THE USE OF THE NATIONAL TUBERCULOSIS AND LEPROSY PROGRAMME SCREENING TOOL IN IDENTIFYING PATIENTS ELIGIBLE FOR ISONIAZID PREVENTIVE THERAPY AND THE ROLE OF TUBERCULIN SKIN TEST AMONG PATIENTS ATTENDING MUHIMBILI NATIONAL HOSPITAL HIV CLINIC.

Lilian Tina Minja, MD

MMed (Internal Medicine) Dissertation
Muhimbili University of Health and Allied Sciences
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By

Lilian Tina Minja, MD

A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences

Muhimbili University of Health and Allied Sciences
October, 2013

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled: **"The use of the National Tuberculosis and Leprosy Programme screening tool in identifying patients eligible for Isoniazid Preventive Therapy and the role of Tuberculin Skin Test among patients attending Muhimbili National Hospital HIV clinic"** in partial fulfillment of the requirements for the degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences.

……..

Dr. Grace Shayo

(Supervisor)

Date ……..……..

……..

Professor Ferdinand Mugusi

(Co-Supervisor)

Date …….……..……..

DECLARATION

AND

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I, Lilian Tina Minja, 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

To Jason Thomas, our son

Zoe Margareth, our daughter

Hans Warburg, my husband

ABSTRACT

Background: Screening and treatment for latent TB infection is necessary in the clinical settings where people with HIV infection receive their care. Tanzania's National TB and Leprosy Program (NTLP) has started to provide Isoniazid Preventive Therapy (IPT) to HIV infected patients with latent TB infection in 14 pilot sites. A screening tool which includes fever = 2 weeks, cough = 2 weeks, hemoptysis, noticeable weight loss for new patients or 3 kg weight loss in a month and excessive sweating at night for = 2 weeks is used to rule out active TB infection. Patients are considered to possibly have active TB when they present with any of the 5 symptoms in the tool and are further subjected to other TB investigations.

Objective: To determine the usefulness of the NTLP screening tool in identifying patients eligible for IPT and the role of Tuberculin skin test (TST) among patients attending Muhimbili national hospital (MNH) HIV clinic.

Study design and setting: Descriptive cross sectional study among HIV infected patients.

Methodology: Socio demographic data was obtained using structured questionnaires. Patients underwent physical examination, chest x-ray (CXR), TST, induced sputum for acid fast bacilli (AFB) microscopy and mycobacterial culture, CD4 count and complete blood count.

Results: A total of 373 patients were enrolled, 72.1% being females. Active TB was found in 4.1% (using culture) and 9.2% (NTLP TB definition) of the participants. The sensitivity and specificity of the NTLP TB screening tool was 71.4% and 75.9% respectively, with PPV and NPV of 11.4% and 98.4% respectively. A CXR identified 3 of the 4 participants with culture confirmed MTB that were missed by the screening tool. Cough = 2 weeks and ARV use were independent predictors of sputum culture defined TB. A positive TST was found among 24% of the participants and no relationship was observed between TST reactivity and TB.

Conclusion and recommendation:

The prevalence of PTB among patients attending MNH HIV clinic is high (4.1% and 9.2% using culture and NTLP PTB definition respectively). The screening tool showed a good sensitivity and specificity for TB with a high negative predictive value, making it a good screening tool in ruling out active TB. Whenever possible a CXR should be done as this may improve the sensitivity of the tool. No relationship was observed between TST and TB.

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ABBREVIATIONS:

AFB	Acid Fast Bacilli
AIDS	Acquired Immune Deficiency Syndrome
BCG	Bacille Calmette-Guérin
CBC	Complete blood count
CPT	Cotrimoxazole Preventive Therapy
CTC	Care and Treatment Clinic
CXR	Chest X-ray
DST	Diagnostic Sensitivity Testing
EPTB	Extra pulmonary Tuberculosis
ESR	Erythrocyte Sedimentation Rate
HAART	Highly Active Anti Retroviral Therapy
HIV	Human Immunodeficiency Virus
INH	Isoniazid
IPT	Isoniazid Preventive Therapy
LTBI	Latent Tuberculosis Infection
MTB	Mycobacterium tuberculosis
NTLP	National Tuberculosis and Leprosy Programme
PCR	Polymerase Chain Reaction
PITC	Provider Initiated Testing and Counseling
PPD	Purified Protein Derivative
PPV	Positive Predictive Value
PTB	Pulmonary Tuberculosis
TB	Tuberculosis
TST	Tuberculin skin test
UNAIDS	United Nations Programme on HIV/AIDS
WHO	World Health Organization

CHAPTER ONE

1.0 BACKGROUND

Tuberculosis, a disease caused by *Mycobacterium tuberculosis* is a global threat to public health. According to the World Health Organization (WHO) one-third of the world's population harbors Mycobacterium tuberculosis (MTB) in an asymptomatic form (latent TB infection [LTBI]) but retain a lifelong risk of future disease. Each year between 8 and 9 million people develop Tuberculosis (TB), and approximately 2 million die from TB Worldwide [1].

1.1 BURDEN OF TUBERCULOSIS

1.1.1 Global burden of tuberculosis

The 2010 WHO Global TB control report, estimated 9.4 million new cases of TB worldwide in 2009, including 1.1 million cases among people with HIV. TB incidence in 2009 was 137 per 100,000 (from 142/100,000 in 2004). The fall in incidence is attributed to provision of IPT, voluntary HIV screening and widespread use of co-trimoxazole preventive therapy [2].

An estimated 0.38 million people who were HIV infected died of TB in 2009, as did 1.3 million people who were not infected with HIV, making a total of 4700 deaths per day [2]. It was also estimated that in 2009, 3.3% of all new TB cases had MDR-TB. Almost 50% of the MDR-TB cases worldwide were estimated to occur in China and India, but estimates show that 69,000 cases emerged in Africa in 2009, of which a vast majority went undiagnosed [2].

1.1.2 Burden of tuberculosis in Tanzania

Tanzania ranks 15th among 22 high-burden TB countries in the world and 6th in SSA with a prevalence of 337 per 100,000. Of the estimated 120,191 new TB cases in the year 2007, 56,233 were sputum smear positive, the remaining being sputum smear negative and Extra Pulmonary TB (EPTB) combined. A male to female ratio of 1:7 and an estimated mortality of 78 per 100,000 population/year was reported in 2007 [3] The regions which report high TB cases in the country include Dar-es-salaam (24%), Mwanza (8%), Arusha (7%), Iringa (7%), Morogoro (6%), Tanga (6%) and Mbeya (6%)[4].

1.2 BURDEN OF HIV

1.2.1 Global burden of HIV

UNAIDS estimated that there were 33.3 million people living with HIV/AIDS at the end of 2009, 30.8 million being adults, of which 15.9 million were women. About 2.6 million people became newly infected with HIV and about 1.8 million deaths occurred due to AIDS in 2009 [5].

1.2.2 Burden of HIV in Sub Saharan Africa (SSA)

Sub Saharan Africa is the world's most severely affected region. In 2009, there were an estimated 22.5 million (68% of the global total) people living with HIV and AIDS, with more women than men being affected. An estimated 1.3 million people died of HIV related illnesses in SSA in 2009, comprising 72% of the global total of 1.8 million deaths attributable to the epidemic [5].

1.2.3 Burden of HIV in Tanzania

In 2009, around 1.2 million people aged 15 and over were living with HIV. About 100,000 were newly infected with HIV, that is around 275 new infections every day [6]. Some regions reported a prevalence of less than 2% (Arusha) and others as high as 16% (Iringa) [5]. In 2007 the estimated adult HIV prevalence was 6.2%, and a total of 96,000 deaths due to HIV/AIDS occurred [5].

1.3 HIV INFECTION AND TUBERCULOSIS

The WHO estimates over 4 million people are TB/HIV co-infected worldwide, the majority of them reside in Africa. Up to 70% of TB patients are HIV infected in SSA and Asia. About 60% of untreated HIV patients develop active TB during their lifetime [7, 8].

The risk of progression from TB infection to disease depends on the status of the immune system and is greatest in the first 2 years after infection [9-11]. Reactivation of TB occurs in about 7-10% of persons who have a positive TST [12]. Patients with TB/HIV co-infection

exhibit higher rates of mortality than CD4 matched controls with TB but without HIV infection[13].

The diagnosis of TB in HIV infected patients may be difficult not only because of the increased frequency of sputum smear negativity but also because of atypical radiographic findings, a lack of classic granuloma formation in the late stages, and negative results in TST[8].

Approximately 60% increase in active TB in Tanzania has been attributed to HIV/AIDS epidemic. Fifty percent of notified TB cases were tested for HIV in 2007, and the prevalence of HIV infection among TB patients was estimated at 47% [14], whereas the prevalence of TB among HIV patients was found to be 15% [15].

1.3.1 Tuberculosis diagnosis

Cultures

This is the gold standard for TB diagnosis. *Mycobacterium tuberculosis* can take 6 weeks or longer to grow on solid culture media (egg-based Lowenstein-Jensen medium or the agar-based Middlebrook 7H10 or 7H11). More rapid results are obtained from liquid media, which usually grows *Mycobacterium tuberculosis* in 7 to 28 days[16]. Cultures are also good in the identification of Mycobacterium based on morphology, growth and biochemical characteristics[16]

Microscopic smears

Sputum smears are routinely done and whenever positive used for initiation of TB treatment while awaiting culture and DST results[16]. However, high rate of sputum smear negativity among HIV infected patients is a hindrance to early TB diagnosis [16].

Other techniques

Rapid gene probes are less sensitive than cultures and are often requested when it is important to differentiate the diagnosis of MTB from other Mycobacteria for which treatment may be

different. Polymerase Chain Reaction (PCR) requires culture and it is known that a negative PCR does not exclude TB[17].

Chest radiography

Radiographic findings suggesting tuberculosis include upper-lobe infiltrates, cavitary infiltrates, and hilar or paratracheal adenopathy. Many patients with primary progressive disease and those with HIV infection, have more subtle radiographic findings and can include lower-lobe infiltrates or a miliary pattern[17].

Drug susceptibility tests

These are useful when drug resistance is suspected and usually available within 10-21 days of the laboratory receipt of the isolates[18].

Tuberculin skin testing

The tuberculin test demonstrates the presence of host hypersensitivity to the proteins of the tuberculous bacillus, most often acquired as a result of infection with M. tuberculosis. Hypersensitivity can however be induced by bacille Calmette-Guérin (BCG) vaccination or infection with environmental mycobacteria[19].

Testing for tuberculosis infection using TST should be performed only in persons who are at high risk for infection since the performance of the test can lead to intervention (treatment or preventive chemotherapy). Groups that are at high risk for tuberculosis infection and should be targeted for TST include contacts of sputum smear positive TB patients, HIV-infected persons, immigrants from countries with high rates of tuberculosis, health care professionals, and persons living or working in long-term care facilities [19].

1.3.2 TB screening

An essential strategy for decreasing the burden of TB and preventing its spread in people with HIV, includes TB screening and active case finding in the clinical settings where people with HIV infection receive their care[22]. All HIV positive patients should undergo routine

screening to determine whether they may have tuberculosis. Screening for TB disease can be done with the administration of a questionnaire asking about symptoms related to possible TB disease. If patients answer positively to any of the questions, this suggests that the patient may have TB disease. This patient should be considered a TB suspect and an evaluation for TB disease should begin. If patients answer no to all the questions, they are considered to be free of active TB and counseled on initiation of IPT[19].

1.3.3 TB preventive therapy

TB chemoprophylaxis for patients co-infected with HIV and *M. tubeculosis* is very important and has been recommended by the UNAIDS and WHO[15]. Many regimens exist and include:-

- 2 months of rifampin and pyrazinamide
- 3 – 4 months of INH and rifampin
- 6 – 9 months INH
- 4 months rifampin[23]
- 18 weeks INH plus rifapentine[25]

The key recommendations of the WHO guidelines for intensified TB case finding and IPT for adults and adolescents living with HIV/AIDS in resource constrained settings are:

- Adults and adolescents living with HIV should be screened for TB with a clinical algorithm and those who do not report any one of the symptoms of current cough, fever, weight loss, or night sweats are unlikely to have active TB and should be offered IPT.
- Adults and adolescents living with HIV and screened with a clinical algorithm for TB, and who report any one of the symptoms of current cough, fever, weight loss, or night sweats may have active TB and should be evaluated for TB and other diseases.
- Adults and adolescents living with HIV who have an unknown or positive TST status and are unlikely to have active TB should receive **at least 6 months of IPT as part of a comprehensive package of HIV care**. IPT should be given to such individuals

irrespective of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women.

- Adults and adolescents living with HIV who have an unknown or positive TST status and who are unlikely to have active TB should receive at least 36 months of IPT. IPT should be given to such individuals irrespective of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women.
- TST is not a requirement for initiating IPT in people living with HIV. People living with HIV who have a positive TST benefit more from IPT; TST can be used where feasible to identify such individuals.
- Providing IPT to people living with HIV does not increase the risk of developing isoniazid-resistant TB. Therefore, concerns regarding the development of isoniazid resistance should not be a barrier to providing IPT[24]

1.4 LITERATURE REVIEW

A population-based survey carried out in 2005–2006 among a random sample of adults in Harare showed that screening failures can be anticipated when either TB symptoms alone or *M. tuberculosis* culture alone is used to screen for previously undiagnosed TB. In this survey, the prevalence of TB symptoms was higher in HIV infected participants (21.2%) than in HIV uninfected participants (9.9%) when at least one symptom was used ($P < 0.001$). TB was asymptomatic in 18 culture-positive individuals, 8 of whom (4 in each HIV status group) had positive sputum smears. Cough of any duration, weight loss and, for HIV+ participants only, drenching night sweats were independent predictors of TB[26].

An IPT pilot study conducted in Botswana in 2001 found that a combination of symptoms was superior to a single symptom in diagnosing active TB. The sensitivity of initial symptom screening in these individuals ranged from 47.9% when chronic cough was used to define a TB suspect to 81.3% when any of the five TB symptoms considered was used. Symptom screening was more sensitive than sputum culture on a solid medium, whose sensitivity was 64.6%[26].

A study conducted in South Africa between April 1999 to July 2001 included 899 HIV-positive gold miners attending a preventive therapy clinic. A screening tool that included new or worsening cough, new or worsening sputum production, haemoptysis, night sweats, fever and self-reported weight loss was administered. Chest radiographs were performed and compared to any prior chest radiographs. It was found that symptoms with the greatest sensitivity (59.1%) and negative predictive value (97.3%) were night sweats, new or worsening cough and weight loss. The inclusion of chest radiographs in the screening process significantly increased the sensitivity (90.9%) and NPV (99.1%) of TB screening. Active TB was identified in 44 (4.9%) miners, and was most common in those with a lower CD4 count of = 200cells/µL[27,28].

Another study conducted in Cape Town in 2003 screened 129 patients with advanced HIV disease for TB. A questionnaire that inquired about weight loss, coughing, night sweats and fever was used. The study found active TB in 11 (8.5%) of the 129 patients. When patients had two or more of the symptoms included in the questionnaire (including measured weight loss), the questionnaire had a sensitivity of 100%, a specificity of 88.1%, and a positive predictive value of 44%[29]

A study in Tanzania among 161 screened subjects during the period of October 2001 to February 2003, to determine the prevalence of active TB among ambulatory HIV-infected persons with CD4 cell counts of =200 cells/mm3 and a BCG vaccination scar found baseline active TB in 15% of the first 93 subjects who were enrolled: 71% had clinical TB (symptoms or chest radiograph findings), and 29% had subclinical TB (positive sputum AFB stain or culture results but no symptoms or chest radiograph findings). It was concluded that clinical and subclinical TB are common among ambulatory HIV-infected persons, and some cases can only be identified by sputum culture[15].

Another study conducted between 1996 and 2005 to determine the long-term incidence of TB and associated risk factors among 346 individuals receiving HAART in South Africa showed that the TB incidence was highest among patients with baseline CD4 cell counts < 100 cells/ml and those with WHO clinical stage 3 or 4 disease. Risk of TB was independently associated with CD4 cell count < 100 cells/ml and age < 33 years. Risk of TB was not independently associated with plasma viral load, previous history of TB, low socioeconomic status or sex[31].

In HIV infected patients there is a reduction in the proportion of those reacting to PPD as the CD4 count falls, from 50%-90% in those who have a CD4 count of =500 cells/ul and down to 0% - 20% in those patients who have AIDS or advanced HIV infection with CD4 count of =200cells/ul [20]. The cutoff value of the TST is often reduced from an induration of 10 mm in diameter to one of 5 mm in diameter to compensate for loss of sensitivity. The effectiveness of this reduction depends on the underlying mechanism: a gradual decrease in skin test

responsiveness with decreasing immunocompetence or an all-or-nothing switch to complete anergy[21]

Studies have shown that IPT is effective for HIV-infected patients with latent TB infection (LTBI) who are at high risk of progressing to active tuberculosis (TB) disease[32,33] Preventive therapy could significantly reduce TB incidence in populations with high TB prevalence[34].

In a study published in 1982 by the International Union Against Tuberculosis Committee on Prophylaxis (IUATCP) on 28,000 people, the preventive effect of Isoniazid was seen after the first 12 weeks on treatment with a 31% reduction in incidence of active disease, the effect increased to 69% after 24 weeks of IPT, and to over 93% at 52 weeks in adherent/completer patients[35].

In settings of high TB infection (>30%), the WHO policy is that preventive therapy should be provided to all eligible people with HIV (WHO/UNAIDS 1998) regardless of the TST response. But reports have shown that IPT reduces the risk of developing active disease in people with HIV and a positive TST by about 64% and the risk of mortality by 26%[32].

Specific investigations on whether prophylaxis with INH is equally effective in TST - positive and negative persons, revealed that IPT for 6 months effectively reduces the incidence of TB in HIV-infected people and that the risk reduction is larger in TST-positive than in TST-negative persons[32,36]. The data suggests that INH prophylaxis in HIV infection may be limited to individuals with positive TST[36]

In a study done on 2376 participants in Maryland (USA), among 800 HIV-positive participants, 649 (81%) had a TST placed and read. TST positivity differed significantly between HIV-positive participants (16%) and HIV negatives (39%); $P < 0.01$. Among HIV positives, TST positivity had an inverse association with CD4 count, with only 4.1% of those with CD4 < 200/mm3 (P=.02) having a positive result[37].

A cross-sectional study of TST responses and HIV infection among patients with sputum smear positive PTB was conducted in 6 hospitals in Tanzania during the period of 2000 to 2003. Of 991 patients with complete results, 451 (45.5%) had HIV infection. The sensitivity of the TST among HIV-infected patients was 64.3% at a cutoff value of 10 mm and 71.2% at a cutoff value of 5 mm[38].

1.5 DEFINITION OF TERMS

Pulmonary tuberculosis – Tuberculosis affecting the lungs

Extra pulmonary Tuberculosis – Tuberculosis affecting organs other than the lungs such as pleura, lymph nodes, peritoneum, pericardium, spine and joints.

The Tanzania NTLP defines PTB in the presence of two of the following:

1. Symptoms of tuberculosis (cough, fever, night sweats, loss of weight for more than 2 weeks)
2. AFB visible by direct Ziehl Nielsen staining of sputum specimen or *M.tuberculosis* cultured from sputum in Lowenstein Jensen media
3. Chest radiograph independently interpreted as highly suggestive of tuberculosis
4. For patients with culture negative tuberculosis, a clinical response to anti tuberculosis medication

Alcohol abuse is defined as repeated drinking of alcohol in quantities in excess of 21U/week in men and 14U/week in women which leads to harm in one's work or social life. 1U ˜ 9g ethanol ˜ 1 spirits measure ˜ 1 glass of wine ˜½ pint of beer[39].

1.6 PROBLEM STATEMENT:

Over the past few decades, there have been many studies conducted on different ways of diagnosing and managing HIV infected patients with active TB. Despite this, the prevalence of TB disease is still increasing at an alarming rate and this has largely been attributed to the increase in HIV disease especially in the developing world.

The World Health Organization (WHO) recommended a 6-month course of IPT for persons living with HIV (PLWH) in TB-endemic countries in 1993[40]. Although policies for IPT exist, the WHO reported that, provision of IPT remains at very low levels, with reported numbers treated with IPT reaching only 27,056 in 2006 equivalent to less than 0.1% of the estimated 33 million people estimated to be infected with HIV globally[41].

Although the prevalence of TB symptoms is high in HIV positive patients, the effectiveness of symptomatic screening in ruling out active TB in TB/HIV co infected patients remains unclear. This study aimed to evaluate the usefulness of the NTLP screening tool in identifying patients eligible for IPT and the role of TST among patients attending MNH HIV clinic.

1.7 RATIONALE:

Various studies conducted showed differing results on diagnostic effectiveness when certain symptoms or combination of symptoms and/or laboratory and radiological findings were considered in ruling out active TB in PLWHA[26, 42-44].

There is no data in Tanzania on what symptoms or combination of symptoms is most sensitive in ruling out active TB in PLWHA prior to initiation of IPT. In order to start countrywide IPT provision, the Tanzania NTLP has launched a pilot study on IPT in PLWHA at 14 different sites in the country. A screening tool involving five questions (cough = 2 weeks, fever = 2weeks, haemoptysis, excessive night sweats = 2weeks and noticeable weight loss or weight loss of = 3Kg in 4 weeks) is being used to rule out active TB prior to initiation of IPT. The addition of haemoptysis in the screening tool is thought to increase the sensitivity of the screening tool.

This study was therefore conducted to provide data on the usefulness of the NTLP screening tool in identifying patients eligible for IPT and the role of TST among patients attending MNH HIV clinic.

CHAPTER TWO

2.0 OBJECTIVES:

2.1 BROAD OBJECTIVE:

To assess the usefulness of the NTLP screening tool in identifying patients eligible for IPT and the role of TST among patients attending MNH HIV clinic.

2.2 SPECIFIC OBJECTIVES:

1. To determine the prevalence of TB through clinical screening among patients attending MNH HIV clinic by using the Tanzania NTLP TB screening tool.
2. To determine the sensitivity and specificity of the Tanzania NTLP TB screening tool in ruling out active TB among patients attending MNH HIV clinic.
3. To determine the prevalence of TST positivity among HIV infected patients attending MNH HIV clinic.
4. To determine the relationship between TST reactivity and TB among HIV infected patients attending MNH HIV clinic

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

This was a descriptive cross sectional study.

3.2 Study duration

This study was conducted in a period of 3 months, from September 2011 to November 2011

3.3 Study site

The study took place at the Muhimbili National Hospital HIV clinic in Dar-es-Salaam. MNH is Tanzania's largest tertiary hospital in the country. The MNH HIV clinic receives patients from the different districts and from inpatients discharged from the medical wards through the clinic. It is a 5 day per week clinic, patients attend on a monthly basis for clinical evaluation and ART refill, with a daily attendance of 70 to 100 patients. This site was chosen because it is one of the pilot sites for IPT.

Dar es Salaam is located at $6^0$48' East and is an administrative province in Tanzania. There are three administrative districts; Kinondoni to the North, Ilala in the center of the region and Temeke to the South. According to the 2002 National census, this region had a population of 2,497,940.

3.4 Study population

Study participants were outpatients attending Muhimbili National Hospital HIV clinic. Both HAART naïve and those on HAART were included in the study.

3.5 Sampling and Sample size

The sample size was obtained using the following formula

$n = Z^2 pq/ d2$

n = the required sample size

z = 1.96 (96% confidence interval)

d = maximum likely error, 4%

p = prevalence of TB in HIV patients - 15%[15]

= 306 patients

Thus the minimum sample size was round figured to 310

3.6 Sampling technique

Consecutive recruitment of subjects was done in the clinic starting from September to November 2011.

3.7 Inclusion criteria

- Known HIV infected patients attending MNH HIV clinic (HAART naïve and those on HAART)
- Age above 18 years
- Consent to take part in the study

3.8 Exclusion criteria

- Current TB or TB treatment = 2 years
- Pregnant women (verbal response)
- Alcohol abuse

The inclusion and exclusion criteria have been taken from the National TB guidelines for IPT in Tanzania. Age above 18 years in this study was taken for ethical reasons.

3.9 Data collection methods and procedures

Patients attending the MNH HIV clinic were enrolled into the study if they met the inclusion criteria. A structured questionnaire was used to obtain the patient's information.

All consenting individuals were interviewed at the MNH HIV clinic doctor's room by the investigator and trained research assistants. Personal particulars, clinical history and physical examinations information were obtained and filled into a structured questionnaire.

The structured questionnaire also included the NTLP's 5 screening tool (cough = 2 weeks, fever = 2weeks, haemoptysis, excessive night sweats = 2weeks, and noticeable weight loss or weight loss of = 3Kg in 4 weeks) used by the NTLP in screening for TB suspects prior initiation of IPT (Refer next page).

Subjects were recruited on Mondays, Tuesdays and Fridays. On recruitment, the following was done: General clinical evaluation to all the study participants, clinical examination including anthropometric measurements. Weight was measured using an analogue scale (SECA) without shoes and in light clothing and was recorded to the nearest 0.5kg and height was measured using a measuring rod after the patient had removed his/her shoes and cap and was recorded to the nearest centimeter. Temperature was measured in degrees Celsius using a digital thermometer. Systemic examination included the lymphatic system, skin and mucous membranes, respiratory system, GIT, cardiovascular, central nervous system and musculoskeletal examination. Any abnormality was documented as yes or no and specified.

An intradermal injection of 0.1ml of 2TU of PPD, was injected on the volar surface of the forearm using a disposable 1.0ml graduated syringe fitted with a short steel bevel needle gauge 26. No antiseptic was used to clean the injection site. The site was slightly stretched and the needle point held almost parallel to the skin surface. With the bevel upwards and inserted into the superficial layer of the dermis, the solution was slowly injected with appearance of a small papule. If a papule did not appear, another injection was repeated into the other volar surface of the forearm[45]. Reading of the Mantoux response was done 72 hours after the injection. A reaction response was defined as a flat, uneven, slightly raised and palpable induration measured transversely at its widest diameter against the long axis of the forearm using

Annex ….: TB Screening Questionnaire

MINISTRY OF HEALTH AND SOCIAL WELFARE COLLABORATIVE TB/ HIV ACTIVITIES

TB SCREENING QUESTIONNAIRE FOR ABOVE AGE 5 YEARS AND ADULT HIV/AIDS PATIENTS

Patient's name: ..... CTC Reg. Number: ..... Date of birth: ../...../.... Sex: □ Male □Female

Physical Address: ..... Area leader/ neighbor: ..... Contact telephone (if available).....

Date																							
Tick appropriate response	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y
Cough for ≥ 2 weeks?																							
Coughing up bloodstained sputum (haemoptysis)?																							
Fevers for ≥ 2 weeks?																							
Noticeable weight loss for new patients or a 3 kgs weight loss in a month (subsequent visit)?																							
Excessive sweating at night for ≥ 2 weeks?																							

If 'YES' to one or more questions enter the code "*TB Susp*" in the TB status column of the CTC2 form and complete the respective column in the table below:

Date												
Do sputum smear for AFB and enter results (*pos / neg*)												
If sputum negative, do chest X-ray and enter result (*suggestive* or *not suggestive*)												
Outcome of assessment (*TB* or *No TB*)												

If 'No' to all questions: Do not initiate TB investigations and repeat screening at the subsequent visit. Enter the code "NO" in the TB status column of the CTC

Figure 1: Ministry of Health and Social Welfare - NTLP TB screening tool

a clear, flexible plastic ruler and recorded in millimeters (mm). The results of the Mantoux test were interpreted as Negative TST response when the induration measured = 4mm, and positive TST response when the induration measured = 5mm[46]

Sputum samples were collected from all patients. Sputum specimens from all participants were obtained through sputum induction with an Omron NE-U17 ultrasonic nebulizer, which has a maximum flow rate of 17L/min and a spraying speed of 0-3ml/min with a particle size of 4.4m mass median aerodynamic diameter (MMAD). This was done in an open space that was well ventilated. Prior to sputum induction each patient received pretreatment with a bronchodilator i.e salbutamol 200-400µg from a standard metered dose inhaler. For each induced patient one sputum sample was collected then transported in cool boxes to the NTLP reference laboratory at the Central Pathology Laboratory (CPL) located within the MNH. Each sputum sample was divided into two parts which were kept at -4^0C awaiting processing. One sample was stained with Ziehl Neelsen stain for AFB and the other was processed for growth in Lowenstein Jensen Culture media.

Sputum smear for microscopy was graded as:

+ 1 when 10 – 99 AFB were seen per 100 immersion fields in a smear,

+2 when 1 – 10 AFB were seen per 1 immersion field in a smear,

+3 when more than 10 AFB were seen per 1 immersion field in a smear[47]

Laboratory blood investigations:

Venepuncture was done from the antecubital veins in a recumbent position, 10mls of blood were collected and put into 3 different tubes; one contained an anticoagulant EDTA, the others had no anticoagulant. For determination of peripheral blood counts an automated counter was used i.e. Cell Dyn System 1200 (Abbott Diagnostics division). ESR was obtained using the Westergreen method. ALAT and ASAT were determined using direct spectrophotometric measurement. CD4+ cell counts were determined by flow cytometry using Becton Dickson Facs count machine. Samples were analyzed at the hematology and biochemistry laboratory at the Central Pathology Laboratory of the Muhimbili National Hospital.

Radiological investigations:

Chest radiographs were obtained from all participants. A radiologist who was blinded to the HIV status of the participants reported whether the radiograph was suggestive or not suggestive of TB.

Case definitions:

Pulmonary TB

For study purposes, patients were classified as having TB if they fulfilled the Tanzania NTLP TB definition. The Tanzania NTLP defines TB in the presence of two of the following:

- Symptoms of tuberculosis (cough, fever, night sweats, loss of weight for more than 2 weeks)
- AFB visible by direct Ziehl Nielsen staining of sputum specimen or *M.tuberculosis* cultured from sputum in Lowenstein Jensen media
- Chest radiograph independently interpreted as highly suggestive of tuberculosis
- For patients with culture negative tuberculosis, a clinical response to anti tuberculosis medication

Operational PTB definition:

In Tanzania, sputum samples for MTB are rarely done in the normal hospital setting. An operational PTB definition in this study excludes mycobacterial culture and defines PTB as the presence of two of the following:-

- Symptoms of tuberculosis (cough, fever, night sweats, loss of weight for more than 2 weeks)
- AFB visible by direct Ziehl Nielsen staining of sputum specimen
- Chest radiograph independently interpreted as highly suggestive of tuberculosis
- For patients with culture negative tuberculosis, a clinical response to anti tuberculosis medication

3.10 Disposal of the patients

Symptoms and signs of TB together with radiological and laboratory results were used to diagnose active TB. Subjects with active TB were referred to the District TB and Leprosy co-coordinator for initiation of anti TB as per Tanzania NTLP guidelines.

Patients considered free of active TB were referred to the nurse and counseled on initiation of daily 300mg INH tablets[48]

3.11 Ethical consideration:

Ethical clearance to conduct the study was sought from Muhimbili University of Health and Allied Sciences Ethical Review Board. Permission to do the study was obtained from the Hospital management. A written informed consent to participate in the study was sought from the study participants. Clinical evaluation and laboratory investigation procedures and interpretations were done by qualified registered doctors. Results were communicated to the patients and were treated according to the available guidelines.

Confidentiality

All participant records and laboratory results were kept locked in secure storage areas. Data entered in the database bared no names but numbers allocated to the participants.

3.12 Data entry, cleaning and analysis:

Collected data was checked for completeness and consistency, and errors or discrepancies found were promptly corrected. Data was entered by the investigator into the computer using EPI info version 6 and checked for clarity.

Data analysis was performed using SPSS version 18. Cross tabulations and Pearson's Chi – square test were used to obtain the associations and strength of relationship between variables. Multivariate analysis was done to calculate predictors of PTB from the various symptoms used in the screening tool. Student t test was used to compare means of two variables. P-value of 0.05 or less was taken as significant.

CHAPTER 4

4.0 RESULTS

A total of 474 participants were screened, 373 fulfilled the inclusion criteria and were enrolled in the study. Those who did not meet the inclusion criteria were due to pregnancy/suspected pregnancy in 4 (0.84%) , anti TB treatment in 19 (4.04%), use of Isoniazid Preventive Therapy in 23 (4.9%) , and 55 (11.6%) would not be able to come for the tuberculin skin test reading.

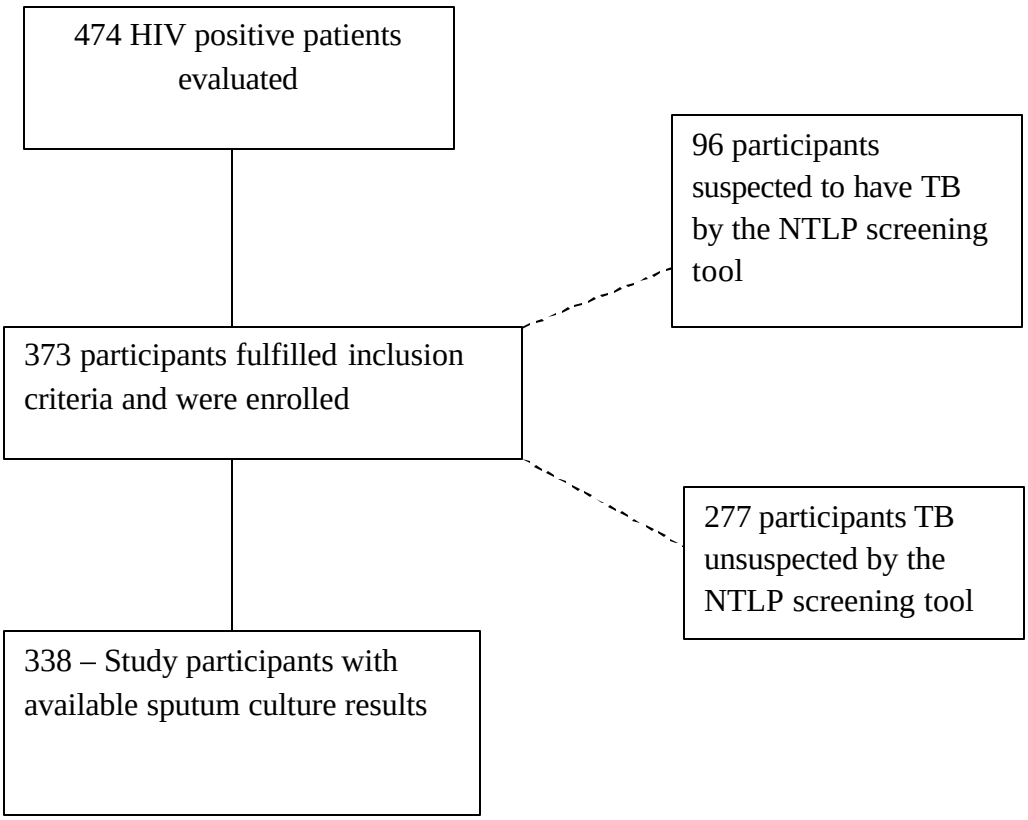

Figure 2: Flow chart of study participants

4.1 Socio-demographic and clinical characteristics of the study participants.

Majority of the participants were women 269/373 (72.1%). The overall mean (SD) age was 41 (± 9.6) years, being 44.4 (±10.32) years for males and 36.7(±8.99) years for females. Almost half of the participants (46.1%) were in the age group 35-44 years (Table 1).

Majority of the study subjects (57.1%) were married or cohabiting. The commonest occupation was petty business (42.1%), and about a quarter (23.3%) was unemployed. The occupation category "others" comprised of subsistence farmers, drivers, housewives, shopkeepers, watchmen and students, and accounted for 20.4%. Most of the participants had primary level education (63%) (Table 1).

Half of the participants 188/373 (50.4%) had normal weight, while 41.3% (154/373) were overweight or obese. Majority of the participants 197/373 (52.8%) were in WHO HIV stage II while 101/373 (27.1%) were in WHO stage III or IV. About fifty three percent (52.8%) had a CD4 count = 350 cells/μL. Twenty nine (7.8%) had their CD4 results missing (Table 1).

About 90% of the participants were on ARV, majority 151/373 (40.5%) were on AZT+3TC+EFV. Only 9/373 (2.4%) of participants were on protease inhibitors based regimen (Table 1).

Peripheral neuropathy was reported in 29.2% of the study participants, whereas jaundice was rare with a frequency of 0.5% (Table 1).

Table 1: Socio-demographic and clinical characteristics of the study participants (N=373)

VARIABLE		FREQUENCY	PERCENTAGE
Gender	Female	269	72.1
Age	18 – 24	10	2.7
	25 – 34	80	21.4
	35 – 44	172	46.1
	45 – 54	78	20.9
	=55	33	8.8
Marital status			
	Single	109	29.2
	Married/cohabiting	213	57.1
	Divorced	26	7
	Widowed	25	6.7
Occupation			
	Unemployed	87	23.3
	Civil servant	29	7.8
	Health care worker	17	4.6
	Petty business	157	42.1
	Large scale business	7	1.9
	Others	76	20.4
Education level			
	No formal education	39	10.5
	Primary school	235	63
	Secondary school	94	25
	Post secondary	5	1.3
Body mass index (Kg/m^2)			
	<18.5	31	8.3
	18.5 – 24.9	188	50.4
	=25	154	41.3
WHO HIV stage			
	I	75	20.1
	II	197	52.8
	III	86	23.1
	IV	15	4
CD4 count			
	=50	5	1.3
	51-199	59	15.8
	200-349	83	22.3
	=350	197	52.8
	Missed CD4 results	29	7.8
ARV treatment			
	No ARVs	40	10.7
	AZT+3TC+EFV	151	40.5
	AZT+3TC+NVP	110	29.5
	d4T+3TC+NVP	28	7.5
	d4T+3TC+EFV	22	5.9
	TDF+FTC+EFV	13	3.5
	ABC+ddI+L/r	9	2.4
Jaundice		2	0.5
Peripheral neuropathy		109	29.2

4.2 Prevalence of TB using sputum culture for MTB in LJ media (gold standard)

Of the 373 enrolled patients, mycobacterial culture was available for 338 participants. Of the 338 participants, 88 responded yes to one of the 5 screening questions of the NTLP screening tool. Sputum culture was positive for MTB in 10 of the 88 TB suspects and 4 of the 250 TB unsuspected. Thus the prevalence of PTB by sputum culture was 4.1% (14/338) (Figure 3).

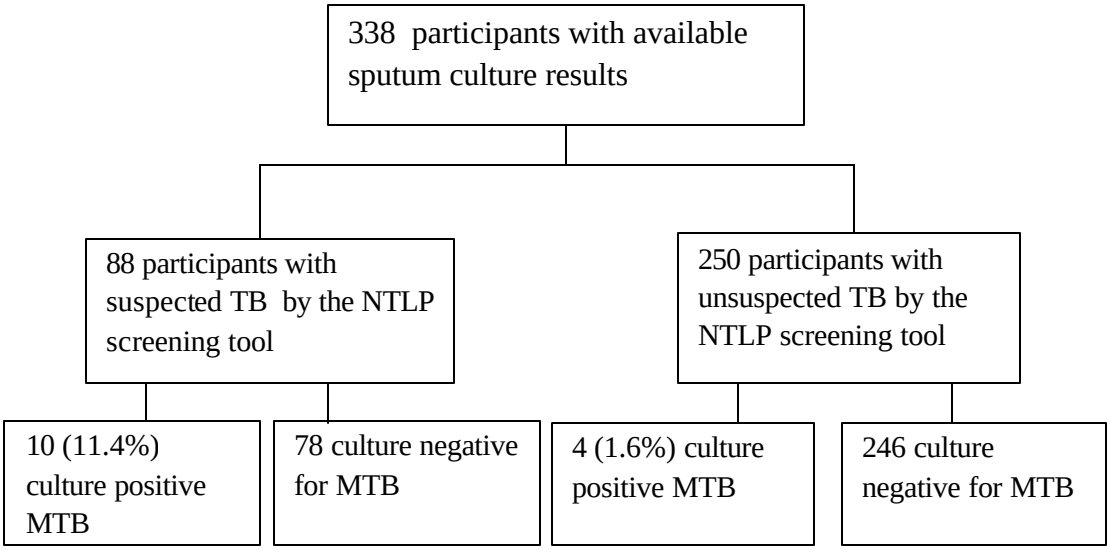

Figure 3: Flow chart of study participants showing TB patients as defined by sputum culture

4.2.1 Sensitivity and specificity of the screening tool using sputum culture for MTB as a standard for the diagnosis of PTB.

The NTLP symptom screening tool had an overall sensitivity of 71.4% (10/14) and a specificity of 75.9% (246/324). Positive predictive value was found to be 11.4% (10/88) whereas the negative predictive value was 98.4% (246/250). Four participants (4/250, 1.6%) with culture positive MTB reported no symptoms. These would have been missed by the screening tool and counseled on initiation of IPT (Table 2).

Table 2: Sensitivity and specificity of the screening tool using sputum culture for MTB as a standard for the diagnosis of PTB.

		Sputum culture		
		Positive	**Negative**	**Total**
NTLP screening tool	**TB suspect**	10 (71.4%)	78 (24.1%)	88 (26%)
	Not TB suspect	4 (28.6%)	246 (75.9%)	250 (74%)
Total		14 (100%)	324 (100%)	338 (100%)

4.3 Prevalence of TB using the NTLP TB definition for the diagnosis of PTB:

Among the 373 patients enrolled 338 participants had culture results available. Of the 338 patients with culture results available, 88 (26%) were TB suspects (i.e responded "yes" to one of the 5 screening tool questions) whereas 250(74%) were not TB suspects (responded "no" to all the 5 questions in the screening tool). Those who fulfilled the NTLP PTB definition were 28 among the TB suspects and 3 among the TB unsuspected. Thus the prevalence of PTB as per the NTLP definition was 9.2% (31/338).

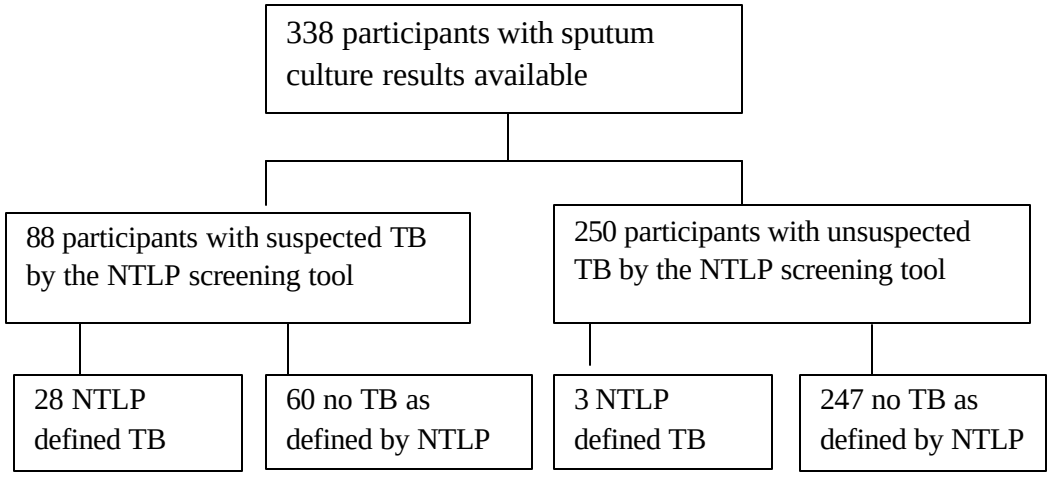

Figure 4: Flow chart of study participants showing TB patients as defined by NTLP PTB definition

4.3.1 Sensitivity and specificity of the screening tool against the NTLP TB definition.

The sensitivity and specificity of the screening tool against the NTLP PTB definition was 90.3% (28/31) and 80.5% (247/307) respectively. The PPV was 31.8% (28/88) and the NPV was 98.8% (247/250) (Table 3)

Table 3: Sensitivity and specificity of the screening tool against the NTLP TB definition.

		NTLP TB definition		
		TB	**Not TB**	**Total**
NTLP screening tool	**TB suspect**	28 (90.3%)	60 (19.5%)	88 (26%)
	Not TB suspect	3 (9.7%)	247 (80.5%)	250 (74%)
Total		31 (100%)	307 (100%)	338 (100%)

4.4 Prevalence of TB using the Operational PTB definition:

The NTLP PTB definition includes sputum culture as one of the components in making a diagnosis of TB. However, sputum culture is rarely done in routine practice. In the operational PTB definition, the sputum culture component was excluded from the NTLP PTB definition. Among the 373 participants enrolled in the study, 96 responded "yes" to one of the 5 screening tool questions, whereas 277 participants responded "no" to all the 5 screening tool questions. Twenty nine of the 96 TB suspects fulfilled the operational PTB definition. Thus the prevalence of PTB as per the Operational PTB definition was 7.8% (29/373) (Figure 6).

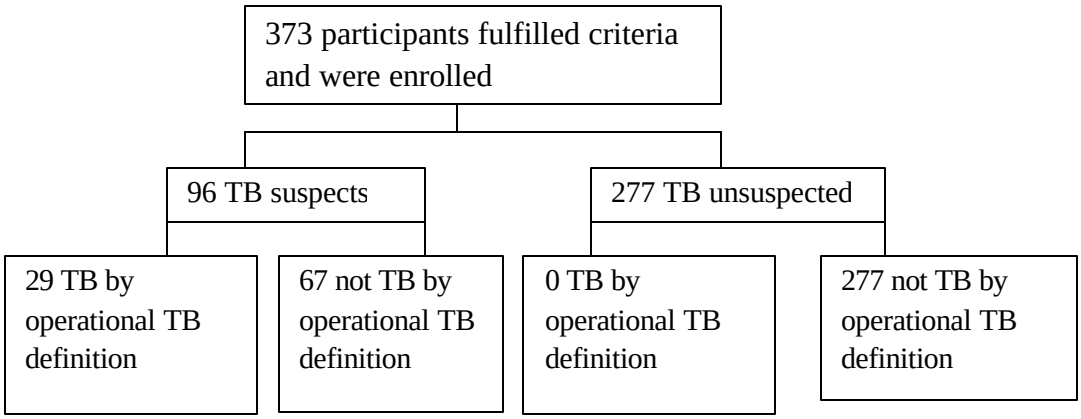

Figure 5: Flow chart of study participants showing TB patients as defined by the operational PTB definition

4.4.1 Sensitivity and specificity of the screening tool against the Operational PTB definition.

The sensitivity of the screening tool against the operational PTB definition was 100% (29/29) and specificity of 80.5% (277/344), the PPV was 30.2% (29/96) and NPV was 100% (277/277) (Table 4).

Table 4: Sensitivity and specificity of the screening tool against the Operational PTB definition.

		Operational PTB definition		
		Positive	**Negative**	**Total**
NTLP screening tool	**TB suspect**	29 (100%)	67 (0%)	96 (100)
	Not TB suspect	0 (0%)	277 (100%)	277 (100)
Total		29 (100%)	344 (100%)	373 (100%)

4.5 Socio-demographic characteristics of the study participants by TB status

The socio-demographic characteristics of the study participants in relation to TB status are shown in Table 5. Widowed participants constituted the highest proportion of the TB patients, being 17.4% an 34.8% as defined by sputum culture and NTLP TB definition respectively. The difference observed across the marital status is statistically significant with p values of 0.009 and < 0.001 by culture and NTLP respectively (Table 5).

Table 5: Socio-demographic characteristics of study participants by TB status as defined by positive sputum culture and the NTLP PTB definition (N= 338)

		PTB by positive sputum culture		PTB by NTLP definition	
Characteristic	**Total no.**	**Number (%)**	**P value**	**Number (%)**	**P value**
Gender					
Male	89	6 (6.7)		11 (12.4)	
Female	249	8 (3.2)	0.211	20 (8.0)	0.283
Age group					
18 – 24	10	0 (0)		1 (10)	
25 – 34	70	2 (2.9)		5 (7.1)	
35 – 44	157	5 (3.2)		13 (8.3)	
45 – 54	73	4 (5.5)		6 (8.2)	
=55	28	3 (10.7)	0.347[ᵀ]	6 (21.4)	0.132[ᵀ]
Marital status					
Single	102	2 (2)		6 (5.9)	
Married	191	7 (3.7)	**0.009**[†]	16 (8.4)	**<0.001**[†]
Divorced	22	1 (4.5)		1 (4.5)	
Widowed	23	4 (17.4)		8 (34.8)	
Occupation					
Unemployed	82	1 (1.2)		3 (3.7)	
Civil servant	23	2 (8.7)		2 (8.7)	
Health care worker	16	0 (0)	0.453[ᵀ]	2 (12.5)	0.052[ᵀ]
Petty business	141	8 (5.7)		11 (7.8)	
Large scale business	5	0 (0)		0 (0)	
Others	71	3 (4.2)		13 (18.3)	
Education level					
No formal education	35	2 (5.7)		2 (5.7)	
Primary school	210	7 (3.3)	0.728[ᵀ]	19 (9.0)	0.723[ᵀ]
Secondary school	88	5 (5.7)		9 (10.2)	
Post secondary	5	0 (0)		1 (20)	

[ᵀ] The P value determined by Fischer's exact test

4.5.1 Presenting clinical features and laboratory investigations of the TB patients.

Patients with cough constituted the highest proportion of patients with TB (21.4%), followed by night sweats (7.1%), and fever (6.1%). However, only cough was significantly associated with TB as defined by sputum culture. By using NTLP TB definition, cough, fever and weight loss were significantly associated with TB, seen in 39.3%, 30.3% and 30.0% respectively, p value < 0.001 in all the three (Table 6).

The highest proportion of TB patients was found in underweight (BMI < 18.5) participants. The proportion is 6.9% with culture defined TB and 20.7% with NTLP defined TB, p values 0.731 and 0.06 respectively (Table 6).

A higher proportion of TB patients had CD4 values < 200cells/µL. The proportion being 6.3% with culture defined TB and 15.9% with the NTLP defined TB, p values of 0.307 and 0.057 respectively (Table 6).

Both culture defined TB and NTLP defined TB patients presented with a raised ESR and lymphocytosis though this was not statistically significant (Table 6).

Table 6: Clinical and laboratory characteristics of study participants by PTB status as defined by positive sputum culture and by NTLP TB definition (N = 338)

		PTB by positive sputum culture		PTB by NTLP definition	
Variable	**Total no.**	**Number. (%)**	**P value**	**Number (%)**	**P value**
***Symptoms**					
Cough = 2 weeks	28	6 (21.4)	<0.001ᵀ	11 (39.3)	<0.001ᵀ
Hemoptysis	3	0 (0)	1.0ᵀ	1 (33.3)	0.251ᵀ
Fever = 2 weeks	33	2 (6.1)	0.636ᵀ	10 (30.3)	<0.001ᵀ
Night sweats	14	1 (7.1)	0.453ᵀ	3 (21.4)	0.127ᵀ
Weight loss	40	2 (5)	0.675ᵀ	12 (30.0)	<0.001ᵀ
Body mass index (Kg/m^2)					
<18.5	29	2 (6.9)		6 (20.7)	
18.5 – 24.9	174	7 (4)	0.731ᵀ	16 (9.2)	0.06ᵀ
=25	135	5 (3.7)		9 (6.7)	
WHO HIV stage					
I	65	2 (3.1)		2 (3.1)	
II	181	10 (5.5)	0.538ᵀ	21 (11.6)	0.198ᵀ
III	77	2 (2.6)		6 (7.8)	
IV	15	0 (0)		2 (13.3)	
****CD4 count (cells/ul)**					
< 200	63	4 (6.3)		10 (15.9)	
=200	274	10 (3.6)	0.307ᵀ	21 (8.8)	0.057ᵀ
Lymphocytosis					
Yes	42	3 (7.1)		5 (11.9)	
No	296	11 (3.8)	0.396ᵀ	26 (8.7)	0.752ᵀ
****ESR**					
=20mm/Hr	141	5 (3.5)		8 (5.7)	
>20mm/Hr	196	9 (4.6)	0.785†	23 (11.7)	0.084†
ARVuse					
Yes	308	11 (3.6)		28 (9.1)	
No	30	3 (10.0)	0.118†	3 (10.0)	0.747†

* Participants could report presence of more than one symptom

**CD4 count and ESR (n=337)

† The P value determined by Fischer's exact test

4.6 Predictors of PTB using MTB sputum culture.

Using MTB sputum culture, predictors for TB were cough = 2 weeks OR (95% CI) = 13.4 (3.9-46.5), p < 0.001 and ARV use, OR (95% CI) = 4.6 (1.1-19.7) p= 0.042 (Table 7).

Table 7: Predictors of TB using MTB sputum culture (N = 338)

	Univariate			Multivariate		
	OR	**95% CI**	**p-value**	**OR**	**95%CI**	**p-value**
Cough = 2 weeks	10.3	3.3-32.3	**<0.001**	13.4	3.9-46.5	**<0.001**
Haemoptysis	0	0	0.999	.000	0	.999
Fever = 2 weeks	1.6	0.3-7.4	0.564	1.4	0.2-7.9	.716
Night sweats	1.8	0.2-15.1	0.571	1.9	0.2-20.5	.600
Weight loss	1.3	0.3-5.8	0.772	.6	0.1-3.3	.554
ESR	1.3	0.4-3.9	0.636	1.0	0.3-3.4	.985
Lymphocytosis	0.5	0.1-1.9	0.306	.5	0.1-2.1	.353
ARV use	3.0	0.8-11.4	0.107	4.6	1.1-19.7	.042

4.7 Predictors of TB using the NTLP PTB definition.

Using the NTLP PTB definition, predictors for TB were cough = 2 weeks, fever = 2weeks, noticeable weight loss or weight loss of = 3Kg in 4 weeks (Table 8).

Table 8: Predictors of TB using the NTLP PTB definition (N = 338).

	Univariate			Multivariate		
	OR	**95% CI**	**p-value**	**OR**	**95%CI**	**p-value**
Cough = 2 weeks	9.4	3.9-22.7	**<0.001**	8.1	3.0-21.7	**<0.001**
Haemoptysis	5.1	0.5-57.7	0.190	1.5	0.1-33.1	.802
Fever = 2 weeks	5.9	2.5-14.0	**<0.001**	4.6	1.7-12.5	**.003**
Night sweats	2.9	0.8-11.0	0.120	1.3	0.3-6.5	.722
Weight loss	6.3	2.8-14.3	**<0.001**	4.7	1.8-12.2	**.002**
ESR	2.2	1.0-5.1	0.063	1.6	0.6-4.1	.322
Lymphocytosis	0.7	0.3-2.0	0.514	1.0	0.3-3.7	.959
ARV use	1.1	0.3-4.0	0.869	1.0	0.3-4.2	.970

4.8 Prevalence of Tuberculin skin test (TST) positivity

All 373 participants underwent a TST, however TST results were available for 354 (94.9%) participants. A positive tuberculin skin test (TST = 5mm) response was seen in 24% (85/354) of the participants. The mean (SD) diameter of tuberculin skin test (TST) induration was 4.1 (± 7.9) mm.

Of the 354 participants with TST results, 340 had CD4 count values available for analysis. Of the 340 participants with TST and CD4 count values available, 81 (23.8%) participants had a positive TST. About 28% of participants with CD4 =200 cells/µl had positive TST results as compared to 6.3% of patients with CD4 < 200 cells/µl, p value <0.001(Table 9)

Table 9: TST reactivity by CD4 cell count among the study participants (N=340)

CD4 counts (cells/µL)		**<200**	**=200**	**Total**	**P value**
TST induration	**0 – 4mm**	60 (93.8%)	199 (72.1%)	259 (76.2%)	**<0.001**
	= 5mm	4 (6.3%)	77 (27.9%)	81(23.8%)	
	Total	64 (100%)	276 (100%)	340 (100%)	

4.9 TB status by TST reactivity among the study participants

Two of the 338 participants with culture results had no TST results. Of the 336 participants with sputum culture and TST results available, 81 participants had a positive TST. Six (7.4%) of the 81 participants with a positive TST had PTB as defined by positive sputum culture, p = 0.111, whereas 7/81(8.6%) had TB as per the NTLP PTB definition, p value 1.000.(Table 10)

As per the TB screening tool, 85 participants had a positive TST (Table 10). TB was not suspected in 64 (75.3%) participants, whereas TB was suspected in 21 (24.7%) participants, p value 1.000.

Table 10: TB status as defined by MTB positive sputum culture and NTLP PTB definition by TST reactivity among the study participants (N=336)

TB status		**MTB sputum culture**			**NTLP PTB definition**		
		TB	Not TB	Total	TB	Not TB	Total
TST induratio	0-4mm	8 (3.1)	247 (96.9)	255 (100)	23 (9.0)	232 (91.0)	255 (100)
	=5mm	6 (7.4)	75 (92.6)	81 (100)	7 (8.6)	74 (91.4)	81 (100)
Total		14 (4.2)	322 (95.8)	336 (100)	30 (8.5)	306 (91.5)	336 (100)
P value		0.111			1.000		

5.0 DISCUSSION

The present study aimed at evaluating the ability of the NTLP screening tool to rule out active TB among patients eligible for IPT and the role of TST among patients attending MNH HIV clinic.

Active TB was diagnosed in 4.1% (sputum culture) and 9.2% (NTLP PTB definition) of the patients attending the MNH HIV clinic. The sensitivity and specificity of the NTLP TB screening tool in the present study was 71.4% and 75.9% respectively, with PPV and NPV of 11.4% and 98.4% respectively. Four (1.6%) participants with culture positive MTB were missed by the NTLP screening tool. The sensitivity and specificity of NTLP PTB definition was 90.3% and 80.5% respectively, with a PPV of 31.8% and NPV of 98.8%. Cough = 2 weeks, fever = 2weeks, noticeable weight loss or weight loss of = 3Kg in 4 weeks were found to be independent predictors for PTB as per NTLP PTB definition while Cough = 2 weeks and ARV use were predictors for TB when positive MTB sputum culture was used to define TB. A positive TST was found among 24% of the participants, and TST positivity was associated with CD4 values of = 200cells/µL. No relationship was observed between TST and TB.

A significantly higher proportion of women constituted the study participants. The preponderance of females in the HIV clinic could be due to the fact that a higher proportion of women in Tanzania are HIV infected compared to men, the prevalence in 2008 was 6.8% in females and 4.7% in males. Another reason for the high female preponderance could be a poor and delayed uptake of HIV services amongst men[49]. This finding is comparable to studies in Ethiopia and South Africa that found significantly higher proportions of women with HIV infection than men[43].

5.1 Prevalence of TB

The NTLP defined PTB prevalence in the present study is similar to a study done in Rural Northern Tanzania in 2008 among HIV patients receiving HIV care which had a prevalence of 8.5%[50]. Another study done among police officers in Dar es Salaam Tanzania between

October 2001 and February 2003 before ARVs became widely available identified active TB among 15% of the participants[15], a higher prevalence than that of Rural Northern Tanzania and that of the present study. The difference can be attributed to unavailability of ARVs at the time of the police officers' study and thus many HIV infected patients succumbed to TB. Another study in Iringa region in Tanzania among 83 patients who were investigated for *Pneumocystis jiroveci* pneumonia and PTB found a prevalence of PTB at 38.5% [30]. The high prevalence in the Iringa study could be due to the fact that it included only symptomatic patients while the present study included symptomatic and asymptomatic patients.

A study done in Cambodia, a South East Asian country between September 2006 and July 2008 had a prevalence of 9%, a figure comparable to that found in this study[44].

5.2 The sensitivity and specificity of the screening tool using sputum culture for MTB as a standard for the diagnosis of PTB.

The sensitivity and specificity of the NTLP TB screening tool using sputum culture for MTB as a standard for the diagnosis of PTB in the present study was 71.4% and 75.9% respectively. The NPV and PPV in the present study was 98.4% and 11.4% respectively. A study done in Ethiopia in 2005 had similar values of 78% sensitivity and a PPV of 12% when cough, fever and night sweats of any duration were used in the screening questionnaire[43]. Predictive values vary based on the prevalence of TB disease in the screened population[43] Ethiopia has an estimated TB incidence of 341/100,000 population per year[43] incidence of TB in Tanzania is 312/100,000 population per year[43]). A study conducted in South Africa evaluating the TB screening algorithm among HIV infected persons had a higher sensitivity of 91%, however this could be due to the fact that a combination of fever and cough of any duration in the previous 4 weeks was used in their study[42] while in the present study fever and cough of = 2 weeks was used.

5.3 The sensitivity and specificity of the screening tool against the NTLP PTB definition

In this study the sensitivity and specificity of the screening tool using the NTLP PTB definition was 90.3% and 80.5% respectively, with PPV of 31.8% and NPV of 98.8%. This means that the when the screening tool was tested against the NTLP TB definition the sensitivity and specificity improved, however the NPV remained the same. The findings in this study are similar to those of a study conducted in Cape Town South Africa in 2003 which had a TB prevalence of 8.5%. In the 2003 study, TB was classified as definite (culture-positive together with appropriate symptoms or radiographic appearances), probable (smear-positive) and possible (clinical diagnosis together with a response to therapy). By using a screening tool of two or more of the symptoms of measured weight loss, cough, night sweats or fever, a sensitivity of 100% and specificity of 88.1% were obtained with PPV and NPV of 44% and 100%, respectively[27]. However, no studies have been done in Tanzania looking at the sensitivity and specificity of the screening tool by using the NTLP PTB definition.

5.4 Sensitivity and specificity of the screening tool using the operational PTB definition

In Tanzania, two government hospitals have the facilities to investigate sputum by culture and DST in the diagnosis of TB i.e Muhimbili National Hospital in Dar-es-Salaam and Kibong'oto hospital in Kilimanjaro. The NTLP PTB definition includes a component of sputum culture (rarely done in our routine practice) for MTB in the diagnosis of PTB. Sputum culture is usually reserved for TB treatment failures, retreatment cases or others considered "high risk" for drug resistant TB in WHO guidelines. This is largely because of limited resources and high cost and complexity of culture techniques[43]. In this study, the sensitivity and specificity of the operational PTB definition was 100% and 80.5% respectively. The PPV and NPV were 30.2% and 100% respectively.

Haemoptysis as a symptom was not common in this study (3/373 -0.01%) and thus cannot be used to predict TB. This was also a finding in other studies[44]. In a study among 1748 HIV infected patients from eight outpatient clinics in Cambodia, Thailand, and Vietnam on an algorithm for TB screening and diagnosis in people with HIV, haemoptysis was reported in 3% of all the participants [44]. In a meta analysis of 12 studies, of which 77% of the patients

were from SSA and the remaining patients from South East Asian countries, the most sensitive single symptoms in the meta analysis was weight loss with a sensitivity of 49.3% (95% CI 27.0-71.9), with haemoptysis having the lowest sensitivity of 5.9% (95% CI 2.3-14.5)[52]. This means that, adding haemoptysis to the screening tool does not improve the sensitivity, specificity or the PPV of the screening questionnaire.

5.5 Diagnosis of PTB using sputum smear microscopy.

Sputum smears performed poorly in this study. This is similar to a study conducted in Ethiopia, in which direct smear microscopy by Ziehl–Nielson method detected 3 of 32 TB cases (9%)[43]. Smear negative microscopy for AFB is common in HIV infected patients with PTB. The paucibacillary nature of TB disease in immunodeficient patients reduces the performance of sputum smear microscopy, which requires 5000 – 10,000 bacilli for detection.

5.6 The role of CXR in the diagnosis of TB.

In the present study CXR abnormalities suggestive of TB (in combination with sputum culture results) identified 3 of the 4 participants that were missed by the screening tool. A study conducted in Ethiopia showed that chest radiography screening for HIV-positive clients diagnosed 10% more TB cases.[43] In another study conducted among gold miners in South Africa, the addition of CXR abnormalities compatible with TB reduced the proportion of TB cases that would have been missed from 40.9% to 5.1%. In the gold miners study, the CXR was in combination of symptoms that would have missed the smallest proportion of active TB (i.e any one of night sweats, new or worsening cough and measured weight loss of = 5%) [27]. Therefore, if not for economical constrains especially in developing countries like Tanzania, adding CXR to the screening tool may improve the sensitivity and specificity of the screening tool.

Although the symptom screening tool missed to detect some patients diagnosed with TB by sputum culture and CXR, it is still an effective means of ruling out active TB. It demonstrated a sensitivity of 71.4% when using sputum culture for MTB as a standard for the diagnosis of

PTB. The NPV of 98.4% means that 98.4% of patients reporting no symptoms are unlikely to have tuberculosis and thus can be used to identify patients eligible for IPT.

5.7 Tuberculin Skin Test

Tuberculin skin test in this study was found to be positive among 24% of the participants, a lower prevalence than the 33% found in a study on completion of IPT among 1932 HIV-infected patients with a CD4 = 200cells/µL[53]. This higher prevalence could be explained by the reduced number of participants with severe immunosupression as only participants with CD4 = 200cells/µL were recruited. In the current study TST positivity was associated with CD4 values of = 200cells/µL. No relationship was observed between TST and TB.

STUDY LIMITATIONS:

Symptomatic patients who needed a course of antibiotic treatment (as per NTLP TB screening algorithm) before re-evaluation for likelihood of having active TB were not followed up. This could have caused an underestimation of the TB prevalence.

The main strength of this study is that all participants were screened and underwent sputum induction with an ultrasonic nebulizer despite the presence or absence of clinical symptoms.

Despite these limitations, this study provides critical prospective evaluation of routinely available TB diagnostic tools.

CHAPTER SIX

6.0 CONCLUSION AND RECCOMENDATIONS

6.1 CONCLUSION:

- This study has shown high levels of active TB among patients attending MNH HIV clinic, being 4.1% and 9.2% using culture and NTLP PTB definition respectively.
- The NTLP screening tool for PTB has a good sensitivity (71.4%) when using sputum culture for MTB as a standard for the diagnosis of PTB in a clinic setting.
- The addition of a CXR could improve the sensitivity of the tool as the screening tool missed 4 patients with culture confirmed MTB, of which 3 were picked by a CXR
- Predictors of PTB using MTB culture were cough = 2 weeks and ARV use.
- TST positivity in this setting has no value in the diagnosis of PTB, however it was associated with higher CD4 cell count.

6.2 RECCOMENDATIONS:

? The use of the screening tool is highly recommended (mandatory) in all HIV clinics to identify people without TB especially in centers providing IPT as it useful in excluding active TB.

? Whenever possible CXR should be done as this may improve the sensitivity of the tool.

? A follow up study is needed to determine the incidence of TB during IPT as the screening tool and NTLP PTB definition missed patients who had culture positive MTB.

CHAPTER SEVEN

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CHAPTER 8

8.0 APPENDICES:

8.1 APPENDIX NO. 1

INFORMED CONSENT ENGLISH VERSION

PARTICIPANT INFORMATION LEAFLET AND INFORMED CONSENT

Each participant must receive, read and understand this document before any study-related procedure

STUDY TITLE:

THE USE OF THE NATIONAL TUBERCULOSIS AND LEPROSY PROGRAMME SCREENING TOOL IN IDENTIFYING PATIENTS ELIGIBLE FOR ISONIAZID PREVENTIVE THERAPY AND THE ROLE OF TUBERCULIN SKIN TEST AMONG PATIENTS ATTENDING MUHIMBILI NATIONAL HOSPITAL HIV CLINIC.

INVESTIGATORS: Dr. Lilian Tina Minja, Dr Grace Shayo and Professor Ferdinand Mugusi
INSTITUTION: Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

WHY ARE WE CONDUCTING THIS STUDY?

A significant proportion of persons continue to be infected with the HIV virus. The prevalence of Tuberculosis among HIV infected people in Tanzania is significantly high, ranging from 8.5% in rural areas to 15% in urban settings. As a response to World Health Organization (WHO) recommendation, the Ministry of Health and Social Welfare (MoHSW) of Tanzania will be providing Isoniazid Preventive Therapy (IPT) to all HIV patients who will screen negative to active TB disease. The aim of providing IPT is to reduce the burden of Tuberculosis among people living with HIV and AIDS (PLWHA).

WHO WILL PARTICIPATE IN THE RESEARCH?

Persons attending the HIV clinic aged 18 years and above who are willing to participate in the study. We are happy to inform you that you have been identified as a potential participant for this study.

WHAT WILL YOU BE ASKED TO DO?

If you agree to participate in the study, you will be asked several questions to know whether you have active TB or not. Those who will present with symptoms of TB will undergo TB screening as per Tanzanian NTLP guidelines (These will include sputum sample, chest X-ray and blood). Those confirmed to have active TB will receive treatment for TB as per the Tanzania NTLP guidelines.

Those who present with no symptoms of TB will undergo a Tuberculin Skin Test (TST) which is an intradermal injection of a drug that will help us know whether the individual is infected with TB mycobacteria or not. TST will be done on Mondays, Tuesdays and Fridays and will be read after 3 days. These participants will then be sent for IPT for 6 months as per Tanzania NTLP guidelines.

WHAT ARE THE POSSIBLE RISKS OF PARTICIPATING?

There are no major risks anticipated on your participation. You will experience minor pain from the injection site. TST can cause local skin itching or a blister.

Sputum induction can cause minor throat irritation which subsides thereafter

WHAT ARE THE BENEFITS?

The benefit to the participant as an individual is a golden chance to be diagnosed either with active TB and receive a full course of anti-TB treatment or not having active TB and receive a prophylactic treatment against TB.

The benefit to the community as a whole is a reduction of TB burden and sources of TB infection. This is expected to increase survival of PLWHA because TB is the leading cause of death in these patients.

RIGHTS AS A PARTICIPANT IN THIS STUDY:

Your participation in this study is entirely voluntary and you can refuse to take part, or stop at any time, without stating any reason. Your withdrawal will not affect your access to health services.

CONFIDENTIALITY

Your name, registration number, physical contact and telephone number(s) will be recorded to aid tracing or in case you are required at the health facility. All the documents bearing your identity will be handled with great confidentiality. Information collected for this study will be reported to the study sponsor. All reported information will be coded by a number to protect your identity. Any report or publication of the information you provide to us will not use your name or identify you personally.

PROBLEMS OR QUESTIONS

If you have any questions about the study you may contact:

1. Dr. Lilian Tina Minja,
   Resident, Internal Medicine, MUHAS
   P.O.Box 65001 Dar es Salaam.
   Tel: 0713 254563
2. Dr. Grace Shayo,
   Lecturer, Department of Internal Medicine MUHAS,
   P.O.Box 65001 Dar es Salaam.
   Tel. +255 754 564924
3. Prof. Ferdinand Mugusi,
   Professor, Department of Internal Medicine MUHAS,
   P.O.Box 65001 Dar es Salaam., Tel: 0784 613354

I_____ have understood the above information concerning this research and have been satisfied with responses to my questions and thus have agreed to participate.

Signature / thumb print of the participant: _____

Name and signature of a witness: _____

Researchers name & signature: _____

Date of consenting: __ __/ __ __/ __ __ __ __

8.2 APPENDIX NO 2

FOMU YA MAELEZO NA KUKUBALI KUSHIRIKI

Kila mshiriki anapaswa kusoma na kuelewa maelezo haya kabla ya kufanya jambo lolote linalohusiana na utafiti

UTAFITI: UTAFITI WA KUCHUNGUZA NJIA YA KUGUNDUA KAMA MTU HANA UGONJWA WA KIFUA KIKUU KWA KUTUMIA MASWALI YALIYOPANGWA NA KITENGO CHA TAIFA CHA KIFUA KIKUU NA UKOMA KABLA YA KUANZISHIWA MATIBABU YA KUZUIA KUPATA UGONJWA WA KIFUA KIKUU PAMOJA NA MATOKEO YA KIPIMO CHA TST KWA WAATHIRIKA WA VIRUSI VYA UKIMWI.

Watafiti: Dr. Lilian Tina Minja, Dr Grace Shayo na Professor Ferdinand Mugusi

Kitengo: Chuo Kikuu cha Afya na Sayansi Shirikishi cha Muhimbili, Dar es Salaam, Tanzania

KWANINI TUNAFANYA UTAFITI HUU?

Idadi kubwa ya watu wanaendelea kuambukizwa na virusi vya ukimwi. Idadi ya watu wenye kifua kikuu katika waathirika wa VVU Tanzania ni kubwa, kati ya asilimia 8.5% vijijini mpaka 15% katika makazi ya mjini. Kutokana na mapendekezo ya Taasis ya Afya Duniani (WHO), wizara ya Afya na Ustawi wa Jamii ya Tanzania itaanza kutoa dawa (Isoniazid) ya kuzuia kupata ugonjwa wa kifua kikuu kwa waathirika wote wa ukimwi watakaogundulika hawana ugonjwa wa kifua kikuu. Dawa hii itatolewa ili kupunguza idadi ya watu watakaougua kifua kikuu miongoni mwa waathirika wa VVU. Sababu ya kuendesha utafiti huu ni kuchunguza njia ya kugundua kama mtu hana ugonjwa wa kifua kikuu kwa kutumia maswali yaliyopangwa na kitengo cha Taifa cha kifua kikuu na ukoma kabla ya kuanzishiwa matibabu ya kuzuia kupata ugonjwa wa kifua kikuu kwa waathirika wa VVU.

NANI ANRUHUSIWA KUSHIRIKI?

Mtu yeyote muathirika wa VVU, anayehudhuria kliniki ya Muhimbili mwenye umri wa miaka 18 au zaidi.

UTAOMBWA KUFANYA NINI?

Iwapo utakubali kushiriki katika utafiti huu, utaulizwa maswali, ili kuweza kutambua kama na ugonjwa wa kifua kikuu au la, na utachukuliwa kipimo cha makohozi na kipimo cha damu.

Washiriki watakao kuwa na dalili za kifua kikuu watafanyiwa uchunguzi wa ziada kwa kufuata utaratibu wa kitengo cha Taifa cha kifua kikuu na ukoma Tanzania. Watakaogundulika wana kifua kikuu wataanzishiwa matibabu ya kifua kikuu

Watakaogundulika hawana ugonjwa wa kifua kikuu watachomwa sindano ya Tuberculin Skin Test (TST) ambayo ni sindano itakayoonyesha kama mshiriki ana maambukizi ya kifua kikuu au la. TST itachomwa siku za Jumatatu, Jumanne na Ijumaa na mshiriki ataombwa kurudi baada ya siku 3 ili kusoma majibu ya kipimo hicho. Baada ya hapo, mshiriki atapelekwa katika kitengo husika cha kuanzishiwa dawa ya kuzuia kupata ugonjwa wa kifua kikuu kutokana na utaratibu wa Taifa wa kitengo cha kifua kikuu na ukoma Tanzania.

JE MGONJWA ANAWEZA KUPATA MADHARA GANI?

Hakuna madhara makubwa yanayotegemewa katika utafiti huu. Utapata maaumivu kidogo kwenye eneo utakalochomwa sindano.

Kipimo cha makohozi kinaweza sababisha hali ya mkwaruzo kidogo kwenye koo. Ni kipimo au jinsi tutakavyo kuomba toa makohozi.

FAIDA ZA KUSHIRIKI

Faida ya kushiriki ni utagundulika kama una ugonjwa wa kifua kikuu na matibabu ya kifua kikuu kuanzishwa au kama huna kifua kikuu na dawa ya kuzuia kupata ugonjwa wa kifua kikuu kuanzishwa.

Faida kwa jamii ni kupunguza idadi ya watu wenye ugonjwa wa kifua kikuu, na kupunguza maambukizi ya kifua kikuu na vifo vitokanavyo na kifua kikuu kwa waathirika wa VVU katika jamii.

HAKI ZAKO KAMA MSHIRIKI:

Ushiriki wako katika utafiti ni wa hiari, na endapo utaamua kujitoa katika utafiti baada ya kuanza, utaruhusiwa kufanya hivyo. Na hii haitaathiri matibabu yako kwa upande wowote.

USIRI:

Jina lako, namba yako ya CTC, anuani yako vitachukuliwa ili kusaidia katika njia za kukutafuta iwapo utahitajika. Maelezo yako yote yatatunzwa kwa usiri mkubwa sana na hayataonyeshwa kwa mtu yeyote asiyehusika na utafiti huu. Ripoti zozote zitakaztokana na utafiti huu hazitatumia jina lako katika maelezo yoyote.

KAMA UNA MASWALI YOYOTE KUHUSIANA NA UTAFITI HUU UNARUHUSIWA KUWASILIANA NA WAFUATAO:

1. Dr. Lilian Tina Minja
   Daktari, Idara ya Internal Medicine, MUHAS
   S.L.P 65001 Dar es Salaam.
   Simu # : 0713 254563
2. Dr. Grace Shayo,
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   Simu:. +255 754 564924
3. Prof. Ferdinand Mugusi,
   Professor, Idara ya Internal Medicine MUHAS,
   S.L.P 65001 Dar es Salaam. Simu; 0784 613354

Mimi_____

nimeelewa maelezo ya utafiti huu na nimeridhika na majibu ya maswali nilyouliza na nimekubali kushiriki katika utafiti huu

Sahihi / alama ya dole gumba la mshiriki: _____

Jina na sahihi ya shahidi:_____

Jina na sahihi ya mtafiti: _____

Tarehe: __ __/ __ __/ __ __ __ __

8.3 APPENDIX NO 3

TB screening Questionnaire at baseline

1. Questionnaire #: ☐☐☐ 2. Age (yrs): ☐☐ 3. Sex: F(1) M(2)

4. Patients name: ☐

5. CTC registration #: ☐☐☐☐☐☐☐☐☐ 6. Study site: ☐

7. Physical address: ☐

8.a) Marital status: b) Level of education: ☐

9. Contact Telephone(s): 1. Patient: ☐

2. Close relative/treatment supporter: ☐

3. Others:(specify names) ☐

10. Occupation (tick the appropriate response):

1. Unemployed: ☐ 2. Civil servant: ☐ 3. Health care worker: ☐

4. Petty business ☐ 5. Large scale business: ☐ 6. Others (specify): ☐

---

11. Do you have any of the following symptoms? (Tick the appropriate response)

	Yes	No
1. Cough = 2 weeks	1	2
2. Coughing up blood (Haemoptysis)	1	2
3. Fevers = 2 weeks	1	2
4. Noticeable weight loss or = 3kg weight loss per month	1	2
5. Excessive sweating at night for = 2 weeks	1	2

12. Have you ever had TB disease? | 1. Yes | 2. No |

13. If YES, date of last anti-TB treatment completion : __ __ /__ __ / __ __ __ __

14. Duration of HIV disease since diagnosis (in months)

15. Are you on anti-retroviral drugs (ARVs) 1. Yes 2. No

16. If yes, what ARV's are you on (circle the appropriate combination):

1. Zidovudine, Lamivudine and Efavirenz (AZT, 3TC, EFZ)
2. Zidovudine, Lamivudine and Nevirapine (AZT, 3TC, NVP)
3. Stavudine, Lamivudine and Nevirapine (d4T, 3TC, NVP)
4. Stavudine, Lamivudine and Efavirenz (d4T, 3TC, EFZ)
5. Tenofovir, Emtricitabine and Efavirenz [Atripla] (TDF, FTC, EFZ)
6. Abacavir, Lopinavir/ritonavir (Kaletra), Didanosine (ABC, L/r, ddI)
7. Emtricitabine, Tenofovir, Lopinavir/ritonavir (Kaletra), (FTC, TDF, L/r)

17. Have you ever changed ARVs 1. Yes 2. No

18. If yes, what ARVs were you previously on (write the appropriate number from Qn. 16 above) 19. What was the reason & date for change of ARVs

20. Date of ARV initiation DD/MM/YYYY: __ __/__ __/ __ __ __ __

21. Duration of ARV use (in months): _____

22. 1. Last recorded CD4 count (cells per cm^3) _____ 2. Date taken __ __/__ __/ __ __ __

Date last recorded CD4 was checked DD/MM/YYYY. __ __/__ __/ __ __ __ __

23. Vital signs

1. Weight (kg)	_____.____ Kg	3. Temperature (^oC) _____
2. Height (M)	_____ M	

24. Is there any evidence of: Jaundice 2. Peripheral neuropathy

25. Examination	Normal	Abnormal	Specify
1. Respiratory system	1	2	
2. Cardiovascular system	1	2	
3. Gastrointestinal system	1	2	
4. Central nervous system	1	2	
5. Lymphatic system	1	2	
6. Skin and mucous membranes	1	2	
7. Musculoskeletal system	1	2	

26. Is a BCG scar present? 1. Yes 2. No

Presence or absence of an intradermal scar above the right deltoid muscle

27. Investigations results:

1. Haemoglobin: ESR:	5. Creatinine:
2. WBC & differentials:	6. CD4 count:
3. ALT:	7. Viral load:
4. Albumin:	8. Sputum results:

28. Radiological diagnosis (X-rays):

1. Normal 1. Yes 2. No
2. Suggestive of TB 1. Yes 2. No

29. WHO HIV stage:

30. Tuberculin skin test record form:

Manufacturer of PPD solution:_____

Expiry date of PPD solution: _____

Lot number: _____

1. Name & signature of administrator: _____
2. Date of TST administration: __ __/__ __/ __ __ __ __
3. Forearm administered: 1. Left 2. Right
4. Mantoux induration: _____ mm
5. Time read after administration: _____ _HRS
6. Name & signature of the reader: _____
6. Adverse reactions (specify)_____

_____

* It is very unlikely that a side effect to the test will occur. If such an event does happen, the most common reaction is pain or redness at the test site. In very rare cases, a person who is hypersensitive to the solution could have a severe allergic reaction near the injection site. Such rare reactions may include blistering or a skin wound.

Date:	Name:	Signature:

8.4 APPENDIX NO 4

Dodoso la mshiriki (Swahili)

2. Dodoso #:		2. Umri (miaka):		3. Jinsia:	Ke(1) Me(2)
4. Jina la mshiriki:					
5. Nambari ya CTC:			6. Kituo cha utafiti:		

7. Anuani ya mshiriki:

8a) Marital Status: b) Kiwango cha elimu:

9. Namba za simu(s): 1. Mshiriki

2. Ndugu wa karibu:

(taja jina)

10. Kazi ya mshiriki (tiki jibu sahihi):

1. Sija ajiriwa: ☐ 2. Mfanyakazi wa serikali: ☐ 3. Mhudumu wa afya: ☐

4. Biashara ndogo ☐ 5. Mfanyabiashara kubwa: ☐ 6. Nyingine (taja): ☐

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11. Je, una dalili zozote zifuatazo? (Tiki jibu sahihi)

	Ndio	Hapana
1. Kikohozi cha wiki 2 au zaidi	1	2
2. Kukohoa damu	1	2
3.Homa za wiki mbili au zaidi	1	2
4.Kupungua uzito au kupungua kilo 3 au zaidi kwa kipindi cha mwezi mmoja...	1	2
5.Jasho jingi kutoka usiku kwa kipindi cha wiki mbili au zaidi	1	2

12. Je, umewahi gundulika una ugonjwa wa kifua kikuu? 1. Ndio 2. Hapana

13. Kama Ndio, ulimaliza lini matibabu ya kifua kikuu? (Tarehe) : __ __ /__ __ / __ __ __ __

14. Unafahamika una maambukizi ya virusi vya ukimwi tangu lini? (miezi mingapi))

15. Je, upo kwenye dawa za kurefusha maisha (ARVs) 1. Ndio 2. Hapana

16. Kama Ndio, unatumia dawa zipi? (zungushia jibu sahihi):

8. Zidovudine, Lamivudine and Efavirenz (AZT, 3TC, EFZ)
9. Zidovudine, Lamivudine and Nevirapine (AZT, 3TC, NVP)
10. Stavudine, Lamivudine and Nevirapine (d4T, 3TC, NVP)
11. Stavudine, Lamivudine and Efavirenz (d4T, 3TC, EFZ)
12. Tenofovir, Emtricitabine and Efavirenz [Atripla] (TDF, FTC, EFZ)
13. Abacavir, Lopinavir/ritonavir (Kaletra), Didanosine (ABC, L/r, ddI)
14. Emtricitabine, Tenofovir, Lopinavir/ritonavir (Kaletra), (FTC, TDF, L/r)

23. Vipimo vya muhimu

1. Uzito (kg) _____.____ Kg
2. Kiwango cha joto cha mwili (^{o}C) _____
3. Urefu (M) _____ M

24. Je, kuna viashiria vya: 1. Macho ya manjano: 2. Ganzi katika viganja vya mikono na miguu:

25. Kipimo	Kawaida	Isiyokawaida	Elezea
1. Respiratory system	1	2	
2. Cardiovascular system	1	2	
3. Gastrointestinal system	1	2	
4. Central nervous system	1	2	
5. Lymphatic system	1	2	
6. Skin and mucous membranes	1	2	
7. Musculoskeletal system	1	2	

26. Je, kuna kovu la BCG? 1. Ndio 2. Hapana

Kuwepo au kutokuwepo kwa kovu la BCG katika mkono wa kulia eneo la msuli wa deltoid

27. Majibu ya vipimo vya damu:

1. Haemoglobin: ESR:
5. Creatinine:

2. WBC & differentials:	6. CD4 count:
3. ALT:	7. Viral load:
4. Albumin:	8. Sputum results:

28. Majibu ya kipimo cha X-ray ya kifua:

4. Hakina tatizo 1. Ndio 2. Hapana

5. Kinaashiria kifua kikuu 1. Ndio 2. Hapana

29. WHO HIV stage:

Tarehe:	Jina la mtafiti:	Sahihi ya mtafiti: