appendix II: Informed Consent Form- Swahili Version

FOMU YA OMBI LA RIDHAA

Ridhaa ya kushiriki katika utafiti kuhusu ‘‘Utendaji hafifu wa mapafu kabla na baada ya matibabu miongoni mwa wagonjwa wanaotibiwa kifua kikuu katika baadhi ya vituo vya afya Dar es Salaam’’.

Namba ya utambulisho.....

Kwa Bibi/Bwana,

Utangulizi: Jina langu ni Dr. Reinhard Lema, dakitari mwanafunzi wa shahada ya uzamili, idara ya magonjawa ya ndani, Chuo Kikuu cha Afya na Sayansi Shirikishi (MUHAS). Nafanya utafiti kuhusu mabadiliko ya utendaji kazi wa mapafu miongoni mwa wagonjwa watu wazima wanaotibiwa kifua kikuu Dar Es Salaam. Karibu sana ushiriki katika utafiti huu.

Nia na madhumuni ya utafiti huu. Ninafanya utafiti huu kwasababu Tanzania inauwingi wa wagonjwa wa kifua kikuu. Ugonjwa huu husababisha uharibifu wakudumu wa mapafu. Hupelekea kuathirika kwa utendaji kazi wa mapafu na magonjwa ya mapafu ya muda mrefu kwa asilimia 74 ya wagojwa pamoja na kupona kifua kikuu. Utafiti huu ni wa muhimu kwa sababu unachunguza maadiliko ya utendaji kazi wa mapafu na magojwa ya mapafu ya muda mrefu yanayohusiana nayo kwa wagonjwa wa kifua kikuu kwenye mazingira yetu. Yatokanayo na utafiti huu yatasaidia maboresho ya tiba ya muda mrefu kwa wagonjwa wa kifua kikuu Tanzania.

Jinsi ya kushiriki katika utafiti huu: Kama utakuwa tayari kushiriki kwenye utafiti huu, utaweka sahihi yako kwenye fomu hii ya idhini kuonyesha utayari wa kushiriki. Nitakuuliza maswali machache kuhusu historia ya ugonjwa wako na kisha nitakufanyia uchunguzi wa mwili wako. Nitakufanyia vipimo , nitakutoboa na sindano kidoleni kupata sampuli kidogo ya damu kwa ajili ya kupima kiwango cha sukari kwenye damu. Nitatumia sindano kuchukua sampuli ya damu kwenye mshipa wa mmoja wapo ya mikono yako mara moja kwa ajili ya kupima viashiria vya Inflamesheni. Utafanya kipimo cha X-ray ya kifua

hapa hospitali kama hukuwahi kukifanya tangu ugonjwa huu uanze. Mwisho nitapima utendaji kazi wa mapafu yako na kipimo kinachoitwa Spirometer.

Spirometer hupima kiasi cha hewa ambacho mtu anaweza kuvuta kuingia kwenye mapafu na kukitoa kwa nguvu zake zote. Ukiwa umesimama, utatakiwa kuvuta hewa ndani kwenye mapafu kisha kuitoa yote mdomo wako ukiwa umeunganishwa kwenye sehemu ya kuwekea mdomo ya spirometer. Zoezi hili litafanyika kwa uchache mara tatu kupata vipimo vya utendaji kazi wa mapafu yako. Taarifa zako zote zitaandikwa kwenye fomu maalum ya utafiti. Ninategemea shughuli zote kuchuku wastani wa saa moja. Majibu ya kipimo cha sukuri na Spirometer utayapata baada ya vipimo.

Utunzaji wa siri: Taarifa zote zitakazochukuliwa katika utafiti huu zitatunzwa kwa usiri. Namba ya utambulisho itatumika badala ya jina lako. Kama matokeo ya utafiti yakichapishwa au kutangazawa, jina lako halitatumika. Data zitakazotunzwa kwenye compyuta yitatunzwa kwa kutumia neno siri. Fomu zote za utafiti zitafungiwa kwenye kabati maalum nje ya hospirtali.

Gharama za Ushiriki: Ushiriki katika utafiti huu ni bure yaani hakuna gharama yeyote kwa mshiriki. Hutalipwa fedha yoyote kwa ushiriki wako.

Hiyari ya kushiriki na kujitoa katika utafiti huu Ushiriki katika utafiti huu ni wa hiyari na pia ni haki yako kujitoa katika utafiti huu muda wowote unapohisi kufanya hivyo. Maamuzi yako ya kuamua kutoshiriki au kujitoa katika utafiti huu hayataathiri haki yako ya kupata huduma na matibabu.

Hatari/Maudhi yatokanayo na Kushiriki Utafiti huu: Kipimo cha Spirometer kinaweza kuleta usumbufu mdogo na hali ya mpito ya muda mfupi ya mapigo ya moyo kwenda mbio hasa kwa watu wenye maradhi ya moyo. Ipo hatari ya maambukizi kwa kushika sehemu za Spirometer na maambukizi mengine kwa njia ya hewa wakati wa kupuliza hewa ndani ya Spirometer. Nimechukuwa tahadhari ya kudhibiti hatari hii kwa kuzingatia kanuni za kitabibu za kudhiti maambukizi.

Maswali: Kwa maswali au maoni kuhusiana na utafiti huu au kuhusu haki zako kama mshiriki, tafadhali wasiliana na Prof. Tumaini Nagu**,** msimamizi mkuu wa utafiti huu, MUHAS, S.L.P 65001, Dar es Salaam**,** Tanzania. Simu: +255 743 265 265. Barua pepe: jtjoyce20@gmail.com.

Dr. Bruno Sunguya, Mkurugenzi wa Tafiti na Uchapishaji wa tafiti. MUHAS, S.L.P 65001, Dar es Salaam, Tanzania. Simu: 022-2152489. Barua pepe: drp.muhas.ac.tz

Kauli ya Mshiriki: Nimekubali kushiriki kwenye utafiti huu wa maadiliko ya utendaji kazi wa mapafu miongoni mwa watu wazima wanaotibiwa kifua kikuu Dar es Salaam.

Asili na madhumuni ya utafiti yemeelezwa kwa ufasaha kwangu.

Sahihi ya Mshiriki……

Sahihi ya Mtafiti…….

Tarehe ……..

Appendix III: Questionnaire (Clinical Research Form)

LUNG FUNCTION ABNORMALITIES BEFORE AND AFTER TREATMENT FOR PULMONARY TUBERCULOSIS IN SELECTED HEALTH FACILITIES IN DAR ES SALAAM.

ID NUMBER:……

PTB Number ……..

Hospital Name / TB Clinic ……..

Date of starting treatment of PTB ……

Treatment of TB(New case):

a) On Anti TBs ( ) Number of days on Anti-TB chemotherapy ……..
b) Not started Anti TBs ( )

Address:

Street…… P.O Box……..

Phone number …….. ……. Next of

Kin……

Ward……

District……

Region……..

Part 1: Socio-Demographic Data

1. Age……..
2. Gender
    a) Male
    b) Female
3. Marital Status
    a) Single
    b) Married
    c) Divorce
    d) Separated
    e) Widow
    f) Others

4. Education Level
    a) No formal education
    b) Primary school education
    c) Secondary school education
    d) College/University education
5. Family size……
6. Occupation
    a) Office / white color job
    b) Mining
    c) Automobile industry
    d) Petty trader
    e) Farmer
    f) Student
    g) Pensioner
    h) Others…….

Part 2: Factors associated with change in Lung functions.

7. Alcohol use
    a) Never
    b) Current
    c) Past
8. Smoking
    a) Never
    b) Current
    c) Past
9. HIV status
    a) Positive
    b) Negative
    c) Unknown
10. If the answer is positive, which regime are you currently using?……..……..
11. Baseline CD4 count ……..

12. Diabetes Mellitus history
    a) Yes
    b) No
    c) Don't know

Part 3: Clinical features presented with Pulmonary TB

	Yes	No	Duration (days)
13. Fever	☐	☐	
14. Cough	☐	☐	
15. Drenching Night sweats	☐	☐	
16. Weight loss	☐	☐	
17. Hemoptysis	☐	☐	
18. Chest pain	☐	☐	
19. Difficulty in breathing	☐	☐	
20. Loss of appetite	☐	☐	
21. Yellow coloration eye	☐	☐	
22. Nausea	☐	☐	
23. Vomiting	☐	☐	

Part 4: Physical examination findings

24. Temperature _____ ^{o}C
25. Weight _____kg
26. Height _____cm
27. BMI……..m^2/kg
28. Waist Circumference……..cm
29. BCG scar
    1. Present
    2. Absent

General	**Yes**	**No**	
30. Cervical LN:	☐	☐	cm _____
31. Sub mental/ mandibular	☐	☐	cm _____
32. Pre auricular LN	☐	☐	cm_____
33. Post auricular	☐	☐	cm _____

34. Oral candidiasis ☐ ☐
35. Angular stomatitis ☐ ☐
36. Respiratory exam

RR:_____/Min

	Yes	No
Crackles	☐	☐
Rhonchi	☐	☐
Consolidation	☐	☐
Pleural effusion	☐	☐

Other _____

	Normal	Abnormal	Specify
37. Neurology	☐	☐	_____
38. Abdomen	☐	☐	_____
39. Cardiovascular	☐	☐	_____

40. Random blood glucose level……..mmol/L
41. Systolic blood pressure _____mmHg
42. Diastolic Blood Pressure _____mmHg
43. Sputum AFB microscopy results
    1. Negative
    2. Scanty
    3. +
    4. ++
    5. +++

Part 5: CHEST RADIOGRAPHICAL FINDINGS

1. Abnormalities	**Upper**	**Middle**	**Lower**
i. Cavities			
ii. Fibrosis			
iii. Infiltrates			
iv. Nodules			
v. Collapse			
vi. Others (specify below)			

2. Pleural Abnormalities	**Yes**	**No**	**R**	**L**
Apical cap				
Pleural thickening				
Pleural Effusion				
CP Angle obliteration				

3.Central structure abnormalities	**Yes**	**No**
i. Tracheal Deviation		
ii. Hilar Elevation		
iii. Mediastinal shift		
iv. Pericardial effusion		

4.Lymphadenopathy	**Yes**	**No**	**R**	**L**
i. Hilar				
ii. Mediastinal				

5. Any other abnormalities	**Yes**		**No**	
Specify				

Part 6: Lung function test findings at treatment initiation

FEV_1	
FVC	
FEV1/ FVC	

Part 7: Lung function test findings at treatment completion

FEV_1	
FVC	
FEV1/ FVC	

Appendix IV: Questionnaire (Swahili- Version)

UTENDAJI KAZI HAFIFU WA MAPAFU KABLA NA BAADA YA MATIBABU MIONGONI MWA WAGONJWA WANAOTIBIWA KIFUA KIKUU KATIKA BAADHI YA VITUO VYA AFYA DAR ES SALAAM.

Fomu ya utafiti wa kliniki

Namba ya dodoso…….....

Namba ya matibabu ya kifua kikuu…….

Jina la Hospitali au kliniki ya kifua kikuu……..

Tarehe ya kuanza matibabu ya kifua kikuu ……

Tiba ya kifua kikuu:

a) Ameanza dawa ( ) Idadi ya siku za kutumia dawa za kifua kikuu …….
b) Hajaanza dawa ( )

Anwani

Mtaa …… S.L.P……..

Namba ya simu …….. ……. Jamaa wa karibu……

Kata ……

Wilaya ……

Mkoa ……..

Sehemu kwanza: Takwimu za kijamii za mshiriki

1. Umri …….
2. Jinsia
   a) Mwanaume
   b) Mwanamke
3. Hali ya ndoa
   a) Sijaolewa
   b) Nimeolewa
   c) Mtalaki
   d) Tumetengana
   e) Mjane au mgane
   f) Nyinginezo

4. Kiwango cha elimu
    a) Sijasoma
    b) Elimu ya msingi
    c) Elimu ya sekondari
    d) Elimu ya chuo kikuu
5. Ukubwa wa familia……
6. Kazi
    a) Ajira ya Ofisini
    b) Migodini
    c) Kiwanda cha magari
    d) Biashara ndogondogo
    e) Mkulima
    f) Mwanafunzi
    g) Mstaafu
    h) Nyingineyo

Sehemu ya pili: Sababu zinazohusiana na mabadiliko ya utendaji kazi wa mapafu.

7. Matumizi ya vileo
    a) Sijawahi tumia
    b) Natumia
    c) Nilitumia zamani
8. Uvutaji sigara
    a) Sijawahi
    b) Natumia
    c) Nilitumia zamani
9. Hali ya maambukizi ya virusi vya UKIMWI,
    a) Nimeambukizwa
    b) Sijaambukizwa
    c) Haijulikani
10. Kama jibu nimeambukizwa, ni dawa gani za UKIMWI unazotumia?_____
11. Kiwango cha CD4 ulichonacho ……..

12. Historia ya ugonjwa wa kisukari
    a) Ndio
    b) Hapana
    c) Sijui

Sehemu ya tatu: Dalili za kitabibu zinazoambatana na kifua kikuu cha mapafu.

	Ndio	Hapana	Muda
13. Homa	☐	☐	
14. Kikohozi	☐	☐	
15. Jasho tiririka usiku	☐	☐	
16. Kupungua uzito	☐	☐	
17. Kukohoa damu	☐	☐	
18. Maumivu ya kifua	☐	☐	
19. Kushindwa kupumua vizuri	☐	☐	
20. Kupoteza hamu ya chakula	☐	☐	
21. Manjano kwenye macho	☐	☐	
22. Kichefuchefu	☐	☐	
23. Kutapika	☐	☐	

Sehemu ya nne: Matokeo ya vipimo vya mwili

24. Hali joto _____^{o}C
25. Uzito _____kg
26. Urefu _____cm
27. BMI …….m^2/Kg
28. Mzingo wa kiuno…….cm
29. Kovu BCG
    1. Lipo
    2. Halipo

Jumla	**Ndio**	**Hapana**	
30. Tezi za shingoni	☐	☐	cm _____
31. Tezi chini ya taya	☐	☐	cm _____
32. Tezi kabla ya sikio	☐	☐	cm_____
33. Tezi baada ya sikio	☐	☐	cm _____

34. Fangasi ya kinywa ☐ ☐

35.Kuathiriwa kingo za mdomo ☐ ☐

(Angular stomatitis)

36. Uchunguzi katika njia ya upumuaji

Kasi ya kupumua (RR):_____/Dakika

	Ndio	Hapana
Crackles	☐	☐
Mlio kama kukoroma (*Rhonchi)*	☐	☐
Consolidation	☐	☐
Majimaji katika mfuko wa mapafu *(Pleural effusion)*	☐	☐

Nyinginezo _____

	Kawaida	Sikawaida	Taja
37. Mishipa ya fahamu	☐	☐	_____
38. Tumbo	☐	☐	_____
39. Moyo na mishipa	☐	☐	_____

40. Kiasi cha sukari kwenye damu cha muda wowote _____mmol/L.

41. Kiwango cha juu cha msukumo wa damu (systolic) _____mmHg

42. Kiwango cha chini cha msukumo wa damu (diastolic) _____mmHg

43. Matokeo ya kipimo cha makohozi kwa njia ya hadubini

1. Hakuna
2. Kidogo *(scanty)*
3. +
4. ++
5. +++

Sehemu ya tano: Matokeo ya kipimo cha mionzi ya mapafu *(radiographical)*

1. Utofauti	**Juu**	**Katikati**	**Chini**	
i. Matundu *(Cavities)*				
ii. Fibrosis				
iii. Majimaji *(Infiltrates)*				
iv. Viuvimbe *(Nodules)*				
v. Wingi *(Mass)*				
vi. Collapse				
vii. Nyinginezo *(Taja)*				
2. Utofauti wa pleural	**Ndio**	**Hapana**	**Kulia**	**Kushoto**
Apical cap				
Kuvimba kwa kuta za mapafu *(Pleural thickening)*				
Majimaji kuzunguka mapafu *(Pleural Effusion)*				
Uhalibifu wa kona ya CP *(CP Angle obliteration)*				

3.Utofauti katika muundo wa kati	**Ndio**	**Hapana**
i. Kuhama kwa njia ya hewa *(Tracheal Deviation)*		
ii. Kuinuka kwa tezi katika mapafu (*Hilar Elevation)*		
iii. Kuhama kwa eneo lilloko katikati ya mapafu *(Mediastinal shift)*		
iv. Mkusanyiko wa majimaji kuzunguka moyo *(Pericardial effusion)*		

4. *Lymphadenopathy*	**Ndio**	**Hapana**	**Kulia**	**Kushoto**
i. Hilar				
ii. Eneo la kati ya mapafu mawili (*Mediastinal)*				

5. Tofauti zinginezo	**Ndio**		**Hapana**	
Eleza				

Sehemu ya sita:
Matokeo ya kipimo cha ufanyaji kazi mapafu mwanzoni mwa matibabu.

FEV_1	
FVC	
FEV1/ FVC	

Sehemu ya saba:
Matokeo ya kipimo cha ufanyaji kazi mapafu mwishoni mwa matibabu

FEV_1	
FVC	
FEV1/ FVC	