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Pulmonary function and Quality of Life in patients with treated smear positive pulmonary tuberculosis at Riruta, Kangemi and Kibera Tuberculosis Clinics in Nairobi

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A thesis submitted in partial fulfillment of the requirements for the degree of Master of Medicine in Internal Medicine of the University of Nairobi

Declaration

I declare that this research is my original work and has not been presented for the award of a degree at any other university

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Acknowledgement

Abstract

Background: Pulmonary impairment following TB treatment has been described in selected populations. No previous studies have evaluated the effects of treated pulmonary TB on lung function and QOL in Kenya.

Methods: This was a cross sectional study conducted at Riruta, Kangemi and Kibera Health Centres between May and June 2012. Patients with cured smear positive TB in the last 2 years were assessed for their current health status using the St Georges Respiratory questionnaire and pulmonary function using spirometry.

Results: Of 409 eligible patients, 183 (58% males) were enrolled. There were no significant differences in the demographic profiles of the study subjects and non responders.

53 patients (29%) had pulmonary impairment, the commonest being restrictive defects in 42 patients (23%, 95% CI 16.8-29.1%), obstructive defects in 9 patients (5%, 95% CI 1.76-8.08%) and combined defects in 2 patients (1%, 95% CI -0.4-2.61%). Patients with abnormal lung function were younger {median age, 29 years (IQR, 22-36) vs 34 years (IQR, 27-39), p= 0.036}, more likely to be underweight (38% vs 9%, P= <0.005) and had a lower prevalence of HIV (20.8% vs 37.7%, p=0.027). Low BMI was the only independent predictor of pulmonary function abnormality (p=0.001). The median QOL total score from the SGRQ was 3.16 (IQR, 0 – 8.9) signifying good QOL. There was no correlation between QOL and pulmonary function.

Conclusions: The commonest lung function abnormality post TB treatment was restrictive defect. The QOL in this population was good. Body mass index was the only independent predictor of abnormal pulmonary function.

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List of Acronyms

ATS – American Thoracic Society

CDR – Case Detection Rate

CNR – Case Notification Rate

COPD – Chronic Obstructive Pulmonary Disease

EBTB – Endobronchial Tuberculosis

FEV1 – Forced Expiratory Volume in one Second

FVC – Forced Vital Capacity

HIV – Human Immunodeficiency Virus

HRQL – Health Related Quality of life

LTBI – Latent Tuberculosis Infection

OR – Odds Ratio

PFT – Pulmonary Function Test

PTB – Pulmonary Tuberculosis

QALY – Quality Adjusted Life Years

QOL – Quality of Life

TB – Tuberculosis

WHO – World Health Organization

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Chapter one

1.1 Introduction and Background

TB is a global health problem with an estimated 8.7 million new cases and 1.45 million deaths occurring in 2011 (1). There were 5.8 million notifications of new and recurrent TB cases, equivalent to 65% of the estimated number of incident cases in 2011. India and China accounted for 40% of the world's notified cases in 2011, Africa accounted for 24% and the 22 high-TB burden countries accounted for 82% (1)

Kenya is ranked 13th among the 22 high burden countries (1). Based on the 2010 estimates, the number of reported TB cases has increased tenfold from 11,625 in 1990 to 106, 083 cases in 2010. Of the reported cases in 2010, 34% were smear positive, 30% smear negative, 10% retreatment cases, 16% extra-pulmonary TB and 10% did not have smears done (2). Case Notification Rates (CNR) increased from 53/100,000 population for all forms of TB and 32/100,000 population for sputum smear-positive PTB cases in 1990 to 271/100,000 population and 95/100,000 population respectively in 2010. The major reason for the increasing burden of TB in Kenya is the concurrent HIV epidemic (2)

Tuberculosis treatment results for TB patients started on treatment in 2009 show treatment success rates of 85.86% for new smear-positive pulmonary TB cases (2) The case detection rate has also risen to 80% making Kenya one of the African countries that have achieved the WHO targets of 70% case detection rate of new sputum positive cases and 85% treatment success rate.

Although completion of treatment and microbiological cure for active cases of TB is the most important priority of TB control programs, approximately a third of patients who have completed a course of treatment for pulmonary tuberculosis, are often left with significant respiratory disability due primarily to fibrocavitary lung disease (3-7)

Current tuberculosis treatment guidelines suggest that performing a chest radiograph at the completion of therapy may be useful but is not essential (8) Additional evaluation for patients after tuberculosis has been cured is currently recommended only for those patients who have suggestions of disease recurrence (8)

TB is also associated with significant societal and personal loss of health quality of life after a microbiological cure (9-11) Despite the association between economic disadvantage and PTB, (9) little attention has been given to the short- and long-term effects of PTB in terms of disability (and the effect this has on productivity) and quality of life.

No studies have addressed the sequele of TB in Kenya despite Kenya being one of the high TB burdened country. Therefore, the objective of this study was to describe the pulmonary function status and health related quality of life of patients with smear positive TB after achieving a microbiological cure with short course chemotherapy.

Chapter Two

Literature Review

2.1 Introduction

The relationship between impairment of lung function and PTB has been well described in the pre-chemotherapy era and in some chemotherapy era literature. Previous studies in this subject in Sub-Saharan Africa have been done mainly among gold miners in South Africa. The commonest lung abnormality post TB is restrictive lung defect (12-14). However, even in patients with obstructive airway impairment, post pulmonary tuberculosis can be an important cause. PTB has been observed to be an etiologic factor of both COPD (15) and asthma (16)

2.2 Prevalence of Respiratory abnormalities post PTB treatment

TB can cause chronic impairment of lung function which increases incrementally with the number of episodes of TB (17). In a study done in South Africa that evaluated current miners with a history of tuberculosis who had been identified through screening up to 31 years prior to their evaluation, the investigators found that the proportion of impaired subjects increased with episodes of tuberculosis. Impairment was identified in 18%, 27%, and 35% of subjects, respectively; after one, two, or three episodes. (17) The loss of lung function was highest within six months of diagnosis of TB and stabilized after 12 months when the loss was considered to be chronic (17).

In a retrospective cohort study undertaken among black South African miners to determine whether an episode of PTB even though treated i) caused an accelerated loss of lung function in comparison to miners of same age who had not had TB during the study period and ii) causes chronic respiratory symptoms (12) After controlling for age, height, baseline lung function, silicosis, years of employment, smoking and other respiratory diagnoses, pulmonary TB during the follow-up period was associated with a mean excess loss of 40.3 ml/year in FEV1 and 42.7 ml/year in FVC. Lung function loss was greater among those with more severe or later clinical presentation of TB (12) At the time of follow-up lung function testing, miners who had had TB, compared to those who had not had TB, had more than a twofold greater risk of having

respiratory symptoms of cough, breathlessness and wheezing and a tenfold greater risk of having restrictive lung disease, but were not at greater risk of having obstructive lung disease (12)

In a case-control study using pulmonary function tests of patients with culture-confirmed pulmonary tuberculosis and a comparison group with Latent tuberculosis infection (LTBI) (18), survivors of TB were 5.4 times more likely to have a decline in FEV1 and FVC than were LTBI subjects after adjusting for risk (age, BMI, country of birth, gender, and smoking) (18)

In a population based multicentre study carried out by the Latin America Project for the investigation of obstructive disease (PLATINO) team (19) ,the overall prevalence of airflow obstruction (FEV1/FVC post-bronchodilator ,0.7) was 30.7% among those with a history of tuberculosis, compared with 13.9% among those without a history. Males with a medical history of tuberculosis were 4.1 times more likely to present with airflow obstruction than those without such a diagnosis. This remained unchanged after adjustment for confounding by age, sex, schooling, ethnicity, smoking, exposure to dust and smoke, respiratory morbidity in childhood and current morbidity. Among females, the unadjusted and adjusted odds ratios were 2.3 and 1.7, respectively (19). This demonstrates that TB is associated with significant airflow obstruction.

In a study to assess the influence of antimicrobial chemotherapy on spirometric parameters and pro-inflammatory indices in severe pulmonary tuberculosis, Anderson et al; (14) showed that despite radiological improvement during TB treatment occurring in 54% of patients, 28% and 24% of the patients were left with residual airflow obstruction and restrictive defects respectively.

2.3 Effects of PTB on lung function
TB is associated with significant and varying degrees of airflow limitations. TB survivors frequently experience structural and functional lung sequeale. Residual damage after

completion of TB treatment includes varying degrees of fibrosis, brochovascular distortion, emphysema and brochiectasis (19). Studies of pulmonary function in individuals with pulmonary tuberculosis show variable patterns and severity of impairment (17,18, 20).

2.3.1 TB and Restrictive lung disease

2.3.1a Parenchyma lung disease

The pulmonary tissue response to the inhalation of mycobacterium tuberculosis is characterized by hypersensitivity leading to necrosis that is surrounded by inflammatory cells. These cells form a fibrotic tissue encompassing the area involved in the inflammatory process, isolating it from the remaining lung parenchyma. Limitation of infection at this stage has no significant effect on pulmonary function or gas exchange abnormality. Decreased static and dynamic lung volume, reduced FEV1 proportionally to FVC and reduction in diffusion capacity can result from necrotizing tuberculous pneumonitis (21). Massive release of mycobacteria into pulmonary circulation with secondary hyperimmune and inflammatory reaction leads to infiltrative and obliterative endarteritis and basal membrane thickness. Whether partial or complete resolution of the lung function abnormalities will take place depends on the extent of scarring and fibrous tissue deposition after the acute injury (21). Most patients who survive the acute attack will have a mild degree of parallel reduction in both FEV1 and FVC three months after hospital discharge that will continue to improve during the first year. A subset of survivors might end up with permanent residual abnormality (7).

Long and coworkers (20) reported milder changes in pulmonary function in PTB patients with parenchyma lung disease. They prospectively studied 25 patients with PTB. Pulmonary function tests were performed at baseline, 1 and 6 month intervals. Patients with non-cavitary disease (15 cases) had virtually normal lung function while those with cavitary disease (10 cases) had very mild restrictive changes (vital capacity 88% of the predicted). In the same study, some correlation of lung function with structure (number of cavities) was found.

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2.3.1b Pleural disease and fibrothorax

Pleural involvement is common in tuberculous infection. It usually occurs from direct extension from a subpleural focus. Tuberculous pleural effusion and residual pleural thickness may occur in upto 30% of patients (22). The exact pathogenesis behind the development of pleural thickness is probably related to a delayed hypersensitivity reaction rather than to an inflammatory response to infection (22).

Pleural TB leads to the thickening of the pleura due to tuberculous pleuritis. Therefore, delays in diagnosing TB have been shown to relate directly to the severity of pulmonary damage and the frequency of comorbidities, negatively affecting quality of life (23)

2.3.2 TB and obstructive lung disease

Obstructive airway disease came to be recognized as a complication of advanced PTB within a few years of the advent of effective chemotherapy.

Hallet and Martin reported on 710 patients with PTB admitted to Firland Sanitarium (5) The obstructive pattern was found in 34% of these patients and occurred more frequently in men than in women although the difference was not statistically significant. The incident of obstructive abnormality increased with age and duration of cigarette smoking. However, when age factor was controlled, the smoking relationship was no longer significant.

Anno and Tomaschefsky in 1995 reported pulmonary function studies in 25 patients with proven PTB. They demonstrated that airway obstruction and pulmonary hyperinflation were more common in far advanced than in less advanced disease (6)

Lee and Chang,(7) compared lung function in patients with chronic airflow limitation due to tuberculous destroyed lung and COPD patients and concluded that FVC and post bronchodilator FEV1 of post tuberculous patients were lower compared to those of COPD. Hence,

bronchodilator therapy could be useful for treating chronic airflow limitation in post tubercular cases especially those presenting with wheezing.

In a population based study done in South Korea, previous TB as indicated by the presence of a TB lesion on chest x-ray was an independent risk factor for obstructive lung disease even if the lesion is minimal. Evidence of previous TB on chest X-ray was independently associated with airflow obstruction (adjusted Odds Ratio – 2.56) after adjusting for sex, age and smoking history. This study demonstrated that TB can be an important cause of obstructive lung disease in never smokers. (15)

Patients with previous pulmonary TB are also more likely to suffer from acute exacerbation of COPD than those who did not have pulmonary TB. The bronchodilator response of patients with a tuberculous-destroyed lung is lower than that of patients with COPD. Appropriate management and control of TB is as important as smoking quitting for reducing obstructive lung disease (15)

2.3.2a Endobronchial tuberculosis (EBTB)

Endobronchial TB is the most often a complication of primary PTB in children, although it may also occur in adults. The prevalence of EBTB varies among studies ranging from 10-50%. Bronchospically, EBTB may present as endobronchial mass lesion, submucosal infiltration, hyperemia with edema or fibrostenosis. Clinically, cough, mostly non-productive is invariably present and usually persistent. EBTB can result in a purely restrictive or purely obstructive lung function abnormality.

In a study to correlate the evolution of structural and functional abnormalities when pulmonary TB was treated with Directly Observed Therapy (DOT) for 6 months, Long et al, showed that TB is an endobronchial disease which causes parallel reduction in ventilation and perfusion (20)

2.4. Factors influencing lung function outcome post PTB treatment

2.4.1 Number of TB episodes

The impairment in lung function after an episode of TB increases incrementally with the number of episodes of TB (17)

2.4.2 Radiologic extent of the disease

The most significant factor influencing post treatment lung function status is the pretreatment radiographic score which is a marker of pulmonary involvement (3,14)

Hnizdo et al (12) in a study among South African gold miners demonstrated that the radiological presence of extensive post TB scarring and bronchiectasis at the end of TB treatment was also associated with a greater annual loss of FEV1. Extensive radiological TB disease compared to less extensive TB disease at diagnosis was associated with significantly greater loss of FEV1 (153 mls/year versus 103 mls/year) (12).

Willcox et al (3) in a study of seventy-one subjects who had previously been treated for tuberculosis up to 16 years before underwent pulmonary function assessment. Evidence of airways obstruction was found in 48 (68%). There was an inverse relationship between the extent of the disease on the original chest radiograph and the forced expired volume in one second (3)

2.4.3 Time lapse since the TB episode

The average duration of onset of obstructive airway disease has been found variable. Study undertaken by Hnizdo et al found that the loss of lung function was highest within six months of the diagnosis of tuberculosis and stabilized after 12 months when the loss was considered to be chronic (17)

However chronic impairment in lung function after completing of short course chemotherapy is also common. In a cross sectional study to assess the long term status of smear positive PTB patients treated with short course chemotherapy, Banu et al (13), assessed the clinical, bacteriological, radiological status and health related quality of life of PTB patients with a mean period after completion of treatment being 16.5 years. 29% (n= 148) of the participants had persistent respiratory symptoms, 86% had abnormal radiological sequalae and 65% had lung function impairment (45% restrictive, 5% obstructive and 15% combined). The restrictive pattern was more common in females (64%).

2.4.4 Other Factors

Other factors that influence lung function outcome after completing treatment include smoking habit, degree of inflammatory activity as measured by erythrocyte sedimentation rate and concentrations of c-reative protein and alpha1-protease inhibitor (14). Delays in diagnosing TB have also been shown to relate directly with the severity of pulmonary damage and frequency of co morbidities negatively affecting the quality of life (24).

Some studies say that tobacco smoking and biomass smoke inhalation, in addition to the risk of TB, may compound the airflow obstruction caused by TB. A previous study found that smoking history is associated with an increased risk of TB for a cohort of black gold miners, and smoking is known to increase lung function loss (17). Miners who had TB were more likely to be current or exsmokers (82.7% versus 61.6%) than miners who had not had TB. (12)

2.5. Health Related Quality of life (HRQL) in TB

HRQL is defined as patients' self-evaluations of the impact of tuberculosis and the associated treatments on their physical, mental, and social well-being and functioning. HRQL is a complex type of patient reported outcome that evaluates health status. It broadly describes how well individuals function in daily lives and their own perception of well being in physical, physiological and social aspects (9).

In some communities, TB patients are perceived as a source of infection and the resultant social rejection and isolation leads to a long-term impairment on patients' psychosocial well-being. Many TB patients also report to experience negative emotions, such as anxiety and fear. In a study done in Uasin Gichu, Kenya by Liefooghe et al, on the Kenyan community perception of TB showed that the community perceives TB as a "dangerous and difficult to diagnose", the treatment is perceived as exceedingly long, agonizing and cumbersome and they had doubts about its full curability. There was also stigmatization of TB patients enhanced by the isolation of patients in TB wards (25) However, the current goal of TB management is to achieve microbiological 'cure' and there has been little effort taken to consider patients' HRQL.

Overall, the antituberculosis treatment has a positive effect of improving patients' quality of life; their physical health tends to recover more quickly than the mental well-being. However, after patients successfully complete treatment and are microbiologically 'cured', their quality of life remained significantly worse than the general population (26) Tuberculosis has substantially adverse impacts on patients' quality of life, which persist after microbiological 'cure'.

It also results in loss of Quality Adjusted Life Years (QALY) due to the illness itself, pulmonary sequalea, and death related to TB (9) A variety of instruments are used to assess quality of life in Tuberculosis but there has been no well-established tuberculosis-specific instrument.

Although traditional clinical and biological indicators are often intrinsically related to patients' quality of life, they fail to represent one's self-perceived function and well-being in everyday life settings. It is known that patients with chronic diseases place a high value on their mental and social well-being as well as pure physical health. As a result, HRQL has become an area of increasing interest and has been evaluated in many diseases, including TB.

To measure HRQL, two kinds of instruments are often used: generic and disease specific (10,27). Generic instruments are developed to cover the common and important aspects of health and can be used to assess and compare HRQL across different health conditions and sub-

populations (10,27) In contrast, disease- or condition-specific instruments are designed to reflect unique problems most relevant to a given disease and/or its treatment (10,27).

2.5.1 Generic HRQL instruments

The SF-36 is a commonly used tool in assessing HRQL. It consists of 36 items which are aggregated into 8 subscales, including physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), roleemotional (RE), and mental health (MH). From the 8 subscales, the physical component summary (PCS) and mental component summary (MCS) scores can be also calculated (28).

Others include the 24-item Quality of Life Questionnaire (QLQ), which covers 7 domains, including living conditions, finances, leisure, family relations, social life, health, and access to health care.

The long Medical Outcome Study (MOS) core questionnaire (11) is a generic instrument covering multiple dimensions, including physical function, social function, general health, vitality, and limitations due to physical and emotional functioning. The MOS is an extensively validated non-systemspecific HRQoL instrument. Babikako et al, (29) in a cross-sectional study among PTB patients in Kampala Uganda established the feasibility, reliability, and validity of the Medical Outcomes Survey (MOS) in assessing HRQoL.

2.5.2 Specific HRQL instruments

Several instruments have been used in various studies that evaluated quality of life after completing TB treatment.

The DR -12 is a new TB-specific instrument, which was developed in India and first published in 2003. It is composed of 12 items, among which 7 cover TB symptoms (i.e., cough and sputum, haemoptysis, fever, breathlessness, chest pain, anorexia, and weight loss) and 5 relate to socio-psychological and exercise adaptation (i.e., emotional symptoms/ depression, interest in work, household activities, exercise activities, and social activities) (30). All response options are

presented on 3-point scales and equal weights are given to each item when calculating the two domain scores and the total score (30).

The St. George Respiratory Questionnaire (SGRQ) is a widely used specific instrument designed for measuring HRQL in patients with chronic obstructive pulmonary disease, and other types of respiratory diseases. It was developed at the St. George's Hospital Medical School at the UK. Three domains (symptom, activity, and impacts) scores and a total score can be generated (11). The symptoms component (8 items) measures respiratory symptoms, their frequency and severity; the activities component (16 items) measures the impairment of mobility or physical activity; and the impacts component (26 items) measures social, psychological, and other effects of pulmonary dysfunction. The SGRQ is scaled from 0 (optimal health) to 100 (worst health).

Psychometric testing has demonstrated its repeatability, reliability and validity (11). It is highly correlated with paraclinical measures such as oxygen tension in arterial blood (PaO2), exercise tolerance, and symptoms such as dyspnea and fatigue. It has been validated for use in microbiologically cured TB in a study done by Jotam et al in Tarrant County, USA (11). In this study, participants with known pulmonary function and a history of PTB or LTBI completed HRQoL questionnaires. The SGRQ was validated for content and construct using pulmonary function tests and the Medical Outcomes Study questionnaire. There was a mean 13.5-U difference in SGRQ score between PTB patients and a comparison group of LTBI. The minimal and maximal possible scores observed in this study was similar to other studies thus providing evidence that SGRQ is an appropriate instrument for use in subjects with a history of PTB. However, no studies have been done in Africa using this tool.

HRQoL measures are sensitive to smaller losses of functioning and can detect lower levels of ill health than can be detected by spirometry. In the study by Jotam et al (11), Forty-three patients with a history of PTB had > 80% expected vital capacity and were not considered impaired per American Thoracic Society guidelines (31), yet the SGRQ total score of these 43

patients averaged 7.1 points less than the average total score for the comparison group. This difference in scores has been shown to be clinically significant but was not identified by spirometry. This suggests that spirometry alone is inadequate to evaluate post-tuberculosis pulmonary impairment.

2.6. Study justification

According to WHO global TB report for the year 2011 (1), Kenya is one of the high TB burdened countries in the world with an estimated more than 100,000 cases being reported per year (2) including more than 30,000 smear positive TB cases.

The most important priority for the TB control program in Kenya is to achieve a microbiological cure, a task they have done very well with about 85% of smear positive TB cases being cured in the cohort of patients that were started on treatment in 2008 (2) However, structured assessment of patients completing TB treatment does not occur and patients are only evaluated if they have symptoms of disease recurrence.

Lung remodeling associated with pulmonary tuberculosis (healed cavitation, fibrosis, and distorted architecture) is now a recognized complication of pulmonary TB. With new advances in development of novel agents likely to be useful in pulmonary rehabilitation in post TB lung remodeling, quantification of impairment associated with PTB can indirectly estimate the magnitude of lung remodeling in local set up in TB clinics in Nairobi.

Despite the documented evidence in previous studies that a significant number of TB patients are left with severe respiratory disability and significant loss on health related quality of life, no study has been done in Kenya to document the same.

This study was therefore designed to assess the pulmonary function and quality of life of treated smear positive TB patients attending TB clinics in Nairobi. It will form a baseline for further studies on pulmonary function post TB in Kenya and will help estimate the magnitude of lung remodeling post TB treatment in patients attending these clinics.

Research Question

What are the complications of pulmonary tuberculosis that persists beyond completion of treatment?

Study Objectives

Broad objective

To assess the pulmonary function impairment and health related quality of life among smear positive TB patients after successful TB treatment

Primary objectives

1. To determine the prevalence and type of pulmonary function abnormalities among smear positive TB patients after completing anti-TB treatment.

2. To determine the health related quality of life post TB treatment.

Secondary objectives

1. To determine the factors associated with pulmonary impairment following TB treatment

2. To determine the correlation between St. George Respiratory Questionnaire score and pulmonary function

Chapter Three

Research Methodology

3.1 Study site and design

This study was a cross-sectional study that was conducted at Riruta, Kangemi and Kibera Health centres TB clinics. These sites were chosen because of the high number of TB patients registered in the TB clinics, their proximity to Kenyatta National Hospital and good follow up of patients with at least 90 - 95% of all registered smear positive TB patients having smears done at the completion of TB treatment.

3.2 Study population

Patients with confirmed smear positive TB at the initiation of TB treatment and who had completed the six month short course chemotherapy and had a confirmed negative smear at completion of treatment within the last two years.

3.3 Study period

The study was conducted over the period of May and June 2012.

3.4 Sampling and Sample size

Various studies on assessment of lung function impairment post TB treatment varying in sample sizes, timing of assessment and design suggest a prevalence of between 18% (Hnizdo et al) and 59% (Pasipanodyla et al). Other studies reported a prevalence of 30.7% (PLATINO) and 34% (Hallet et al) Using the formula

$$n = \frac{t^2 \times p\,(1-p)}{m^2}$$

Where:

n = required sample size

t = confidence level at 95% (standard value of 1.96)

p = estimated prevalence of pulmonary function impairment post PTB (average at 30% from previous studies)

m = margin of error at 7% (standard value of 0.07) – The choice of 7% was due to financial and time constraints.

The calculated sample size was:

n = $\dfrac{1.96^2 \times 0.3(1\text{-}0.3)}{0.07^2}$

= 3.8416 x 0.3 x 0.7/ 0.0049

= 3.8416 x 0.21/ 0.0049

==0.8067/ 0.0049

= 164.6

The sample was further increased by 5% to account for contingencies such as non-response or recording error.

Therefore the minimum sample size was:

= 164.6 x 1.05

= 172.8

The calculation result was rounded up to the closest number to 173

Consecutive sampling was done from the TB facility registers in the three sites until the desired sample size was achieved.

3.5 Study eligibility criteria

3.5.1 Inclusion criteria

Patients above 15 years of age with smear positive pulmonary TB (initial treatment and retreatment) at diagnosis and confirmed smear negative after completing TB treatment within the last two years

3.5.2 Exclusion criteria

1. Patients with previously confirmed functional or structural lung abnormality prior to starting TB treatment
2. Non-consenting/assenting individuals
3. Pregnant women

3.6 Patient recruitment procedure

Patients were recruited from the TB facility registers by the principal investigator and his assistant. The details of smear positive patients that had completed treatment within the previous two years was retrieved and tabulated. Consecutive sampling was done and patients were called to come to the clinic on a specific day of the week to have pulmonary function assessment done and complete the QOL questionnaire. Demographic data of the patients who did not turn up to the clinic and those that did not have contact details in the registers and were therefore not contacted was obtained and recorded from the TB facility registers. The reason(s) given for not turning up was recorded in subsequent telephone calls.

The treatment details of the patients who turned up to the clinic were verified from the TB facility registers. Those patients that met the eligibility criteria were given consent/assent forms and included in the study following informed consent. Basic social demographic data was recorded including age, sex, marital status, level of education etc.

3.7 Data collection process

After recruiting the study subjects, data collection was done using two study instruments

1. Data abstraction form
2. St. George Respiratory Questionnaire

3.7.1 St. George Respiratory Questionnaire (SGRQ)

The SGRQ assesses patient perceptions of recent respiratory problems and is validated for the recollection of symptoms ranging from one month to two years. It has three components ie the symptoms, activity and impacts components. It was administered by the principal investigator to all the patients. To test internal consistency, 16 subjects selected consecutively completed a retest 7 days after answering the initial questionnaire.

3.7.2 Pulmonary Function Tests (PFTs)

PFT measurements was performed at the end of the interviews (on site) according to the American Thoracic Society recommendations, for subject maneuver, techniques, and quality control using spirolab III (Medical International Research, Italy) – a portable spirometer machine.

 Pre and post bronchodilator (after administration of 200 micrograms of inhaled salbutamol via a spacer device using disposable mouth pieces) PFTs were performed by the principal investigator and a trained research assistant in the patient's preferred posture. Three tests with values within 5% were defined as being acceptable, and the best of three values was used for comparisons. If the variation was more than 5%, the best three results from eight tests were selected. FEV1, FVC, FEV1/FVC ratio and their respective percent predicted values was recorded. Airway obstruction was defined as an FEV1/FVC ratio of <70% and an FVC of >80% predicted, restrictive defects as an FEV1/FVC ratio of> 80% with an FVC of <80% predicted, and combined defects as FVC of < 80% predicted and an FEV1/FVC ratio of < 80%.

The degree of severity of airway impairment was be defined according to American Thoracic Society (31) and the European Respiratory Society (32) guidelines based on FEV1 (for obstructive defects) and FVC (for restrictive defects) as follows:

Degree of Severity	FEV1 (Obstructive) or FVC (Restrictive) (% of predicted)
Mild	70-80
Moderate	60-69
Moderately severe	50-59
Severe	35-49
Very severe	<35

Response to bronchodilator therapy was be defined according to the ATS/ERS (31,32) recommendations for reversibility testing as a 12% increase in FEV1 and an absolute increase of 200mls.

Quality Control: The spirometer machine was calibrated as per the manufacturer's recommendations. Spirometric pulmonary function tests were done meeting the ATS specified criteria on acceptability, repeatability and reproducibility as described above. The results were automatically adjusted for race. Infection control practices including use of disposable mouth pieces, cleaning/ disinfection of spirometer parts as per manufacturer's recommendations and appropriate disposal of used mouth pieces were strictly adhered to.

3.7.3 Body Mass Index (BMI)

The weight of the patients was recorded in kilograms using a standard bathroom scale and the height recorded in centimeters using a standard stadiometer. BMI was categorized according to WHO guidelines as: Underweight <18.5, Normal, 18.5 – 24.99, Overweight, 25.0 – 29.99 and obese > 30.0

3.8 Main Outcome Variables

3.8.1 Primary outcomes

The first primary outcome was abnormal lung function as defined as either Airway obstruction or Restrictive defects or Combined defects. The definition of these defects was as per the ATS/ERS (31,32) guidelines using the pre bronchodilator indices and categorized as follows:

- Airway obstruction: FEV1/FVC ratio of <70% and an FVC of >80% predicted

- Restrictive defects: FVC<80% and FEV1/FVC ratio of> 80% predicted

- Combined defects as FVC< 80% predicted and an FEV1/FVC ratio of < 80%.

The second primary outcome was Quality of Life as determined by the SGRQ Score. This was a continuous variable with a score of zero indicating good quality of life and a score of 100 indicating the worst quality of life.

3.8.2 Secondary outcomes
Secondary outcomes included:

- Severity of obstructive/restrictive defects as defined earlier using the spirometric lung function parameters

- Reversibility of obstructive and combined defects.

3.9 Data Management and analysis

Data was entered using a computer spreadsheet program (Microsoft Office Excel 2010). All analyses were carried out using Stata statistical software (Stata Intercooled version 11, StataCorp, College Station, Texas, USA). Baseline characteristics of the study population were described. Continuous data were assessed for their distribution by histograms and box plots. Means and standard deviations were used to present normally distributed data. Median and interquartile ranges (IQR) were used to present data that were not normally distributed.

Minimum and maximum values were also presented for continuous variables. Some of the continuous variables were recorded and subsequently used in the analysis as categorical variables. Cross tabulations of categorical data with the study site (clinic) was done to describe their distribution by frequencies and percentages.

3.9.1 Univariable analysis

Clinical and respiratory characteristics were compared between those with airway obstruction and/or restrictive defects (abnormal lung function) and those without. Binary and categorical variables were presented as frequencies and percentages while continuous variables were presented as means ±SD or median and inter-quartile range for normally and non-normally distributed data respectively. Baseline differences were determined by Chi square test; chi square test for trend and Fisher's exact test for categorical variables. Unpaired t test or Kruskal-Wallis test were used for continuous variables.

Preliminary analysis was also done to assess the correlation between the lung function and the quality of life scores. This was done by plotting scatter plots and calculating the correlation coefficient. Correlation was assessed visually and using the correlation coefficient. If the resulting correlation coefficient was more than 0.7, the variables were deemed as having correlation.

3.9.2 Multivariable analysis

Since one of the primary outcomes (abnormal lung function) was binary and the main interest was in occurrence of the outcome rather than time to outcome, logistic regression was used for multivariable analysis. A forward stepwise method of variable selection was adopted. Variables were added to the model in descending order of magnitude of association with abnormal lung function, described by the P Value. In addition, variables for which there was a priori assumption of association, based on the literature review (such as the number of time treated, duration from completion of treatment etc) were included. For each predictor added, we compared model fit using a likelihood ratio test. Variables that still had good evidence of association with abnormal lung function were retained in the model. For the other primary

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outcome (quality of life), linear regression was used for multivariable analysis because the outcome was continuous.

Ethical Consideration

The study was undertaken after approval by the department of Clinical Medicine and Therapeutics and the Kenyatta National Hospital/University of Nairobi Ethical Review Committee. Authorization was also obtained from the District Medical Officer of Health, Nairobi City Council and the respective District Medical Officers of Health, Westlands, Dagoretti and Langata Districts as well as from the management of all health centres before starting the study. The objectives and purposes of the study were clearly explained to eligible participants in a language suitable to them prior to inclusion into the study. Only patients who gave informed consent were enrolled. Information gathered from the study participants was kept confidential. Patients with severe pulmonary function abnormalities who were symptomatic were referred to the Kenyatta National Hospital Chest Clinic for further investigations, treatment and follow up. The study results will be disseminated to health care providers at all the three health centres after approval by the University of Nairobi.

Chapter Four

4. Results

4.1 Clinical and demographic profile

4.1.1 Enrollment

Out of a total of four hundred and nine patients who were eligible for enrollment, two hundred and twenty six (55%) were excluded from the study due to the following reasons: Twenty five (11%) had no telephone contacts in the TB registers, ninety eight (43%) had their mobile phones off and could not be contacted, seventy one (31%) were contacted but did not come for enrollment, twenty three (10%) had relocated out of Nairobi, eight (4%) had died after completing TB treatment and one patient was pregnant. A total of one hundred eighty three (45% of the eligible patients) were thus enrolled into the study.

Figure 1: Enrollment of patients

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┌─────────────────────────────────────────────────────────┐
│                 409 Eligible patients                   │
│  (Smear positives completed TB treatment in last 2 years)│
└─────────────────────────────────────────────────────────┘
                    │
                    │        ┌──────────────────────────────────────────────────┐
                    │        │  ▪  25 (11%) No telephone Contacts in the TB registers │
                    ┆┄┄┄┄┄┄▶ │  ▪  98 (43%) mobile phones off, could not be contacted │
                    │        └──────────────────────────────────────────────────┘
                    ▼
┌─────────────────────────────────────────────────────────┐
│        286 patients/relatives contacted for enrollment  │
└─────────────────────────────────────────────────────────┘
                    │
                    │        ┌──────────────────────────────────────────────────┐
                    │        │  ▪  71 (31%) did not turn up for enrollment          │
                    │        │  ▪  23 (10%) had relocated out of Nairobi            │
                    ┆┄┄┄┄┄┄▶ │  ▪  1 patient was pregnant                           │
                    │        │  ▪  8 (4%) had died after completing TB treatment    │
                    │        └──────────────────────────────────────────────────┘
                    ▼
┌─────────────────────────────────────────────────────────┐
│        183 (45%) patients were enrolled for the study   │
└─────────────────────────────────────────────────────────┘
```

The age distribution of those eligible for the study is as shown in figure 2 below. The youngest was aged 15 years while the oldest was 75 years, with a median age of 29.5 years (IQR, 25 – 38 years)

Figure 2: Age distribution of patients eligible for the study
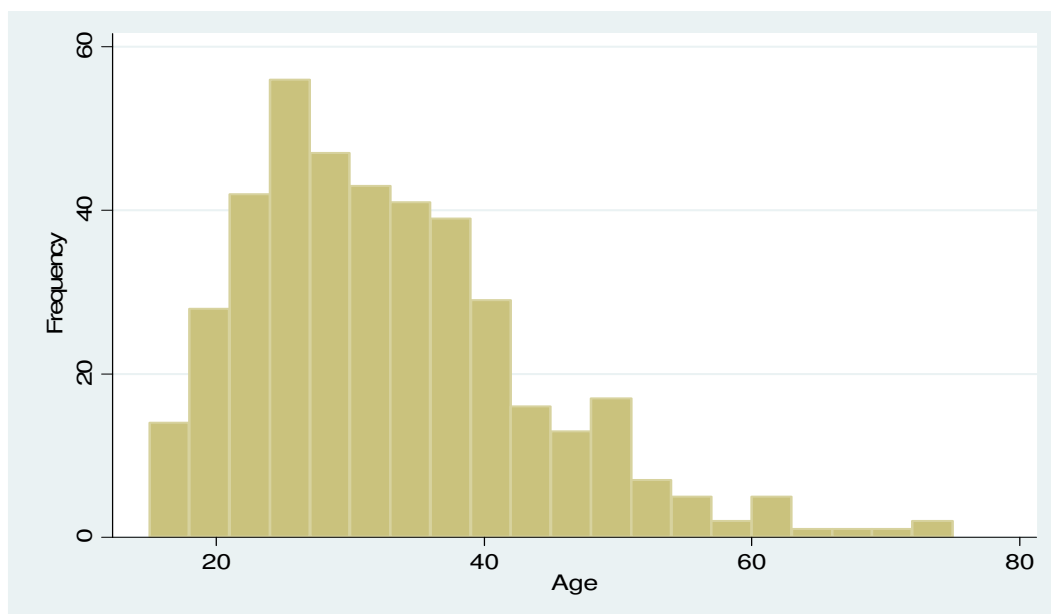
Of the one hundred sixty two eligible patients in Riruta Health Centre, ninety (56%) turned up for enrollment. In Kangemi Health Centre, a total of sixty four (43%) of the one hundred forty nine eligible patients turned up and in Kibera Health Centre, twenty nine (30%) of the ninety eight eligible patients turned up.

4.1.2 Demographic characteristics of participants vis-à-vis non participants

There was no difference in gender and HIV status of participants vis-à-vis the non participants. However, there were more non responders from Kibera Health Centre. Approximately 70% of eligible patients in Kibera did not respond compared to 57% and 44% in Kangemi and Riruta respectively (p=<0.001). Among the non responders, majority (38%) were from Kangemi, compared to 31% and 32% for Kibera and Riruta respectively.

Figure 3: Percentage participants and non participants from the three clinics
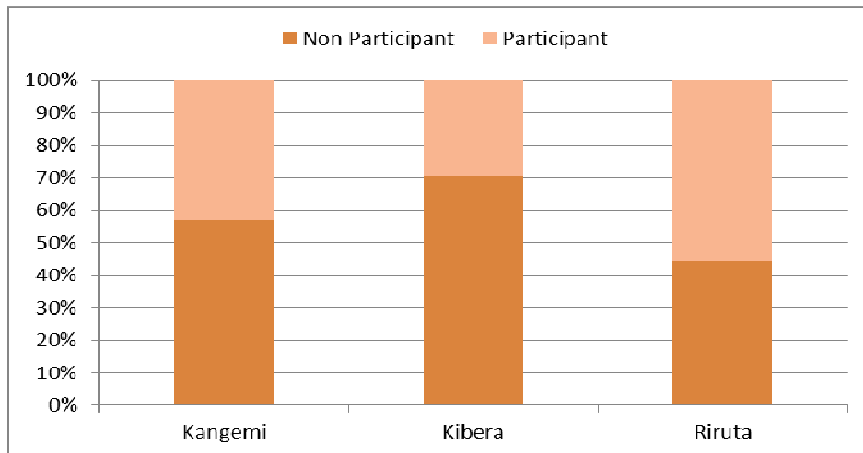
The non responders were younger compared to responders with a median age 29.5 years (IQR, 24–38 years) compared to 32 years (IQR, 25–39 years) for responders (p=0.0867) and had spent longer time since starting TB treatment (median duration of 13 months for non-responders compared to 11.4 months for responders (p=0.0164).

Table 1: Clinical and demographic characteristics of participants vis-a-vis non participants

	Non Participant		Participant		Total		P value
Sex	Freq	%	Freq	%	Freq	%	
Female	94	41.6	77	42.1	171	41.8	
Male	132	58.4	106	57.9	238	58.2	0.921
HIV Status							
Negative	158	69.9	123	67.2	281	68.7	
Positive	68	30.1	60	32.8	128	31.3	0.558
Clinic							
Kangemi	85	37.6	64	35.0	149	36.4	
Kibera	69	30.5	29	15.8	98	24.0	
Riruta	72	31.9	90	49.2	162	39.6	<0.001
Age (yrs)							
Median	29.5		32		30		
IQR	24 – 38		25- 39		25- 38		0.0867
Duration after start of Rx(months)							
Median	13.0		11.4		12.2		
IQR	10.0 -16.5		8.2 - 16.2		9.3 - 16.3		0.0164

4.1.3 Demographic and Clinical characteristics of participants

There were one hundred and six (58%) males and seventy seven (42%) females who participated in the study. The mean and median age of participants was 33.2 years and 32 years respectively with an interquatile range of 25 – 39 years. The participant ages were not normally distributed as shown in the figure 4 below.

Figure 4: Age distribution of the participants
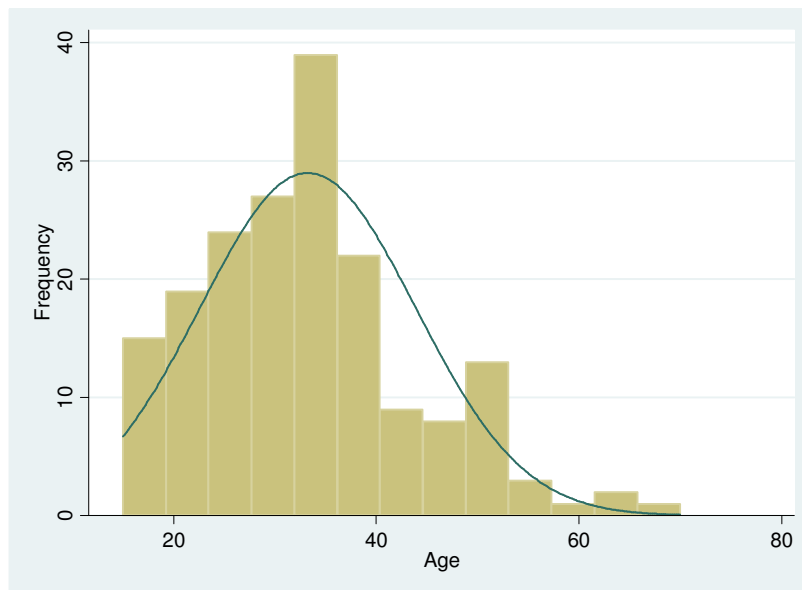
One hundred and twenty three (67%) of the participants were HIV negative and sixty (33%) were HIV positive. Of those who were HIV positive, 85% were on anti-retroviral therapy. One hundred fourty three (78%) of the patients had no prior use of cigarette. However, fourty (22%) were either current or former smokers.

One hundred fifty six (85%) of the patients were new smear positives while twenty seven (15%) were retreatment cases, with twenty one (11%) having been treated twice for TB and the other six (4%), having been treated three or four times. The median duration since starting TB treatment was 11.4 months. The median BMI was 21.1 kg/m^2, with a range of 12.5 to 37 kg/m^2. Majority of the participants (67%) had normal weight, 11% were overweight, 4% were obese and 18% were underweight.

Table 2: Demographic and clinical characteristics of participants (n=183)

Demographics		N	%
Sex	Male	106	58%
	Female	77	42%
Age	Median		32 years
	Mean		33.24 years
	IQ Range		25-39 years
BMI	Median		21.1kg/m^2
	Range		12.5 –37kg/m^2
HIV Status	Positive	60	33%
	Negative	123	67%
HIV patients on HAART		51	85%
Cigarette smoking	Yes	40	22%
	No	143	78%
No of times treated	First	156	85.2%
	Second	21	11.5%
	Third	5	2.7%
	Fourth	1	0.6%
Median duration since diagnosis			11.4 months
Biomass use	Yes	163	89%
	No	20	11%
Clinic	Riruta	90	49%
	Kangemi	64	35%
	Kibera	29	16%

Biomass use was defined using the type of fuel used for cooking. A positive response was indicated for those that used charcoal or firewood as their main source of energy for cooking.

4.1.4 Demographic and clinical profile of participants in different clinics

The demographic characteristics of participants from the three clinics were similar and there was no statistical difference observed when comparing participants from the three clinics.

Table 3: Demographic and clinical profile of participants in different clinics

	Kangemi	Kibera	Riruta	Total	P Value
Biomass use					
No	6	1	13	20	
yes	58	28	77	163	0.227
BMI Median	22.2	20.5	20.9	21.1	0.3019
Smoking					
No	48	27	68	143	
Yes	16	2	22	40	0.183
HIV					
Negative	46	23	54	123	
Positive	18	6	36	60	0.096
Sex					
Female	30	12	35	77	
Male	34	17	55	106	0.611

4.2 Prevalence and Severity of Pulmonary Function abnormalities

A total of fifty three patients (29%) had pulmonary impairment, with the commonest impairment being restrictive defects occurring in fourty two patients (23%), obstructive defects in nine patients (5%) and combined defects in two patients (1%).

Table 4: Prevalence of pulmonary function abnormalities

Type of defect	Freq.	Percent	[95% Conf. Interval]
Normal	130	71.04	64.4 -77.67
Airway obstruction	9	4.92	1.76 – 8.08
Restrictive defect	42	22.95	16.8 - 29.1
Combined defect	2	1.09	-0.4 – 2.61

Of the patients with restrictive defects, 57% (**95% Conf. Interval 41.5- 72.7%**) had mild defects, 26% (**95% Conf. Interval 12.3 – 40%**) moderate defects, 12% (**95% Conf. Interval 1.7 - 22.1%**) moderately severe defects and 5% (**95% Conf. Interval -2.0 – 11.5%**) severe defects.

Table 5: Severity of restrictive defects

Severity	Restrictive defect	95% Conf. Interval
Mild	24 (57%)	**41.5- 72.7%**
Moderate	11 (26%)	**12.3 – 40%)**
Moderately severe	5 (12%)	**1.7 - 22.1%**
Severe	2 (5%)	**-2.0 – 11.5%**
Total	42 (100%)	

4.3 Factors associated with impairment of pulmonary function

4.3.1 Univariable analysis

After univariable analysis, it was observed that, those with abnormal lung function were younger {median age, 29 years (IQR, 22-36) vs 34 years (IQR, 27-39), P= 0.036} and more likely to be underweight (38% vs 9%, P= <0.005). Prevalence of HIV was lower in those with abnormal lung function (20.8% vs 37.7%, P=0.027) There was no association between pulmonary function impairment and time since starting treatment, use of biomass fuel, cigarette smoking and the number of times treated for TB.

Table 6: Univariable analysis – factors associated with pulmonary function impairment

Variable		Normal lung function		Abnormal lung function		P value
		Freq	**%**	**Freq**	**%**	
Age (yrs)						
	Median	34		29		
	IQR	27 – 39		22 – 36		0.036
BMI						
	Underweight	12	9%	20	38%	
	normal	93	72%	29	55%	
	overweight	18	14%	3	6%	
	obese	7	5%	1	2%	<0.005
Number of times treated						
	Median	1		1		
	IQR	1 – 1		1 – 1		0.638
Duration of Rx (months)						
	Median	11.6		11		
	IQR	8.3 - 15.7		7.2 - 17.1		0.906
Biomass use						
	No	13	10.0	7	13.2	
	yes	117	90.0	46	86.8	0.528
Smoking						
	No	99	76.2	44	83.0	
	Yes	31	23.8	9	17.0	0.308
HIV						
	Negative	81	62.3	42	79.2	
	Positive	49	37.7	11	20.8	0.027

4.3.2 Multi-variable analysis

After adjusting for other factors, only BMI was associated with pulmonary function abnormality. A change in BMI category (from underweight to normal weight) was associated with a reduction in odds of having abnormal lung function (Adjusted OR 0.3 CI 0.2 – 0.6, P=0.001). Patients who were underweight had low mean FEV1 and FVC and thus a higher risk of having an abnormal pulmonary function compared to those with normal body weight. There was no association between pulmonary function abnormality and age or HIV status (P>0.05) of the study participants.

Table 7: Multivariable analysis – factors associated with pulmonary function impairment

Variable	Odds Ratio	[95% Conf. Interval]		P Value
Age	1.0	1.0	1.1	0.697
HIV status	0.5	0.2	1.2	0.109
BMI	0.3	0.2	0.6	0.001

### 4.4.1 Quality of life post TB treatment

The median quality of life total score from the St Georges Respiratory Questionnaire was 3.16 (IQR, 0 – 8.9). The median symptom score was 4.24 (IQR, 0-16.5), activity score was 0 (IQR, 0-12.2) and impacts score was 1.63 (IQR, 0-5.3). Forty nine patients (26%) had a total score of zero, one hundred and sixty seven patients (90%) had a total score below twenty and only one patient had a total score above fifty. 26% of patients had the best possible score and none of the patients had the worst possible score. This illustrates that majority of patients had a good quality of life after completing their TB treatment. The SGRQ retest showed stability with no significant difference between the first and second scores.

Table 8: Quality of life scores

Measure	Symptom score	Activity score	Impact scores	Total score
Median	4.24	0	1.63	3.16
IQR	0 - 16.5	0 - 12.2	0 - 5.3	0 - 8.9

The distribution of the various scores is as shown in the graphs below.

Figure 5: Distribution of quality of life scores
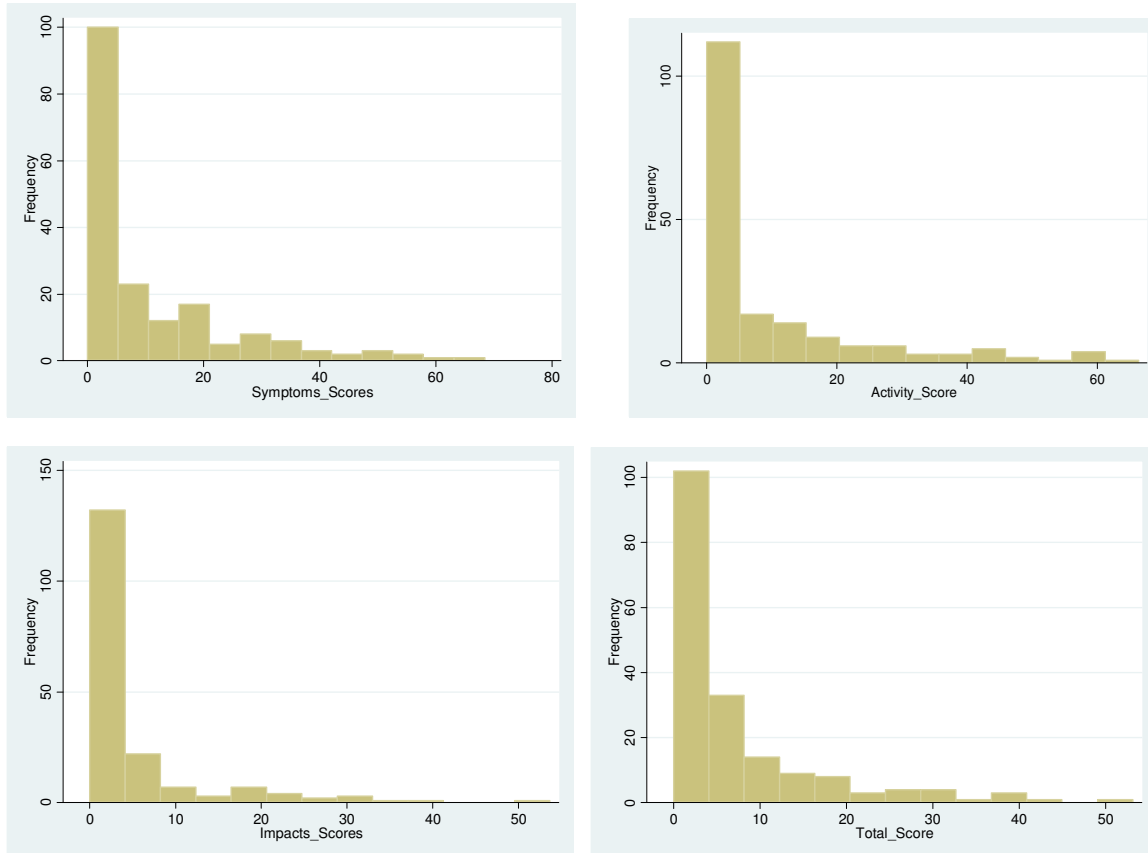
4.4.2 Correlation of QOL scores with pulmonary function

An increase in FEV1 or FVC means improved lung function, while an increase in the total QOL score means a poor quality of life. As such, we would expect that as the FEV1 or FVC increases, the total score decreases i.e. a negative correlation. There was no correlation between the SGRQ total score, symptoms score, activity score or impact score and FEV1, FVC and FEV1/FVC ratio as shown in the graphs below:

Figure 6: Correlation between QOL scores and pulmonary function
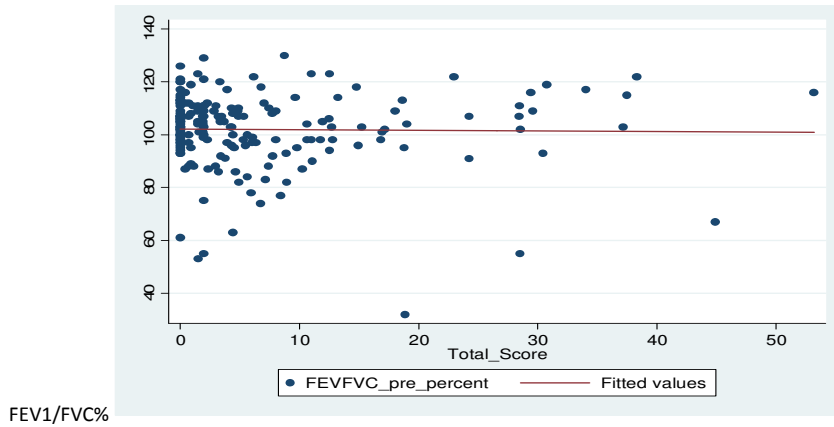
FEV1/FVC%   Correlation coeff= -0.0157
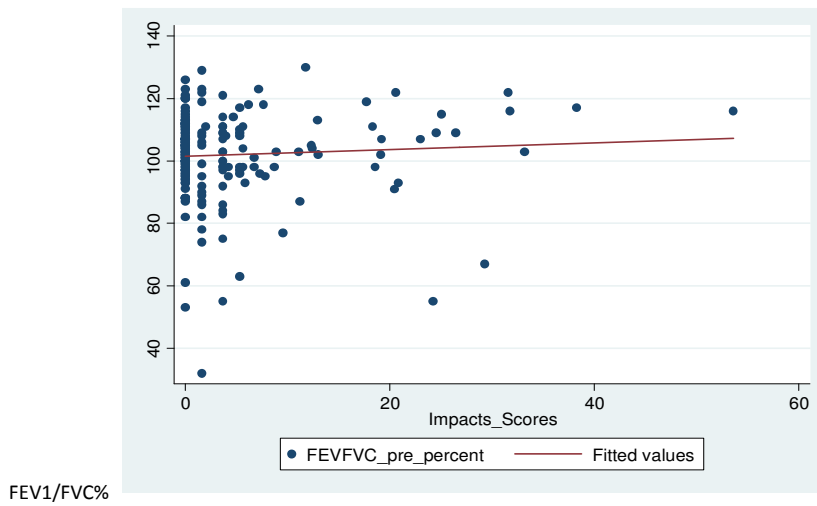
FEV1/FVC%   Correlation Coeff = 0.0629

FEV1/FVC%   Correlation Coeff = -0.0721

FEV1/FVC%   Correlation Coeff = -0.0417

Chapter Five

5. Discussion

5.1 Pulmonary function post TB treatment

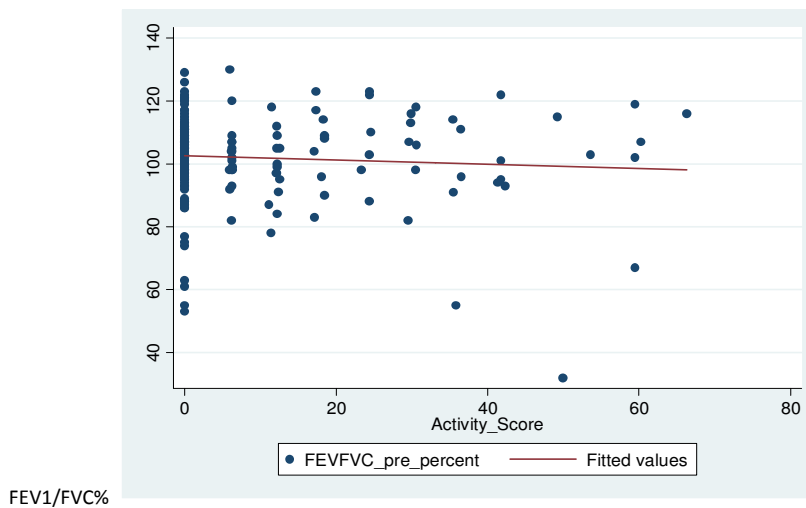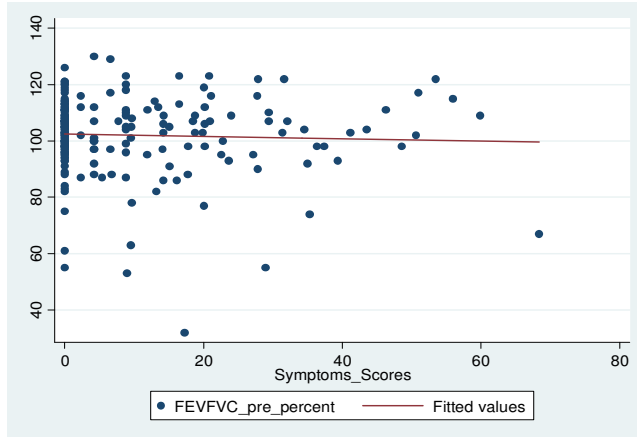This study was a cross sectional study that looked at complications of tuberculosis that persist beyond completion of treatment. We recalled patients who had completed TB treatment and achieved a poor response rate of 45%. The obvious bias in recall studies is the possibility that patients with persistent respiratory symptoms may be more likely to respond to a request for follow up evaluation. This was similar to other recall cross sectional studies by Willcox et al (3) and Krishna et al (33) in which only 40% of the patients could be traced. Similarly, the response rate in the study by Banu et al (13) and Boh et al (34) was low at 54% and 49.5% respectively. However, in our study, similar to the study by Willcox et al, we evaluated for selection bias by looking at the basic demographic characteristic between participants and non-participants. The two groups only differed on time from start of TB treatment. This may explain why the duration from completion of treatment did not appear significant. However, it does not affect the validity of our other findings.

The prevalence of pulmonary impairment in this study was 29% with the predominant lung function abnormality being restrictive pattern. Majority of patients (83% restrictive and 66% obstructive) had mild or moderate defects and were asymptomatic with a low median total SGRQ score indicating good QOL.

There has been a wide variation in prevalence of pulmonary impairment after TB treatment between various studies with the predominant lung function abnormality being restrictive pattern; our findings mirror these studies.

Jotam et al in a prospective case control study done in Tarrant county, Texas, USA (18) showed that 50% (n=107) of patients had pulmonary impairment after completing 20 weeks of TB

treatment compared to 20% in those with LTBI. Restrictive defects were the commonest occurring in 31% of patients. To avoid case selection bias, the study population was derived from a geographical area rather than from a select group that may not fully represent the population with TB. This is unlike our study in which the study population was derived from a select group of patients in three primary health care centers and may not fully represent the population with TB in Kenya.

Similarly, Banu et al (13) in a cross-sectional study done in India showed that 65% of patients (n=363) had pulmonary impairment 14 – 18 years after completing treatment with the commonest abnormality being restrictive defects occurring in 45% of the patients. The mean duration since completing TB treatment in this study was much longer (16.5 years) compared to our study (12.6 months).

Plit et al (14) in a prospective study showed that despite antimicrobial chemotherapy improving lung function in patients with pulmonary tuberculosis, a large population are left with residual impairment with restrictive defects occurring in up to 24% of the study population. The findings in this study were similar to our study despite the differences in the study design.

Hnizdo et al (17) in a retrospective study among South African gold miners with an average time of 4.6 years between diagnosis of last TB episode and lung function test, showed that 18.4% of subjects had chronic airflow impairment after one episode of TB. The prevalence of pulmonary impairment in this study was lower compared to our study possibly due to the longer duration since completion of TB treatment.

After univariable analysis, the factors associated with pulmonary impairment included age, (those patients with pulmonary impairment being younger), low BMI and HIV status. This was unlike the study by Hnizdo et al (17) where the loss of function due to TB was not biased by presence of HIV as both HIV positive and HIV negative subjects had similar losses.

HIV status and pulmonary impairment could be explained by the fact that HIV negative patients are able to mount inflammatory response to the TB bacilli resulting in more fibrosis, cavitations and lung remodeling which results in bigger pulmonary function decline. The other contributing factor was the higher number of HIV negative patients in our study unlike in other previous studies (17,18).

A low BMI was the only independent predictor of pulmonary impairment. A low BMI is an established risk factor for incidence, severity, relapse and mortality associated with TB. The severity of lung disease in adults with PTB is associated with the extent of malnutrition as reflected by BMI (35). Poor weight gain during PTB treatment has also been shown to correlate with poor treatment outcomes (36). Boris et al in a study on effects of body mass index on pulmonary function tests showed that an increase in BMI had a negative effect on total lung capacity and no effect on FEV1 (37) unlike in our study. However, the low mean cut off BMI in Boris's study was 25 unlike in our study which was 18. Previous studies have shown a correlation between the number of TB episodes and pulmonary impairment (17) and no correlation with BMI. However, the number of retreatment patients enrolled in these studies is much larger than our study. A larger sample size would be needed to detect other independent predictors of pulmonary function abnormalities post TB.

Previous studies have showed that cigarette smoking increases the risk of pulmonary impairment (18). However there was no difference in the pulmonary function among smokers and non smokers in our study, similar to the study by Banu et al (13) although our analysis was limited by the fact that we did not provide quantified smoking history of the study participants.

5.2 Quality of life post TB treatment
Patients in this study had a good QOL with low median SGRQ score. This is unlike other previous studies by Banu et al (13) and Jotam et al (18) who showed that post TB patients had a higher mean QOL scores compared to the general population. However, 65% of the participants in the study by Banu et al (13) had abnormal pulmonary function (combined, restrictive, obstructive)

with more than 20% having severe abnormalities with FEV1/FVC <50%. This is unlike in our study in which 29% of the participants had an abnormal PFT with less than 5% having severe abnormalities. It is documented that symptoms of pulmonary impairment generally do not occur in persons with chronic lung disease until FEV1 has fallen to 50% of normal values. This was observed in the study by Jotam et al (18) in which post TB patients with severe pulmonary impairment and FEV1 <50% had an average SGRQ score that were 62% lower than those expected in persons with otherwise similar risk factors. Thus, the big numbers of patients with severe pulmonary function abnormalities in the study by Banu et al means a big number were symptomatic with higher QOL scores implying poor QOL unlike in our study.

Furthermore, data pertaining to SGRQ scores in the general population in Kenya is not available. Normative values for the general population studied in Spain is recommended in the SGRQ manual (and used by Banu et al) but may not be used for comparison in our study due to the differences between the Spanish and the Kenyan population.

Correlation graphs show poor correlation between pulmonary function and QOL scores. This was similar to the study by Banu et al. A larger sample size is required to assess this correlation since this study may not have been powered to assess the same due to the small sample size.

5.3 Study limitations

This study has limitations. First, there was a big number of individual who did not participate in the study. This was due to a number of factors such as death, lack of telephone contact or had relocated out of Nairobi. It is therefore likely that this is a group who had abnormal lung function resulting in death or being unable to perform menial jobs, relocated to their rural home. This is referred to as selection bias. As such, we may have underestimated the prevalence of abnormal lung function and the quality of life scores. However, there was no significant difference between the demographic characteristics of participants and non-participants.

The cross – sectional study design did not allow the determination of causality, as the sequence of exposure to the outcome cannot be proved. There were other risk factors for pulmonary impairment including cigarette smoking and use of biomass. The observations made need not be confined to TB sequelae alone and could be due to the aging and/or health related factors of the study population.

There was also a possibility of recall bias for respiratory symptoms while using the SGRQ with those patients with severe disease and those that completed treatment recently more likely to recall their symptoms. The lack of population based normal values in an African setting for the pulmonary function tests and the SGRQ score was also a limitation. However, we did the standard adjustment for race while conducting the pulmonary function tests.

However, despite these limitations, pulmonary tuberculosis remains the most likely etiology for the identified pulmonary impairment.

5.4 Conclusion

Pulmonary tuberculosis is associated with frequent pulmonary damage despite microbiological cure. However, in majority of these patients, the impairment is mild to moderate and asymptomatic with good quality of life.

5.5 Recommendations

We recommend targeted assessment of lung function post PTB treatment for those at higher risk. This would include those with malnutrition and low BMI. A larger study to implore the relationship between pulmonary function and clinical parameters post TB treatment should also be carried out. This should preferably be a prospective cohort or a comparative study.

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Appendix

1. **Proforma**

(A) Social Demographic Characteristics   Date:

1. Name:

2. DOB: Age (yrs)

3. Sex: (i) Male   (ii) Female

4. Marital Status (i) Single   (ii)Married   (iii)Widowed   (iv)Separated/divorced

5. Residence:

6. Clinic: (i) Riruta HC   (ii) Kangemi HC   (iii) Kibera DO Health Centre

7. Weight (Kg)   Height (cm)

8. Occupation:

9. Level of Education: (i) None   (ii) Primary   (iii) Secondary   (iv) University

10. Date of Start of TB treatment:

11. Date of Completion of TB treatment:

12. How many times have you been treated for PTB? (i) Once   (ii)Twice (iii)Thrice

13. Cigarette Smoking: (i) Never Smoker (ii) Former Smoker (iii) Current smoker

14. If former or current smoker, no of Pack years:

15. Type of fuel used for cooking:

16. Alcohol intake (i) Yes   (ii)No

17. HIV Status (i)Positive   (ii) Negative   (iii) Not done

18. If HIV Positive, (i) Are you on HAART   (i) Yes   (ii) No

                    (ii) Baseline CD4 Count

(B) Spirometric Parameters: **Number:**

Name: **DOB:**   **Age:**

Weight (Kg):   **Height(cm):**   **Sex:**

Parameter	Units	Pre	% Pred	Post	%Pred	% Change
FVC	L					
FEV1	L					
FEV1/FVC	%					
PEF	L/s					
FEF 2575	L/s					

Interpretation:

2. **St Georges Respiratory Questionnaire**
   Part 1

1) **Over the last year, I have coughed:**

Most 80.6

Several 63.2

A few 29.3

Only 28.1

Not 0.0

2) **Over the last year, I have brought up phlegm (sputum):**

Most 76.8

Several 60.0

A few 34.0

Only 30.2

Not 0.0

3) **Over the last year, I have had shortness of breath:**

Most 87.2

Several 71.4

A few 43.7

Only 35.7

Not 0.0

4) **Over the last year, I have had attacks of wheezing:**

Most 86.2

Several 71.0

A few 45.6

Only 36.4

Not 0.0

5)   During the last year, how many severe or very bad unpleasant attacks of chest trouble have you had?

More than three 86.7

3 attacks 73.5

2 attacks 60.3

1 attack 44.2

None 0.0

6)   How long did the worst attack of chest trouble last?

A week or more 89.7

3 or more days 73.5

1 or 2 days 58.8

less than a day41.9

7)   Over the last year, in an average week, how many good days (with little chest trouble) have you had?

None   93.3

1 or 2   76.6

3 or 4   61.5

nearly every day 15.4

every day 0.0

8)   If you have a wheeze, is it worse in the morning?

No 0.0

Yes 62.0

Part 2

9)   How would you describe your chest condition?

The most important problem I have 83 .2

Causes me quite a lot of problems 82.5

Causes me a few problems 34.6

Causes no problem 0.0

10)   If you have ever had paid employment?

My chest trouble made me stop work 88.9

My chest trouble interferes with my work or made me change my work77.6

My chest trouble does not affect my work   0.0

11)   Questions about what activities usually make you feel breathless.

Sitting or lying still 90.6

Getting washed or dressed 82.8

Walking around the home 80.2

Walking outside on the level 81.4

Walking up a flight of stairs 76.1

Walking up hills 75.1

Playing sports or games   72.1

12)   More questions about your cough and breathlessness.

My cough hurts 81.1

My cough makes me tired 79.1

I get breathless when I talk 84.5

I get breathless when I bend over 76.8

My cough or breathing disturbs my sleep 87.9

I get exhausted easily 84.0

13) Questions about other effects your chest trouble may have on you.

My cough or breathing is embarrassing in public 74.1

My chest trouble is a nuisance to my family, friends or neighbours 79.1

I get afraid or panic when I cannot get my breath 87.7

I feel that I am not in control of my chest problem 90.1

I do not expect my chest to get any better 82.3

I have become frail or an invalid because of my chest 89.9

Exercise is not safe for me 75.7

Everything seems too much of an effort 84.5

14) Questions about your medication.

My medication does not help me very much 88.2

I get embarrassed using my medication in public 53.9

I have unpleasant side effects from my medication 81.1

My medication interferes with my life a lot 70.3

15) Questions about how activities may be affected by your breathing.

I take a long time to get washed or dressed 74.2

I cannot take a bath or shower, or I take a long time 81.0

I walk more slowly than other people, or I stop for rests 71.7

Jobs such as housework take a long time, or I have to stop for rests 70.6

If I walk up one flight of stairs, I have to go slowly or stop 71.6

If I hurry or walk fast, I have to stop or slow down 72.3

My breathing makes it difficult to do things such as walk up hills, carry things up stairs, light gardening such as weeding, dance, play bowls or play golf 74.5

My breathing makes it difficult to do things such as carry heavy loads, dig the garden or shovel snow, jog or walk at 5 miles per hour, play tennis or swim 71.4

My breathing makes it difficult to do things such as very heavy manual work, run, cycle, swim fast or play competitive sports 63.5

**16)	We would like to know how your chest trouble usually affects your daily life.**

I cannot play sports or games 64.8

I cannot go out for entertainment or recreation 79.8

I cannot go out of the house to do the shopping 81.0

I cannot do housework 79.1

I cannot move far from my bed or chair 94.0

**17)	Tick the statement which you think best describes how your chest affects you.**

It does not stop me doing anything I would like to do 0.0

 It stops me doing one or two things I would like to do 42.0

It stops me doing most of the things I would like to do 84.2

It stops me doing everything I would like to do 96.7

3. Consent form explanation

My name is Dr Peter Ngaruiya Mugo. I am a postgraduate student studying Internal Medicine at the University of Nairobi. I would like to introduce you to a study I am conducting, tititled:

"Pulmonary function and Quality of Life in patients with treated smear positive pulmonary tuberculosis at Riruta, Kangemi and Kibera Tuberculosis Clinics in Nairobi"

What is the study about?

The study is about assessing the pulmonary function and quality of life for patients with smear positive pulmonary tuberculosis who have already completed their TB treatment and have been declared cured

What does the study involve?

The study involves documenting your demographic characteristics including your age, sex, marital status, level of education, place of residence, smoking status among others. It will also involve taking your weight and height and completing a quality of life questionnaire. An initial test to assess your pulmonary function will also be carried out using a spirometry machine. This test will then be repeated after inhalation of two puffs of a bronchodilator medicine called salbutamol to assess whether for those with pulmonary function abnormalities, the abnormality is reversible or not.

Are there any risks involved?

There are no risks involved by participating in this study since the procedures to be carried out are important in assessing patients with previously diagnosed chronic lung disease including pulmonary tuberculosis. Assessing pulmonary function is also not an invasive procedure and carries no major risks

Are there benefits involved?

Yes, assessing pulmonary function and quality of life will help us detect whether you have any functional lung abnormalities and/or impaired level of functioning/quality of life. The results of the test will be availed to you. For those with abnormalities, they will be referred to the chest clinic in Kenyatta National Hospital for further tests and treatment.

Can I withdraw from the study?

Yes, you are free to withdraw from the study and any point and this shall not affect your care or treatment. However, we encourage you to remain in the study for your benefit and the benefit of other patients.

If you have any further questions, feel free to contact me on 0722480730 or 0733480730 or the secretary of the Kenyatta Hospital Research and Ethics Committee at KNH, telephone no: 726300-9

Thank you for your co-operation

Consent Form (Patient)

I, Dr Peter Ngaruiya Mugo, a postgraduate student in the Department of Clinical Medicine and Therapeutics of the University of Nairobi, is conducting a study on patients with smear positive TB who have completed treatment within the last two years. This study has been approved by my department and by the KNH Ethics Committee

If you agree to participate in the study, I will request you to give me some socio-demographic details including your age, residence, level of education, marital status, smoking history among others. I will also take your weight and height and assess your lung function using a spirometer machine. I will also request you to fill out a quality of life questionnaire.

The results of the study will be availed to you and any advice on whether to seek further treatment or not. Participation is free and you are free to refuse to consent. Your refusal to participate or withdrawal from the study will not in any way affect future care and treatment in this facility. All information obtained will be treated confidentially.

I………………………………………………….. of ………………………………………………………understand the above and voluntarily accept to participate in the study

Signed…………………………………………………. **Date**………………………………………………….

I confirm that I have explained to the patient the above statement

Signed …………………………………………………(interviewer) **Date**………………………………………….

Consent Form (Relative/guarding/Close Friend)

I, Dr Peter Ngaruiya Mugo, a postgraduate student in the Department of Clinical Medicine and Therapeutics of the University of Nairobi, is conducting a study on patients with smear positive TB who have completed treatment within the last two years. This study has been approved by my department and by the KNH Ethics Committee

If you agree to participate in the study, I will request you to give me some socio-demographic details including your age, residence, level of education, marital status, smoking history among others. I will also take your weight and height and assess your lung function using a spirometer machine. I will also request you to fill out a quality of life questionnaire.

The results of the study will be availed to you and any advice on whether to seek further treatment or not. Participation is free and you are free to refuse to consent. Your refusal to participate or withdrawal from the study will not in any way affect future care and treatment in this facility. All information obtained will be treated confidentially.

I……………………………………………….. of ………………………………………………… Relative/ guardian/friend to…………………………………………………………… understand the above and voluntarily accept to participate in the study

Signed…………………………………………………. **Date**………………………………………….

I confirm that I have explained to the patient the above statement

Signed ………………………………………….(interviewer) **Date**……………………………………..