THE CLINICAL CHARACTERISTICS OF TUBERCULOSIS AND ASSOCIATED CO-MORBIDITIES AMONG THE ELDERLY COMPARED TO ADULTS IN DAR ES SALAAM, TANZANIA

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By

Riemann Ray

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

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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 clinical characteristics of tuberculosis and associated co-morbidities among the elderly compared to adults in Dar es Salaam, Tanzania*** in (partial) fulfillment of the requirements for the degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences.

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Professor Kisali Pallangyo

(Supervisor)

_____

Date

DECLARATION AND COPYRIGHT

I, **Riemann Ray**, 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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First and foremost I thank my God for giving me strength, ability and the way to pursue and accomplish this great task.

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DEDICATION

To Dr. Engerasiya J. Kifai my wife and our children Erica, Abigail, Michelle and Joshua-Ariel

To Professor Kisali Pallangyo, my supervisor

To Mwalimu Christopher and Dianna Mwakasege

ABSTRACT

Background: Due to a number of factors life expectancy and the proportion of men and women of 60 years and above continue to increase both globally and locally. Old age has been shown to be associated with impaired immunity (immunoscenensce), increased risk of co-morbidities such as diabetes mellitus, impaired renal function, poverty and malnutrition; factors which increase the risk of developing clinical Tuberculosis. Studies from Europe and America suggest that TB in the elderly often presents with atypical symptoms or atypical radiological findings or both. Furthermore the presenting clinical features may be confused with age related illnesses and hence delay TB diagnosis and treatment with consequent increased morbidity and mortality. The aim of this study was to describe the key characteristics of tuberculosis among the elderly and the associated co-morbidities and compare them to those of adults.

Broad Objective: To describe and compare the clinical characteristics of tuberculosis and associated factors among patients aged 18-59(adults) and those aged 60 years or more (elderly) attending TB clinics in the city of Dar es salaam.

Specific Objectives: (1) To describe and compare clinical characteristics of TB in the elderly and adults aged 18-59 years. (2) To determine and compare the sputum microscopy yield for *Mycobacterium tuberculosis* in elderly and adults with pulmonary TB (PTB). (3) To compare the chest radiological findings in elderly and adults aged 18-59 years with TB (4) To document the treatment outcomes at the end of intensive phase in the two groups (5) To describe and compare the co morbidities associated with TB in the two groups.

Methodology: This was a hospital based prospective cohort study among TB patients aged ≥18 years attending TB clinics in three district hospitals of Dar es Salaam city. All the TB suspects attending the clinics between 2nd August 2014 to 31st December 2014 were investigated as per the NTLP diagnostic algorithm. Patients who consented were asked to provide blood samples for full blood count, random blood sugar, serum creatinine and HIV serology. At the end of two month of intensive therapy study

subjects underwent repeat examinations of sputum for AFB, FBC, serum creatinine, CXR and weight. Adverse effects to drugs and mortality were also compared between the two groups. The estimated sample size for this study was 250 patients with TB.

Results: We recruited 150 (59.3%) and 103 (40.7%) adults and elderly patients respectively. The mean age (SD) for the adults was 35.57 (± 10.3) and it ranged from 18 – 59 years. The mean age (SD) for the elderly was 67.17 (± 6.43) and it ranged from 60 – 90 years. Clinically adults were more likely to present with hemoptysis compared to elderly (23.4% Vs 8.3% p=0.006) while elderly were more likely to present with general body malaise compared to adults. (41.3% Vs 75.7%, p<0.001). Adults had a higher yield for Mycobacterium tuberculosis compared to elderly. (p<0.001). Radiologically a higher involvement of lower zone was observed in a larger proportion of elderly as compared to adults (42.3% Vs 18.5% p<0.001) while adults were more likely to form cavities (50.4% Vs 22.7% p<0.001).Elderly patients were more likely to present with poor treatment outcomes as compared to adults. Co morbidities such as obesity, hypertension, diabetes mellitus and renal insufficiency were observed more among elderly as compared to adults. The mortality rate was higher among elderly as compared to adults. (17.5% Vs 6.7 %, p<0.01)

Conclusion: HIV infection was found to be an important risk factor for TB to both adults and elderly patients in Dar es Salaam. Atypical clinical and/or radiological findings, co-morbidities were significantly more common among the elderly compared to adults.

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LIST OF ABBREVIATIONS

AFB	Acid Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
ARTI	Annual Risk of Tuberculous infection
ATS	American Thoracic Society
BCG	Bacille-Calmette Guérin
BMI	Body Mass Index
C.I	Confidence Interval
CKD	Chronic Kidney Disease
CTC	Care and Treatment Centre
CXR	Chest X Ray
DIB	Difficulty In Breathing
DM	Diabetes Melitus
DMO	District Medical Officer
DNA	Deoxyribonucleic Acid
DOT	Direct Observed Treatment
DTLC	District TB and Leprosy Coordinator
EPTB	Extra Pulmonary Tuberculosis
ESR	Erythrocyte Sedimentation Rate
FBC	Full blood Count
FDC	Fixed Dose Combination
GBM	Generalized Body Malaise
GFR	Glomerular Filtration Rate
HBC	High Burden Countries
HIV	Human Immunodeficiency Virus
IFN	Interferon
IUATLD	International Union Against Tuberculosis And Lung Disease
KDOQI	Kidney Disease Outcome Quality initiative
LAM	Lipoarabinomannan

LTBI	Latent Tuberculosis Infection
MCH	Mean Corpuscular Hemoglobin
MCV	Mean Corpuscular Volume
MDGs	Millennium Development Goals
MDR - TB	Multiple Drug Resistant Tuberculosis
MOHSWF	Ministry of Health and Social Welfare
MOTT	Mycobacterium Other Than Tuberculosis
MTB	*Mycobacterium Tuberculosis*
MUHAS	Muhimbili University of Health and Allied Sciences
NBS	National Bureau of Statistics
NKF	National Kidney Foundation
NTLP	National Tuberculosis and Leprosy Program
OR	Odds Ratio
PCR	Polymerase Chain Reaction
PCT	Patient Centered Treatment
PHC	Population and Housing Census
PI	Principal Investigator
PLWHA	People Living with HIV/AIDS
PST	Prevalence Survey Tanzania
PTB	Pulmonary Tuberculosis
RBG	Random Blood Glucose
SES	Socioeconomic Status
TST	Tuberculin Skin Test
VVU	Virusi vya Ukimwi
WHO	World Health Organization

DEFINITION OF TERMS

1. TB Patient.

Two of the following three criteria were required to define a TB patient:

1) Clinical symptoms of tuberculosis, (cough, fever, night sweats, etc.);
2) Acid-fast bacteria were visible in the sputum, or Mycobacterium tuberculosis was cultured from the sputum;
3) The chest radiograph was independently interpreted as highly suggestive of tuberculosis.

Or for patients without microbiological confirmation, clinical response to anti TB medications was required to make a diagnosis of TB [1]

2. Extra pulmonary TB Patient

This was confirmed if a patient presented with signs and symptoms of the organ/system affected with or without constitutional symptoms and then AFBs were visible in the samples using ZN stain or were cultured using the same samples.

Or radiological and/or clinical findings which were highly suggestive of tuberculosis.

For patients without microbiological confirmation, clinical response to anti TB medications was required to make a diagnosis of EPTB [1]

3. TB Suspect

A person with symptoms of TB based on NTLP but not yet confirmed or ruled out by laboratory and/or radiological investigations [2]

4 Elderly

This was any patient with the age of 60 years and above [87]

5. Adult

This was any patient between 18 and 59 years [87]

6. Co morbidity

This was defined as co-occurrence of multiple diseases or medical conditions in the same individual [88, 89]

CHAPTER ONE

1.0 INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by the bacteria called *Mycobacterium tuberculosis* (MTB).The disease usually affects the lungs (PTB), although in up to one third of cases other organs are also involved (EPTB).Transmission usually occurs through airborne spread of droplet nuclei produced by patients with infectious Pulmonary Tuberculosis (PTB) [1]

In general, 5-10% of people infected with MTB will develop TB disease in their lifetime; however the probability of developing TB is about 10% per year among people infected with HIV[2].Various conditions that cause immunosuppression have been reported to be associated with increased risk of developing clinical tuberculosis. The disease is also more common in men than women and affects mostly adults in the economically productive age groups.

1.0.1 Developing Clinical Tuberculosis

It all starts after inhalation of droplet nuclei which contain TB bacilli. Due to their very small size the droplet nuclei bypass the muco-cilliary defence system of the bronchi and go all the way to the terminal alveoli where they settle.In the terminal alveoli the TB bacilli multiply preferably in the apex where the oxygen concentration is high. This results into the formation of the primary lesion called Ghon focus. [2]From the Ghon focus the bacilli spread to the nearest lymph-nodes, which are in most cases the hilar lymph nodes. This primary lesion combined with the involvement of the hilar lymph nodes is called Primary Complex. [2]The bacilli can also spread hematogenously to any other organ in the body, therefore resulting into disseminated disease such as meningitis, pericarditis, miliary disease etc.

The immune response develops about 4-6 weeks after the infection. The number of bacilli that have been inhaled and the strength of the immune system determine if the infection is stopped or develops into full tuberculosis disease. In the majority of cases the immune system is strong enough to combat this primary attack. Most of the bacilli

are eliminated but a few persist in a dormant stage**.** [2]The dormant TB bacilli can either develop into post primary infection after many months or years or it can undergo reactivation into a full blown TB; this is particularly seen in individuals with immunosuppression due to conditions such as malnutrition, chronic/ recurrent infections, HIV infection and old age**.** [2]

Therefore development of TB is a two stage process in which a susceptible person exposed to an infectious TB case first becomes infected and later on develop a disease, depending on the following factors [2]

1) The risk of exposure to MTB
2) The risk of infection
3) The risk of developing a disease.

1) The Risk of Exposure to MTB.

The first step is to come in contact with an infectious TB case who expectorates the bacilli to the air. The likelihood of contact between a susceptible person and an infectious TB case depends on the prevalence of active PTB in a given population and is influenced by several factors, the most important being overcrowding [3]

2) The Risk of Infection.

This is determined primarily by the combined action of three risk factors:

a) The infectivity of the source case
b) The degree of exposure.
c) Health status of an individual.

a) The Infectivity of the Source Case

Smear positive TB cases are more likely than smear negative ones to infect their contacts and the infectivity of the case is a function of the frequency of coughing, the density of bacilli in the sputum [4] and the virulence of the bacteria [5]

b) The Degree of Exposure

Several factors have been found to influence the balance between exposure and infection; these include HIV infection, immunosuppressive treatment, malnutrition, diabetes mellitus, alcohol and cigarette smoking. These are considered to be *intrinsic* to the susceptible host. [6] Other factors include close proximity to the case [4] overcrowding and low socioeconomic status (SES)

c) Health Status of an Individual.

The degree of susceptibility of an individual to infection depends on the health status of the latter [7,8] and genetic susceptibility which has been observed in certain populations such as the Eskimos in North America, the Yanomami Indians in the Brazilian Amazon and Black Americans in the USA [9] There are several polymorphisms in the human *NRAMP 1* gene that have been identified to increase the relative risk of the susceptible individual to develop a TB disease from latent TB infection.(LTBI) [10] Other genes that have been implicated includes those of vitamin D receptors and the components of the IFN – signaling pathways[11]

3) The Risk of Developing a Disease.

In patients infected with MTB an active disease can develop at variable times through reactivation of the latent infection but can also occur through exogenous re infection[12]The relative contribution of reactivation and re infection is likely to depend on the epidemiologic context[13]It is generally accepted that in populations at high prevalence of TB infection, re infection may be a major contributor to the overall rate of TB in adults, whereas, in populations that have a low prevalence ;most cases of post primary disease in adults probably results from reactivation.[12 – 14]The time from infection to disease ranges from a few weeks to a lifetime. The cumulative lifetime risk of developing the disease has been estimated to be approximately 10 percent.[15]But studies in England and Wales showed that the lifetime risk of developing the disease depends strongly on the time and the contacts' age for the disease to occur[16]

1.0.2 Pathogenesis and Clinical Manifestation of TB.

The clinical manifestation of TB represents a complex interaction between the causative organism, MTB and the human host response [17]

Infection and Macrophage Evasion:

As explained above, MTB comes in contact with the human host when droplet nuclei containing the bacilli from infectious contacts are inhaled. While majority are trapped in the upper airways and expelled, less the 10% reach the lower respiratory tract and settle in the terminal alveoli where the bacilli are phagocytosed by alveolar macrophages thus forming a phagosome. Then the LAM (lipoarabinomannan – a mycobacterial cell wall glycolipid) inhibits further intracellular release of calcium which prevents the formation of the phagosome-lysosome complex. [18, 19] This enables the bacteria to survive within the microphage.

Host Response

If fusion between the phagosome and lysosome is successful, bacillary survival is prevented. Otherwise, mycobacterial replication ensues eventually killing the macrophage with release of bacillary contents. A variety of chemo attractants are release upon cell lysis (including complement and cytokines). These stimulate other mononuclear cells which in turn are responsible for presentation of antigens to T lymphocytes in the draining lymph nodes. These initial phases are usually asymptomatic. In the ensuing 3-4 weeks, 2 host responses are pronounced: a macrophage activating (cell mediated) response and a tissue damaging response (delayed type hypersensitivity response). Although both of these responses can inhibit mycobacterial growth, it is the balance between the two that determines the form of tuberculosis that will develop subsequently.

The Macrophage activating (cell mediated) response is mounted once lymphokines are released by T lymphocytes. These activate other macrophages which aggregate around the center of the lesion and neutralize the bacilli without further tissue damage. A caseating necrosis may occur in the central part of the lesion. However, viable bacilli

may remain dormant within macrophages or in the necrotic material for many years.If the macrophage activating response is weak, further growth can only be restricted by an intensified delayed type hypersensitivity reaction. However, this response is associated with significant damage to the surrounding tissue. Granulomas may forms due to the accumulation of lymphocytes and activated macrophages that evolve toward epithelioid and giant cell morphologies. The caseous necrosis may liquefy and carry large numbers of bacilli to drain into the bronchi as the bronchial walls and vessels are invaded and destroyed. Cavities may also be formed where large numbers of tubercle bacilli multiply and are spilled into the airways and expelled into the environment through coughing or sneezing.

Clinical Presentation.

Now, the symptoms of the disease depend on where in the body the bacteria are multiplying. If the lungs are typically involved the symptoms include Coughing for more than two weeks(sometimes with hemoptysis), Difficulty in breathing, Chest pain plus the overall classical symptoms of TB disease which include Unexplained weight loss, Easy fatigability, Evening fevers, excessive Night sweats and Loss of appetite**.** [20]

1.1.3 Diagnosis of TB

Sputum Smears for AFB.

The most common method for diagnosing TB worldwide is sputum smear microscopy (developed more than 100 years ago) in which the bacteria are observed in sputum samples examined under the microscope. This method is simple, cheap and convenient.

In this technique every tuberculosis suspect should submit three sputum specimens for smear microscopy within 24 hours following the schedule below**;** [2]

Spot

Patient provides on the spot sputum specimen under supervision by a staff member in an open air space or well-ventilated area. The patient is given a sputum container for collection of the second specimen.

Morning

Patient produces the next early morning specimen and returns it to the diagnostic centre and is provided with a container for a third specimen.

Spot

Patient produces last specimen on the spot and submits it to the laboratory.

With this approach approximately 80% of the smear positive patients will be detected on the examination of the first specimen, an additional 15% on the second and another 5% on the third specimen.

The following WHO/IUATLD recommended method of reporting should be used.

Table 1: Reporting of smear results.

Number of bacilli seen in smear	Results	Result Reported
No AFB per 100 immersion fields	Negative	0
1–9 AFB per 100 immersion fields	Positive	Record exact number (1–9)
10-99 AFB per 100 immersion fields	Positive	1+
1-10 AFB per 1 immersion fields	Positive	2+
>10 AFB per 1 immersion field	Positive	3+

Sputum Cultures.

This is a more sensitive method to detect mycobacteria than AFB microscopy and can detect as low as 10 bacilli/ml of sputum. However, culture methods are slow and expensive. Depending on the technique, it takes two to eight weeks before a result is obtained. Materials and equipment needed to perform culture are costly and require complex facilities with highly skilled staff. In Tanzania sputum culture for isolation of mycobacterium is performed on Lowestein Jensen medium (a solid egg enriched) and normally for:

1) Surveillance of tuberculosis drug resistance as an integral part of evaluation of NTLP performance.

2) Follow-up of tuberculosis patients who fail to cure, relapse or become chronic excretors after a standardized course of treatment and who may be at risk of harbouring drug resistant organisms[2]

Chest Radiography

Currently Chest x ray is no longer a pre- requisite for the diagnosis of PTB as per NTLP. Treatment can therefore be initiated immediately without CXR provided that the patient is sputum smear positive. However, CXR can be very useful if one is suspecting pleural effusion, pneumothorax or empyema thoracis, all of which are complications of TB in which the sputum smear is in most cases negative. Therefore the chest x-ray findings suggestive of pulmonary tuberculosis in patients with a smear negative microscopy should always be supported by clinical findings [2]

Tuberculin Skin Test

Tuberculin is a purified protein derived from attenuated mycobacteria. A person who has been infected with tuberculosis develops hypersensitivity to tuberculin, which is measured in millimeters of in duration 48-72 hours after the tuberculin injection has been given in the skin. The test does not indicate the presence of tuberculosis disease; it only indicates mycobacterial infection. The test can be positive in a person who received BCG vaccination and who has never been infected with M. tuberculosis. It is often positive in individuals infected with environmental Mycobacteria Other Than Tuberculosis (MOTT) who are not infected with TB. On the other hand, a negative test does not exclude tuberculosis infection or disease. Immunosuppressive conditions such as HIV infection, malnutrition, severe bacterial infections e.g. TB itself, viral infections e.g. measles, cancers, and incorrect injection of PPD may suppress the tuberculin reaction.

Erythrocyte Sedimentation Rate (ESR)

The measure of the ESR is non-specific and should not be used as a routine diagnostic tool for tuberculosis. In most patients with bacterial infection (including TB) the ESR is raised to more than 20 millimeters per hour but a normal ESR does not exclude TB disease [2]

Biopsy

Biopsy can play a role in the confirmation of the diagnosis of extra-pulmonary tuberculosis (EPTB) particularly TB adenitis. This can be done even in the remote areas provided that the necessary stains and a microscope is available. In this case the excision biopsy is taken then cut and smeared on the glass slide then with ZN stain one can clearly see the AFB. Fine needle aspiration is another method used to obtain tissue/fluid for histopathology/cytology [2] With biopsy one can rule out not only EPTB but malignances such as lymphomas which can clinically mimic TB.

Other Techniques

Following recent breakthroughs in TB diagnostics other more advanced and sophisticated techniques have been invented. These include BacTec technology GeneXpert, and Lipoarabinomanan detection in urine.

Bactec Technology.

As mentioned above the growth of mycobacteria in the Solid media (Lowestein – Jensen) can take up to eight weeks and yet the chances of contamination are very high. However it has been found that growing the mycobacteria in a liquid medium can take only two weeks. This can be achieved by either using the Mycobacterium Growth Indicator Tube (MGIT) or Bactec. These tests can also be used for drug susceptibility. They both have proven to be effective in reducing the waiting time for the diagnosis of TB. However, since they still require culture they are therefore not entirely free from weaknesses; so, a negative result does not necessarily exclude TB [21]

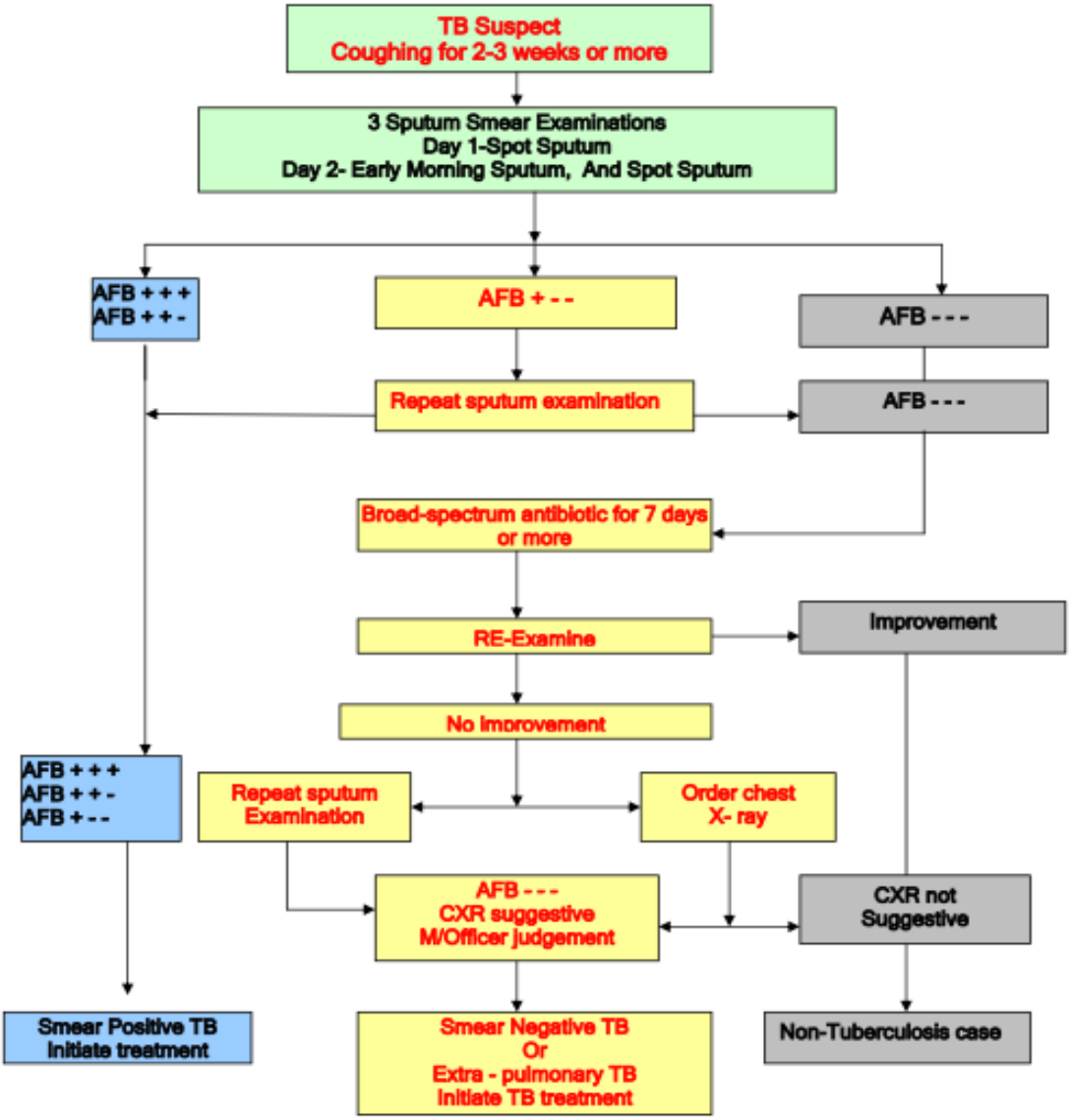
GeneXpert.

This is PCR based nucleic acid amplification test which diagnoses TB by detecting the presence of the bacterial DNA as well as testing for the resistance to the drug Rifampicin. It is highly effective in a sense that compared to culture above, less time is used to diagnose TB (less than 2 hours) and the chances for contamination are very small and this makes this test very accurate and reliable. It actually represents a major milestone for global TB diagnosis and care. The test also requires more trained expertise and it is also expensive compared to others. For this reason WHO has recommended that it should be specifically used in cases where MDR- TB is suspected.

Lipoarabinomannan (LAM)

LAM is the cell wall liposaccharide specific for the genus Mycobacterium and it is released when this bacteria is lysed by the host immune system [22] Recently studies have being done to make use of this biomarker detection in urine to diagnose the disease. [22] It is a very simple and convenient way of diagnosing TB and it requires no highly trained personnel. But it is expensive.

Figure 1: NTLP algorithm for diagnosis of TB in adults



1.0.4 Classification of TB disease.

TB can be classified into the following categories [2]

Smear Positive Pulmonary Tuberculosis (PTB+)

Tuberculosis in a patient with at least two initial smear examinations positive by direct microscopy for Acid Fast Bacilli (AFB+),

OR

Tuberculosis in a patient with one initial smear examination positive by direct microscopy AND positive by culture for mycobacterium.

OR

Tuberculosis in a patient with one initial smear examination positive by direct microscopy for Acid Fast Bacilli (AFB+) AND X ray abnormalities suggestive of active tuberculosis as determined by the treating Medical Doctor.

Smear Negative Pulmonary Tuberculosis (PTB-)

Tuberculosis in a patient with three initial negative smear examinations by direct microscopy for Acid Fast Bacilli (AFB-) AND non-response to a course of broad-spectrum antibiotics, AND again three negative smear examinations by direct microscopy, AND X-ray abnormalities suggestive of active tuberculosis as determined by the treating Medical Doctor.

OR

Tuberculosis in a patient with three initial smear examination negative by direct microscopy but positive by culture for mycobacterium.

Extra-pulmonary Tuberculosis (EPTB)

Tuberculosis in organs other than the lungs proven by one culture positive specimen from an extra-pulmonary site or histopathological evidence from a biopsy.

OR

Tuberculosis based on strong clinical evidence, including macroscopic evidence of specimen inspection, consistent with active extra-pulmonary tuberculosis AND the decision by a Medical Doctor to treat with a full course of anti- tuberculosis therapy.

1.1.5 Treatment of TB.

Early case finding and adequate treatment of tuberculosis patients is the corner stone of tuberculosis control. The aim of treatment is to cure TB patients, to prevent death from active TB or its late effects and to prevent further transmission of tuberculosis to the community. The DOTS strategy is the gold standard to achieve these aims and to prevent the development of anti-TB drug resistance [2] However, in the context of our health care set up, strict Directly Observed Treatment (DOT) was rather difficult and impractical [23] But with the introduction of a fixed dose combination(FDC) in 2006 and

the alteration of the treatment duration from 8 months to 6 months, with Rifampicin being the core in both intensive and continuation phase, Patient Centered Treatment(PCT) proved to be equally effective as the conventional DOT [23]

1.0.6 Prevention of TB.

Primarily this involves avoiding long term direct exposure to the infected TB case. This can be achieved by avoiding overcrowding, maintaining good ventilation and using protective gears when taking care of TB patients.

Secondarily, early case detection and adherence to treatment regimens are the main cornerstones to successful control of the disease.

1.1 LITERATURE REVIEW.

1.1.1 Global Burden of TB

The number of deaths due to TB is unacceptably large given that most are preventable. In 1993, the World Health Organization (WHO) took a bold step and declared tuberculosis a global emergency[24] It was by then estimated that between 2002 and 2020, approximately 1 billion people will be newly infected, over 150 million people will get sick, and 36 million will die of TB - if control is not further strengthened [24] Following that the United Nations in the year 2000 set the strategic goals for the millennium, these are the Millennium Development Goals (MDGs).The MDG 6C specifically addresses TB and the target is for all the countries particularly the HBC to have halted by 2015 and begun to reverse the incidence, prevalence and death rates associated with TB[24] The same thing applies to Proportion of tuberculosis cases detected and cured under DOTS (Directly Observed Treatment Short Course) [24,25]It is now more than ten years and Tuberculosis (TB) is still a major global health problem. In 2012, an estimated 8.6 million people developed TB and 1.3 million died from the disease (including 320 000 deaths among HIV-positive people) [26]

As explained above, global targets for reductions in the epidemiological burden of TB have been set for 2015 and 2050 within the context of the MDG number 6C and separately by the Stop TB Partnership, a global coalition of stakeholders established to coordinate international efforts. The principal MDG target is that the incidence rate should be falling by 2015. The additional targets set by the Stop TB Partnership are that prevalence and death rates should be halved by 2015 compared with their level in 1990, and that TB should be eliminated as a public health problem by 2050 (defined as less than one case per million populations). Now it is one year down the line before re evaluation and we can see that major progress has been made to achieve the target. According to the *Global TB Report 2013* and its accompanying supplement *Countdown to 2015* which assess the progress towards the 2015 targets the rate of new TB cases has been falling globally for about a decade. There is also a fall in incidence rates of TB in all six WHO regions. The rate of decline is 2% per annum but this is still very slow. [26]

Nevertheless, by the year 2012, TB mortality rate had been reduced by 45% since 1990.This means therefore the target to reduce deaths by 50% by 2015 is within reach. [26]The report showed that by the year 2012, the level of active TB disease in the community (prevalence) had fallen by 37% globally since 1990.For that projection the target of a 50% reduction by 2015 is not expected to be achieved. Among the 22 high burden countries (HBC),half of them are actually not on track to reduce the incidence, prevalence and mortality in line with the targets due to financial constraints, conflicts and instability and of course HIV epidemics. Fortunately Tanzania is among the HBC which are on track [26] So in summary if you look at the current global picture of TB you will see that there is continuous progress towards achieving the set goals but it is not fast enough and hence the targets may not be archived in the poor countries where the burden is particularly big.

It has also been observed that most TB cases and deaths occur among men, but women are also potential victims. There were an estimated 410,000 TB deaths among women in 2012, including 160,000 among HIV positive women. In fact, half of the HIV – positive people who died from TB in 2012 were women. Of these estimated 8.6 million new TB cases worldwide in 2012, 2.9 million were women [26] The magnitude of this disease in children is also phenomenal. In the 2013 global report there were an estimated 530,000 TB cases among children under 15 years of age and 74,000 TB deaths among HIV negative children in 2012, this is actually 6% and 8% of the global totals, respectively [26]

The magnitude of this disease among the elderly in Tanzania is however not known.

1.1.2 The Burden of TB in Tanzania.

Tanzania is classified as one of the 22 HBC TB countries according to WHO [26] Despite the efforts made by the National TB and Leprosy program (NTLP) in combating this disease, it still continues to be a major public health problem for more than 30 years since the launch of the program. The burden of TB in the country is usually monitored through a routine notification system. Unfortunately there was no data from national surveys on incidence or prevalence of disease. As a result up to 2007, the case detection

(number of cases identified as percentage of the estimated incidence of disease) of TB was estimated to be below 50% [27] This implies that there was a gross under detection of TB cases. But, a poor reporting system or an overestimation of TB incidence or both could also be a reason why case detection was low. Despite having a consistently routine TB surveillance data over the years, something is still missing in the information and this makes it difficult to use the obtained routine data to approximately derive the TB incidence as an indicator for the burden of disease [27]

Several repeated studies on school children in Tanzania have actually shown a decline in the Annual Risk of Tuberculous infection (ARTI) in both the younger (aged 5-9), and the older children (10-14).This was actually observed through a repeated number of Tuberculin Skin Test (TST) studies in this age group[28] but it was not possible to estimate the TB incidence from these data because the often-used Styblo rule could not apply in a setting with TB-control activities[29, 30]. So, after a thorough assessment of the notification system and additional data sources in 2008 by the WHO team, the case detection was corrected upwards to 70%, despite the fact that a proper insight in the TB incidence and prevalence in the country was still lacking. Being one of the 22 HBC and with the question marks still on regarding the actual burden of the disease in the country, the Ministry of Health and Social Welfare in Tanzania was required to conduct the prevalence survey for this disease in order to find out its current magnitude. This was completed in September 2013 and it actually is the first national TB prevalence survey in the country. In this survey the prevalence of bacteriologically confirmed TB was 295 per 100,000 adults. The prevalence of HIV -infection in identified TB cases was 6.8%. Case Detection of new smear-positive adult TB patients was estimated to be between 42 and 54%. [27]

But the most striking observation in this survey is that the majority of identified TB cases were 55 years or older, indicating a shifting epidemic from young HIV-infected patients. Further, the prevalence was higher in mainland Tanzania compared to Zanzibar, rural compared to urban populations, men compared to women, older

compared to younger participants and in participants with lower compared to higher socio-economic status [27]

The prevalence in Tanzania for bacteriologically confirmed TB according to different subgroups were as follows [27]

Table 2: Prevalence (per 100,000) for Bacteriologically Confirmed TB According to Different sub-groups [27]

Zanzibar	124
Mainland	300
Sex	
Male	410
Female	207
Age group	
15-24	42
25-34	303
35-44	323
45-54	260
55-64	673
65 and older	725
Socioeconomic status	
Low	445
Middle	342
High	268

1.1.3 Global Measures for Control of TB in Tanzania

TB can be controlled by preventing infection, stopping progression from infection to active disease, and rapid detection and aggressive treatment of the active disease[31,32] All these are being aggressively implemented by the Ministry of Health through its Extended Program for Immunization(EPI) by first providing Bacille-Calmette Guérin (BCG) vaccination to more than 80% of the new born annually. But through its NTLP

the effective diagnosis is done and treatment of active disease is being provided. Massive campaigns on TB are being done across the country and awareness has therefore improved. Resistant strains are also been detected by GeneXpert and patients are being subjected to second line treatment although this is still a big challenge due to scarcity of this diagnostic technique particularly in rural areas. Through these initiatives the Ministry of Health has managed to bring up the rate of decline from 1.5% to 2% per annum [33, 34]. This is a fairly good pace but it is not good enough because it is very obvious that the elimination of TB which is projected to be less than 1case per 1000,000 populations by the year 2050 will not be achieved [35]

1.1.4 Challenges in the Clinical Presentation.

Pulmonary tuberculosis (TB) is still a major health problem worldwide. Due to increase in life expectancy in many populations; the absolute number of elderly has increased all over the world **[36]** Elderly patients account for a significant number of TB cases in the world each year. They also account for over 234,000 of cases of smear positive TB worldwide. **[37]**According to 2007 WHO report, 9.8% of sputum smear positive cases of tuberculosis occur in this group **[38]**

In the developing countries in particular, the risk of developing TB is very high among elderly than young adults. In the former, immunosenescence has been described as the potent contributing factor to increased susceptibility to this infection. This is because the pathogenesis of TB is based on CD4+ produced gamma interferon and subsequent macrophage activation. So if this system is dysfunctional as it is in the elderly, the disease ensues**[38]**Other factors such as malnutrition, decreased access to healthcare, diabetes mellitus, renal failure and other co morbidities have also been described as key contributing risk factors in elderly.**[39,40,41,]**Poverty has also been found to be strongly associated with increased TB incidence.**[42,43,44]**

Studies have also shown that, globally the frequency of TB among elderly is three times more than that observed among young adults.**[45]**It has also been found in another study that this disease was more common in un- institutionalized elderly and particularly those living at home.**[46]**These can actually be the potential sources or reservoirs of TB

infection in the communities. It was generally thought that the majority of TB cases among elderly resulted from reactivation of latent infection[47]However, the determination as to whether the case is a result of reactivation of latent infection or of recently acquired infection is often inaccurate particularly when made on clinical and radiographic grounds as demonstrated by a molecular epidemiology study that was done by *Elvin Geng et al* in June 2005 in which a relationship between recently acquired and remotely acquired pulmonary tuberculosis, clinical and demographic variables, and radiographic features by using molecular fingerprinting and conventional epidemiology was thoroughly analyzed[48] It is true that the immune system and particularly the cellular one declines with age and it is therefore reasonable to think that elderly are in fact more susceptible to developing TB by whatever mechanism than young adults[49,50] The effect of age on clinical presentation of TB have been examined in many old studies[51 - 56] and it was found that EPTB, including milliary TB appears to be more common in elderly[36]The classical features which we commonly encounter in young adults with TB, such as cough, fever, night sweats, hemoptysis and weight loss were found to be less frequently in elderly[53- 55] Non specific symptoms such as anorexia generalized body malaise and loss of cognitive function were more pronounced in this group. But these are the symptoms that we encounter in several infectious syndromes among elderly.

So far there is no study that has been published or if at all done in East Africa let alone in Tanzania to address these key presentations of TB in elderly. One of the most thorough reviews of the clinical presentation of tuberculosis in older patients was a meta-analysis done by Perez-Guzmán and his colleagues in which the characteristics associated with tuberculosis in persons over age 60 were thoroughly examined and compared with all other age groups [60] After a thorough search and review of the literature, they found that certain characteristics, including the prevalence of cough, sputum, weight loss, and fatigue or malaise were similar across all age groups. However, fever, night sweats and hemoptysis were all less common in persons over 60[60] Not surprisingly, co-morbid conditions such as cardiovascular disease, diabetes mellitus,

chronic obstructive pulmonary disease and neoplasm, were all more common in older patients.

With regard to radiographic findings which were examined across all age groups; it was found that upper lobe predominant disease was less common in the elderly compared to young adults. Cavities were also less common in this age group. [60]This finding was in line with several other studies which have reported atypical radiographic findings in elderly TB patients, suggesting that pulmonary lesions occur more often in lower lung fields. [60 - 65]

The reason why fever is less frequently observed in elderly is because of a decreased pyrogenic response when aging. This is due to reduced response to hypothalamic thermoregulatory center to prostaglandin E_2.[66,67]or greater sensitivity to alpha - melanocyte stimulating hormone.[68]The lower prevalence of sweating in elderly is likely to be related to the lower presence of fever.[60]

Difficulty in breathing is another clinical feature which has been observed more frequently in elderly than adults with TB and this is mainly due to the fact that pulmonary functions decrease with aging[69,70] Hemoptysis is a clinical feature encountered more in young adults than elderly with TB[71] This may be explained by the formation of cavities in adults.The formation of small Rassmusen's aneurysms along the cavities walls has been described in the past studies[72,73].Bloody sputum and massive hemoptysis can therefore be due to the rupture of these aneurysms.

1.1.5 Challenges in Diagnostic Approach.

The approach to the diagnosis of TB has been well described and written about. [74] In our set up the approach to diagnosis has been clearly described above with regard to NTLP diagnostic algorithm for TB (Fig 1). In this case sputum smear is the cornerstone in the diagnosis of TB across the board. Failure to produce sputum sample by spontaneous expectoration poses a great challenge in the diagnosis of this disease in elderly.

1.1.6 Challenges in Treatment Outcomes.

The basic approach to treatment of TB in elderly is the same as in adults [78] which include two months intensive treatment with Rifampicin, Isoniazid, Ethambutol and Pyrazinamide followed by a 4 month continuous treatment phase with Rifampicin and Isoniazid.

The major concerns related to treatment of TB in elderly are those adverse drug effects, one of them being drug (particularly isoniazid) induced hepatitis with consequent liver damage which has been observed in persons older than 50 years of age [78,79] Adults may also experience drug induced hepatitis but it is in most cases transient and asymptomatic. Ocular toxicity which is a common side effect of ethambutol is usually reversible but in elderly it has been observed to be more frequent and less reversible [80] In addition to this, dietary intake of vitamin B6 is lower in elderly than adults [81] and this makes the elderly patients more prone to Isoniazid induced peripheral neuropathy. In a retrospective cohort study done in southern India in which one of the objectives was to compare the treatment outcomes between elderly (60 years and above) and young TB patients, the former had 38% higher risk of unfavorable treatment outcomes. The treatment outcomes were poor in elderly patients warranting special attention to this group of patients. [81 - 83]

These findings are in line with another twelve years cross sectional study that was done in Mexico in 1995 [46] But poor treatment outcomes and particularly failure in elderly have been described to be due to decreased drugs absorption and this could possibly be due to some age related physiological changes that occur in the stomach, including altered gastric pH, modified gastric emptying rates, slower intestinal transient time and drug intolerance associated with the likelihood of polytherapy [84,85] It has also been found that even after timely diagnosis and completion of treatment mortality is three times higher among elderly than young adults with TB [46].[71]This is again due to high rates of co morbidities and poor treatment outcomes with consequent suspension of treatment [65]

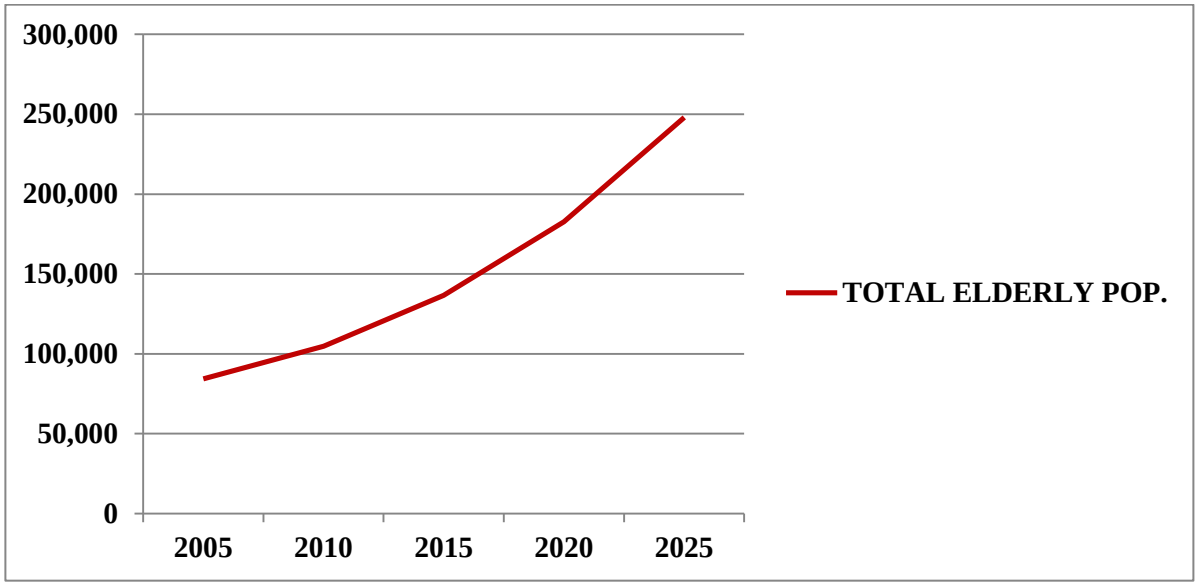
1.1.7 Population of Elderly in Dar es Salaam.

Dar es Salaam is the largest city in Tanzania. As for the 2012 census the population was 4.36 million. [96]This accounted for almost 10% of the country population. But Dar es Salaam is also third fastest growing city in Africa (ninth fastest in the world), after Bamako and Lagos. [99] Currently the population of Dar es Salaam is said to be approximately 5 to 6 million. [99] The main reason for rapid growth of population is rural- urban migration in which young people come looking for greener pastures like job opportunities and business ventures. A fairly conducive infrastructure and availability of social services seem to be the most attractive factor for the rural – urban migration. This has in turn changed the entire age structure of the city. The latter is home for 151,812 (3.5%) of all (2,507,568) elderly in the country. Of these 39.3%, 31.6% and 29.1% reside in Kinondoni, Temeke and Ilala districts respectively. [87]

1.1.8 Projection of Elderly Population in Dar es Salaam by 2025.

The number of elderly in the city is increasing; It is estimated that by 2025 the city will have almost 250,000 elderly **[98].** If this is compared to 151,812, the elderly population as per 2012 population and housing census you will see that the growth of elderly population is faster than expected and the city may by 2025 have more than the projected number of elderly.

Figure 2: Elderly Population Projection in Dar es Salaam by 2025



1.2 PROBLEM STATEMENT

Tuberculosis remains a major global health problem and continues to pose serious public health challenges in spite of multifaceted global efforts to control it. The number of deaths due to this disease is unacceptably high despite availability of effective drug treatment. In 2012, an estimated 8.6 million people developed TB and 1.3 million died from the disease. [26]

Studies have also shown that, globally the frequency of TB among elderly is three times more than that observed among adults, the reason being that old age, cancer and use of immunosuppressive drugs, diabetes mellitus, conditions associated with increased risk to developing clinical TB, are more common among the elderly compared to other age groups.[45] Results from the first Tanzania national TB survey published in 2013 showed a higher TB prevalence among older age groups as compared to younger ones, indicating a shifting epidemic from young to much older patients [27] Studies from Europe, America and Asia have specifically reported that TB in elderly often presents with atypical symptoms and clinical findings which may be confused with other age related conditions and hence delay in diagnosis and treatment with consequent increased morbidity and mortality.

In addition treatment of TB in the elderly can pose peculiar clinical challenges and increased mortality even with timely diagnosis and completion of treatment.

There is no published data on the clinical presentations of TB among the elderly in Tanzania. In deed little has been published on the subject from sub Saharan Africa. Hence this study aims at describing the clinical presentation of TB among the elderly compared to adults in order to improve on the quality of care for this vulnerable group of people.

1.3 RATIONALE

Due to a number of factors diagnosis and treatment for TB in elderly may be more difficult compared to adults. The former being contributed by the atypical presentation and co morbidities and the latter due to poor treatment outcomes which is in a greater way related not only to altered physiological changes but to poor compliance to medication. Reported studies on the subject of tuberculosis among the elderly have largely been from Europe and North America and none from East Africa, let alone Tanzania. Given the increasing numbers of the elderly population and the increasing proportion of reported TB among people aged ≥60 years; there is a need to describe and determine the key characteristics of TB and associated co-morbidities in developing countries like Tanzania.

The aim of this study was to describe the clinical characteristics of TB in the elderly aged ≥60 years compared to adult population aged 18 - 59 years with the purpose of improving clinical care and outcome.

1.4 RESEARCH QUESTIONS

1. What are the clinical characteristics of TB in the elderly and adults?
2. How are the sputum yield microscopy results for *Mycobacterium tuberculosis* in elderly and adults with pulmonary TB?
3. What are the chest radiological findings in elderly and adults with TB?
4. What are the treatment outcomes at the end of two month intensive phase in elderly and adults with TB?
5. What are the co morbidities associated with TB in the in elderly and adults with TB?

1.5 STUDY OBJECTIVES

1.5.1 Broad Objective

To describe and compare the clinical characteristics of tuberculosis and associated factors among patients aged 18-59 and those aged 60 years or more (elderly) attending TB clinics in the city of Dar es salaam.

1.5.2 Specific Objectives

1. To describe and compare clinical characteristics of TB in the elderly and adults
2. To determine and compare the sputum microscopy yield for *Mycobacterium tuberculosis* in elderly and adults with pulmonary TB (PTB).
3. To compare the chest radiological findings in elderly and adults with TB
4. To document the treatment outcomes at the end of two month intensive phase in the two groups
5. To describe and compare the co morbidities associated with TB in the two groups.

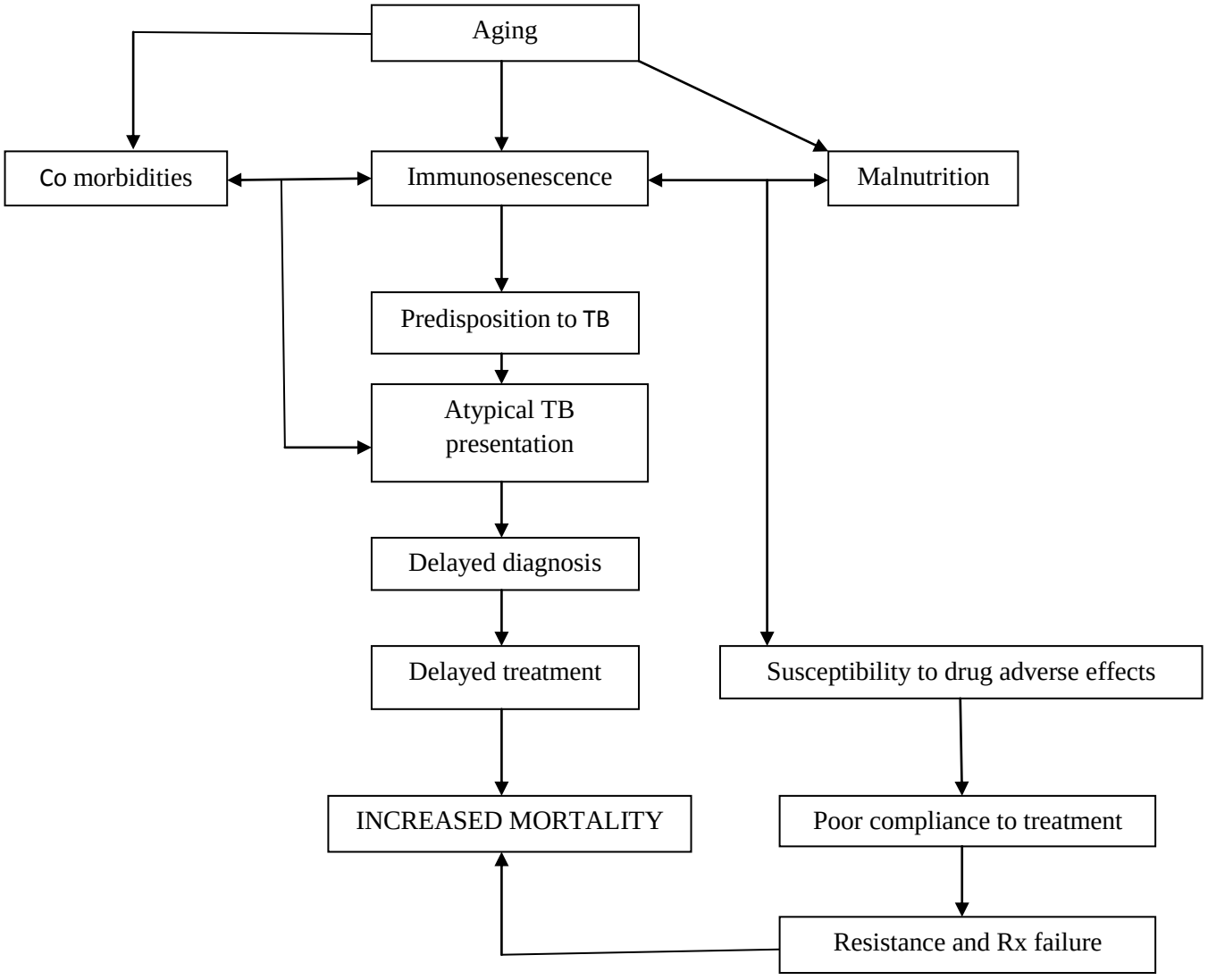
1.6 HYPOTHESIS

This study was based on the hypothesis that unlike adults, elderly TB patients have a unique and atypical presentation. They are therefore more likely to be misdiagnosed and mistreated.

1.7 CONCEPTUAL FRAMEWORK

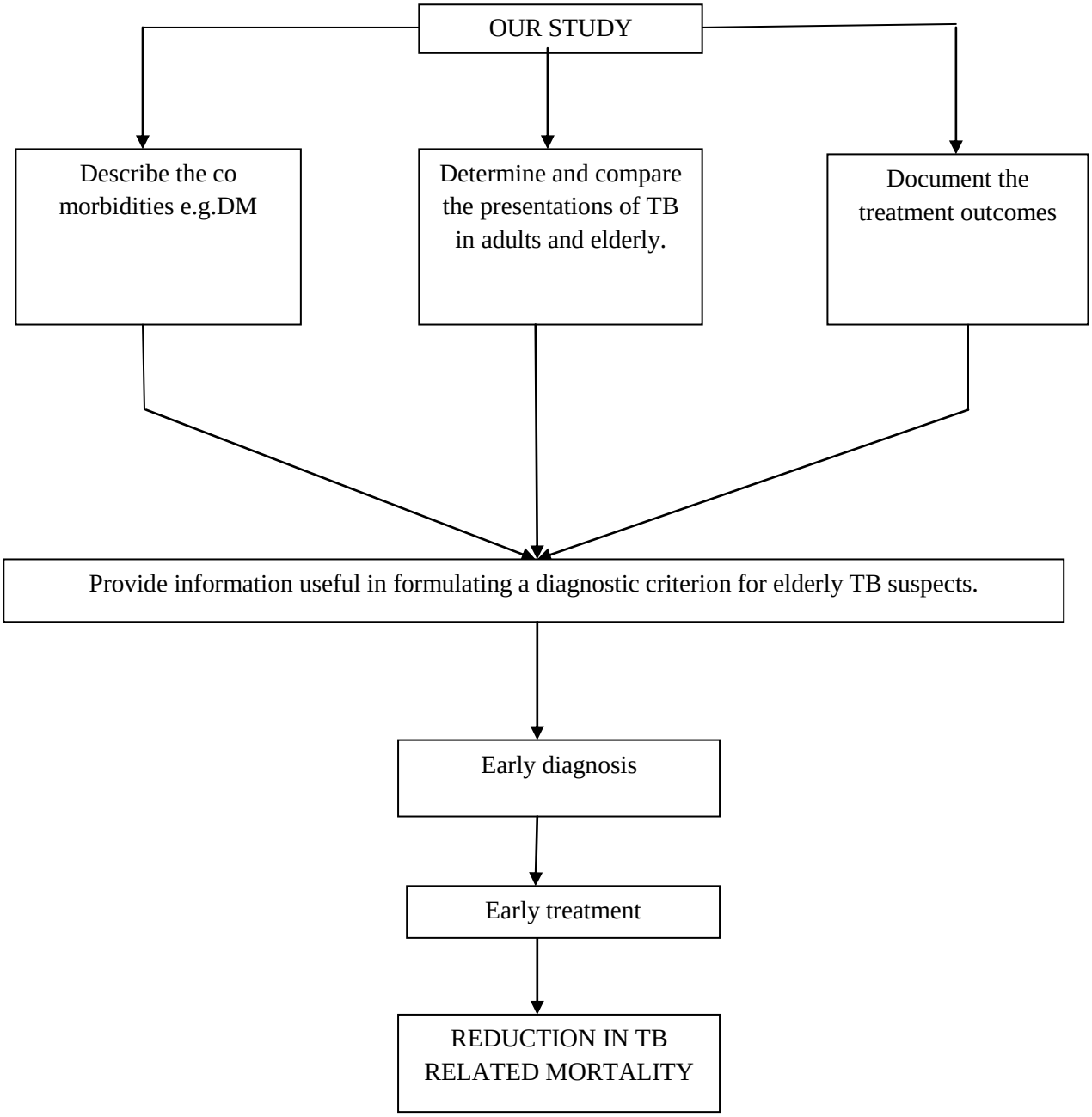
The whole concept can be summarized in the chart below:

Figure 3: Conceptual Framework – 1



Having the whole concept in a clear perspective, the aim of this study can now be summarized as follows:

Figure 4: Conceptual Framework – 2



CHAPTER TWO

2.0 METHODOLOGY

2.1 Study Design

This was hospital based prospective cohort study.

2.2 Study Period.

The study was conducted for seven months**.** Patients were recruited from 2nd August to 31st December 2014. Follow up commenced on 3rd October 2014 to 28th February 2015.

2.3 Study Area

The study was conducted in the TB clinics within three Hospitals in Dar es Salaam City namely, Mwananyamala, Buguruni and Mbagala. These hospitals are located in Kinondoni, Ilala and Temeke districts respectively; three districts of Dar es Salaam city. They were conveniently selected based on their higher throughput of elderly patients with TB as indicated by a pilot study which was done a month prior to the commencement of the research.

2.4 Study Population

This included all new TB patients, 18 years and above, attending the TB clinics in the above mentioned hospitals. Most of these patients were referred from the outpatient clinics in the same hospital but others were self referral following their awareness to symptoms of TB. The TB suspects who turned up not to have TB were not involved in the study and they were therefore not analyzed.

2.5 Inclusion Criteria.

- All TB patients aged ≥18 years who attended the clinics during the study period.

2.6 Exclusion Criteria.

- TB patients who were not willing to participate in the study.

2.7 Key Study Definitions.

2.7.1 Categories of Weight as Defined by The BMI.

These were defined according to WHO as shown below [100]

Table 3: Categories of Weight as Defined by The BMI.

Category	BMI range – kg/m^2
Very severely underweight	less than 15
Severely underweight	from 15.0 to 16.0
Underweight	from 16.0 to 18.5
Normal (healthy weight)	from 18.5 to 25
Overweight	from 25 to 30
Obese Class I (Moderately obese)	from 30 to 35
Obese Class II (Severely obese)	from 35 to 40
Obese Class III (Very severely obese)	over 40

2.7.2 Anemia

This was defined according to WHO criteria as shown below [101]

Table 4: WHO Standard Criteria for Anemia.

(1 g/dL = 0.6206 mmol/L)		
Age or gender group	**Hb threshold (g/dl)**	**Hb threshold (mmol/l)**
Children (0.5–5.0 yrs)	11.0	6.8
Children (5–12 yrs)	11.5	7.1
Teens (12–15 yrs)	12.0	7.4
Women, non-pregnant (>15yrs)	12.0	7.4
Women, pregnant	11.0	6.8
Men (>15yrs)	13.0	8.1

Standard criteria for microcytic (MCV<80fL) and macrocytic (MCV>100fL) anemia and the standard MCH values of 25 -35pg/cell were used as a reference.

2.7.3 Hypertension

This was defined as a systolic blood pressure (SBP) of 140 mm Hg or more or a diastolic blood pressure (DBP) of 90 mm Hg or more or taking antihypertensive medication [102]

2.7.4 Diabetes Mellitus.

This was defined as a Fasting Blood Glucose of ≥7.0 mmol/l. (Fasting is defined as no caloric intake for at least 8 hours) or a Random Blood Glucose of ≥11.1mmol/l). [103]

2.8 Sampling Technique

All patients who attended the TB clinics in those three hospitals mentioned above were sequentially enrolled.

2.9 Sample Size Determination.

With a similar study done in Uttarakhand, India in 2008 as a proxy [36]. The respective sample sizes for each clinical feature of TB were as shown in the table below.

Table 5: Prevalence of Symptomatology of Pulmonary TB in Adults and Elderly Patients.

Clinical Features	Prevalence (%age)		Required Sample Size
	18 – 59 years	60 years +	(95% C.I, 80% Power)
Hemoptysis	29.5	6.0	48
Fever	95.4	76.0	65
Night Sweats	54.5	18.0	31
EPTB	7.0	40.0	31

**Each required sample size above assumes the 80% power and 95% C.I*

The above sample sizes were calculated by using the following formula:

$$n\,(\text{each group}) = \frac{(p_0 q_0 + p_1 q_1)(z_{1-a/2} + z_{1-b})^2}{(p_1 - p_0)^2}$$

Where:

- $p_0 = 0.76$ (proportion with fever in elderly)
- $q_0 = (1 - p_0) = 0.24$ (proportion without fever in elderly)

- p_1= 0.954 (proportion with fever in young adults)
- q_1 =(1- p_1) = 0.046 (proportion without fever in young adults)
- $z_{(1-a/2)}$=value of the standard normal distribution corresponding to a significance level of a (1.96 for a 2-sided test at the 0.0 5 level)
- $z_{(1-b)}$ = value of the standard normal distribution corresponding to the desired level of power (0.84 for a power of 80%, 1.28 for power of 90%)

We used the prevalence of fever as a proxy as it yielded a comparatively larger sample size.

So the required minimum sample size (n) for each group is 65 patients with TB, this made the overall minimum sample size of 130.

But for this particular study we decided to increase the overall sample size to 250 (nearly double) under the assumption that some study subjects may be lost to follow up due to various reasons such as defaulting, being transferred out or simply being unreachable and some might actually die before follow up. But the other good reason is based on the fact that comparability of the outcomes which in this case were the clinical characteristics of TB in elderly and adults would be more robust if the sample size was larger. Nevertheless, the larger sample size also might have increased the power of the study and so is the generalizability.

2.10 Study Procedures.

2.10.1 Recruitment.

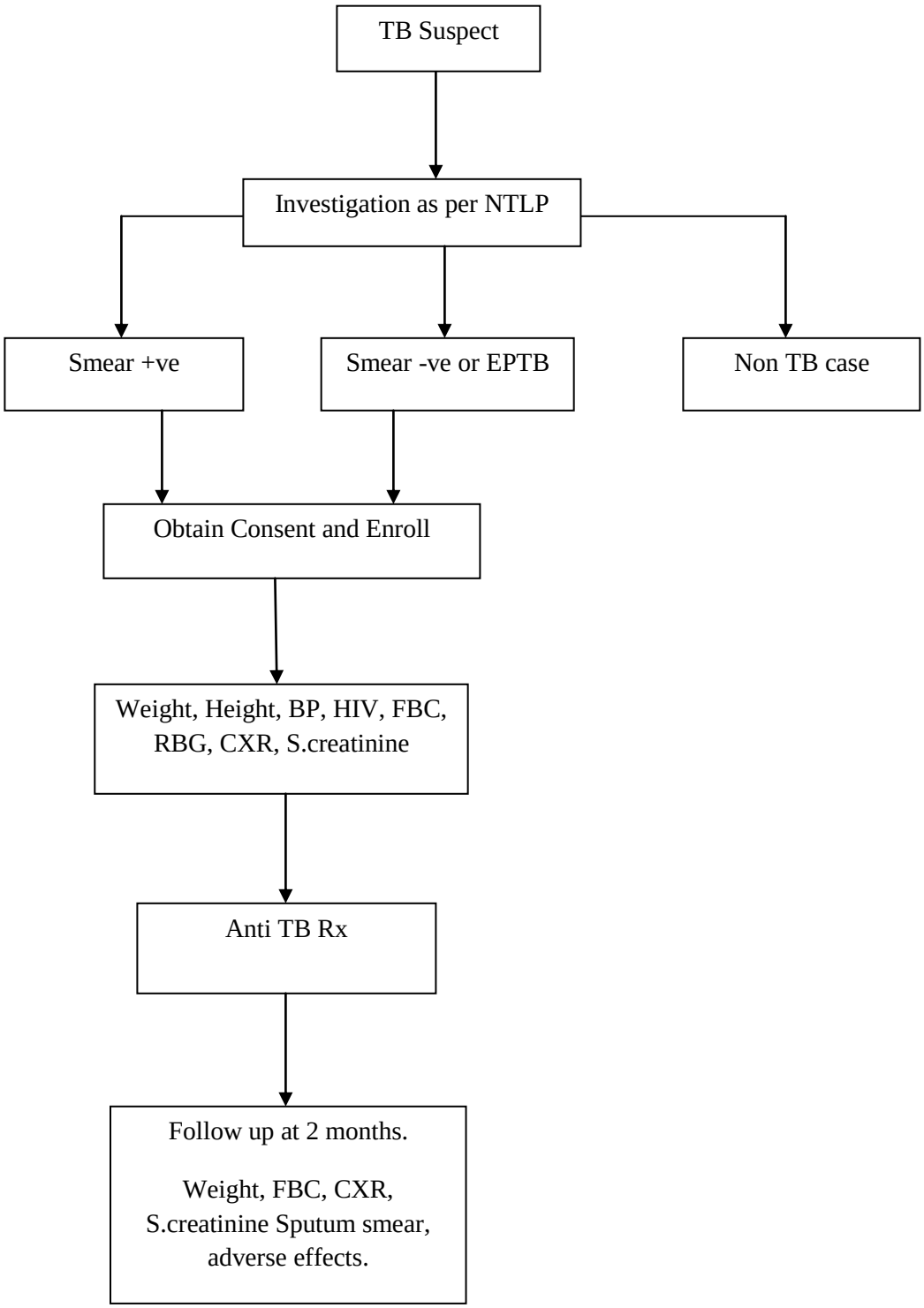
The catchment areas for this study were the TB clinics in Mwananyamala, Buguruni and Mbagala Hospitals in Dar es Salaam city. All new TB suspects with 18 years and above who attended the above mentioned TB clinics during the study period were investigated for tuberculosis by using the NTLP algorithm (Fig 1). This algorithm requires sputum microscopy for AFB be done on three samples (spot, morning sample and spot), if negative antibiotic treatment is given for seven days or more, followed by clinical re-evaluation. If there is no improvement, repeat sputum microscopy for AFB and a chest X ray (CXR) are done. If sputum is still negative but CXR is suggestive of TB the

attending doctor is required to decide to give anti-TB drugs (sputum negative TB and/or extra-pulmonary TB) or otherwise.

All patients who met criteria for diagnosis of TB as per this algorithm were requested to consent participation (in the study) after being adequately informed about the study. Patients who consented, their weight and height were measured, the blood pressure was also measured and they were asked to provide blood samples for full blood count (FBC), random blood sugar (RBG), serum creatinine and HIV serology. In addition a CXR was done if not already done for diagnosis of TB as per the algorithm. Fasting blood glucose (FBG) was done to those who were found to have the RBG of more than 11.1 Mmol/L. Those who were found to be diabetic or hypertensive were referred to the specialized clinics in the respective hospitals for intervention. All these measurements and assessments were done by the trained assistants who included two Assistant Medical Officers and one nurse.

Then treatment with anti TB drugs was initiated as per NTLP guideline. The whole process is summarized in the flowchart below.

Figure 5: Recruitment Flowchart



2.10.2 Follow up.

At the end of two (2) month of intensive therapy study subjects underwent repeat examinations of sputum for AFB, FBC, CXR, serum creatinine and weight. Adverse effects to drugs and mortality was also documented and compared between the two groups. All the chest x rays were reviewed and reported by the consultant radiologist. Except for HIV serology and RBG which were tested on site, the blood samples for FBC and Serum creatinine were on the same day taken to Muhas Research Laboratory for analysis.

The adverse effects that were specifically observed included Peripheral neuropathy which was assessed only during follow up after two months of treatment and this was done by verbally enquiring for the presence of burning sensation of the feet. The presence of jaundice, gastrointestinal disturbances such as nausea, vomiting and diarrhea were specifically assessed to rule out any drug induced hepatitis. Other encountered side effects were also documented.

Follow up by phone call to either the study subject or through their next of kin was done for all the absentees. Those who died during the study were clearly documented including the date of death although the actual primary cause of death was very difficult to elucidate.

2.11 Data Collection

2.11.1 The Data Collection Tool.

A data collection tool (questionnaire) was used to collect data. Primary information such as socio-demographic, chief complaints, past medical history and co morbidities were collected during interviews and physical examination.

The questionnaire was designed to answer all the specific objectives of this study and it had both multiple choice and open end questions. The latter provided more room for the patients to provide more significant information. This tool was available in English version. The Swahili version was not necessary because the latter had to be filled in only by the PI or trained research assistants all of which were fluent in English language. Each questionnaire had a serial number which was also marked on each patient’s blood

samples, CXR film and TB green card. This helped us to avoid confusion during follow up and in the mean time made sure that confidentiality was observed throughout the study.

The process of collecting data was done on a daily basis by a PI and three well trained research assistants two of which were Assistant Medical Officers and one was a well trained nurse.

2.11.2 General Examination.

All study subjects were clinically examined by the PI and the assistants (above).General examination was done not only to rule out TB but to also exclude the co morbidities which were thought to be associated with the disease. Among the clinical findings that we looked for were general appearance, dyspnoea at rest pallor, jaundice, oral ulcers, peripheral lymphadenopathy, finger clubbing and lower limb edema.

2.11.3 Data Processing and Analysis.

All the questionnaires were checked by the PI to make sure that they were accurately and completely filled. Then all the data was on a daily basis entered in the SPSS version 21 software. The latter was then checked for consistency, validity and any other missing information. Finally the analysis was done using SPSS Version 21.T – test was used to evaluate continuous variables while the Chi – square test was used to evaluate categorical variables and a *p- value* of less than 0.05 was considered significant.

2.12 Ethical Approval

Before commencing the study, ethical clearance was sought from the Research and Publications Committee of Muhimbili University of Health and Allied Sciences (MUHAS). Then the permission to conduct the study was sought from the Administration of Mwananyamala, Buguruni and Mbagala Hospitals. None of the participants were enrolled against their will; hence each participant signed an informed consent. The obtained information was handled with utmost confidentiality. In the cases where a second opinion or referral to a tertiary facility was required the researchers did not hesitate to do so in order to save lives. In case of HIV testing, pre and post test

counseling were done on site and those who were found to be HIV positive were immediately referred to the CTC in the same hospital for initiation of treatment and other control measures. Since the study did not interfere but was instead part and parcel of the routine clinical activities, the pre and post counseling were done by the authorized hospital counselor.

2.13 Dissemination of Results

Finally all the laboratory results were given to all study subjects during follow up and necessary interventions were carried out as soon as possible. Fortunately no contagious disease was encountered throughout the study.

The results of the study were disseminated to the MUHAS department of Internal Medicine, the medical library, three hospitals which participated in the study and the NTLP.

2.14 Validity and Reliability of the Study Tools

The questionnaire which was used for data collection had been pre tested on 10 patients and found to be very valid and reliable for the task. Nevertheless the instruments which were used for examination (BP Machine and Glucometers) were the ones recommended by WHO and they were calibrated. All the blood samples were within twelve hours sent to one laboratory (MUHAS Research Laboratory) for analysis. The latter has been internationally recommended for research purposes. All Chest x rays were read and interpreted by one and the same consultant radiologist at MUHAS**.**

CHAPTER THREE

3.0 RESULTS

This study recruited index cases from the TB clinics in Mwananyamala, Buguruni and Mbagala hospitals between 2nd August 2014 and 31st December 2014.All patients attending the clinics were sequentially enrolled and screened for TB as per the NTLP algorithm and those who fulfilled the criteria for the latter were enrolled, evaluated and then started on anti TB. Follow up commenced on 3rd October 2014 and ended on 28th February 2015.A total of 150 adults and 103 elderly new TB patients were enrolled into the study (Fig 1).

The mean age (SD) for the adults was 35.57 (± 10.3) and it ranged from 18 – 59 years. The mean age (SD) for the elderly was 67.17 (± 6.43) and it ranged from 60 – 90 years. The overall mean age (SD) of the study population was 48.23(±17.8) and it ranged from 18 – 90 years.

Out of 150 adults enrolled 116 (77.3%) made it to follow up compared to 79/103 (76.7%) among the elderly group ($p>0.05$). In the adult group ten (6.7%) patients died before two months and 24 [16%] were lost to follow up compared to eighteen (17.5%) and six (5.8%) respectively in the elderly group. (Fig 1)

Figure 1: Flow Chart

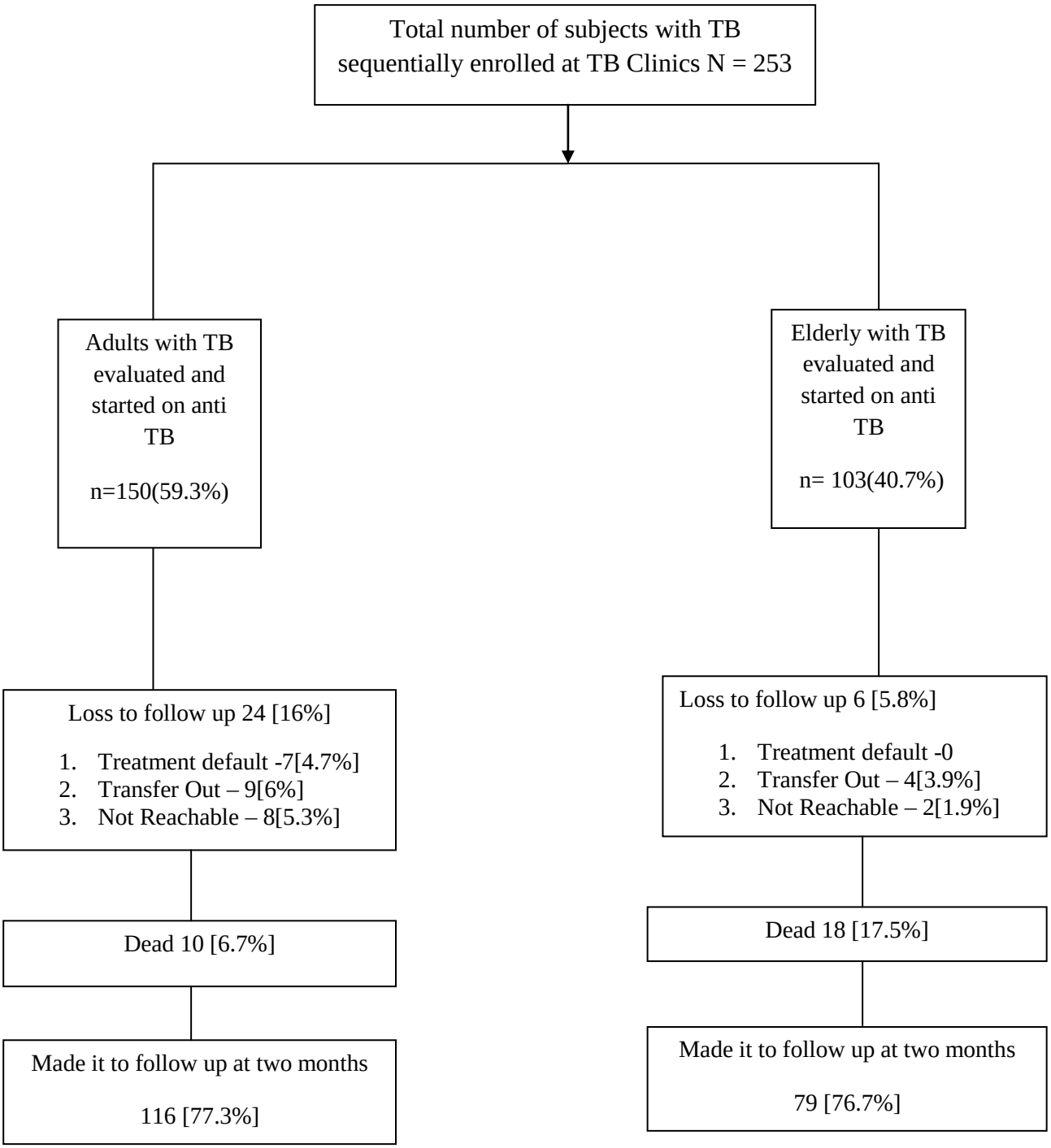


Table 1: Socio-Demographic Characteristics of Adults Compared to Elderly TB Patients

Character	Total (n_1+n_2) 253	Adults (n_1, %) N=150	Elderly (n_2, %) N =103	p-value
Sex				
Male	168 (65.4)	103 (68.7)	55 (63.1)	
Female	85 (33.6)	47 (31.3)	38 (36.9)	0.358
Marital status				
Single	75 (29.6)	69 (46)	5 (5.8)	
Married	119 (47)	51 (34)	68 (66)	
Cohabiting	4 (1.6)	4 (2.7)	0 (0)	
Divorced	28 (11.1)	21 (14)	7 (5.8)	
Widowed	27 (10.7)	4 (2.7)	22 (21.4)	<0.001
Education level				
Non-formal	52 (20.6)	16 (10.7)	36 (35)	
Primary school level	159 (62.8)	95 (63.3)	64 (62.1)	
Secondary school and above	42 (16.6)	39 (26.)	3 (2.9)	<0.001
Occupation status				
Unemployed	189 (74.7)	116 (77.3)	73 (70.9)	
Employed	38 (15)	29 (19.3)	9 (8.7)	
Retired	26 (10.3)	5 (3.3)	21 (20.4)	<0.001

Table 1 compares the socio-demographic characteristics of the study subjects in the two groups. With respect to gender nearly two third of all the study subjects were males; the proportion of males in the two groups (adults and elderly) was not statistically significant (p= 0.358). With respect to marital status nearly half (47%) of all our study subjects were married. Two thirds of the elderly (66%) were married while 46% of adults were single. A significantly higher proportion (21.4%) of elderly patients were widowed compared to 2.7% in the adults group (p< 0.001).The proportion of divorcees was higher among adults (14%) compared to (5.8%) among the elderly (p< 0.001).In terms of level of education majority of all the subjects had attained primary school education (62.8%) but adults displayed a greater proportion (26%) of subjects with secondary school education and above compared to (2.9%) in the elderly group (p<0.001). With regard to occupation 74.7% of all study subjects were unemployed.

Table 2: Baseline Physical Examination and Laboratory Investigations Findings among Adults Compared to Elderly TB Patients.

Finding	Total n (%)	Adults (n, %)	Elderly (n, %)	*p*-value
BMI category				
Severely underweight	32 (12.6)	25 (16.7)	7 (6.8)	
Underweight	57 (22.5)	35 (23.3)	22 (21.4)	
Normal weight	132 (52.2)	76 (50.7)	56 (54.4)	
Overweight	18 (7.1)	8 (5.3)	10 (9.7)	
Obese	10 (4)	4 (2.7)	6 (5.8)	
Severely obese	4 (1.6)	2 (1.3)	2 (1.9)	0.141
Blood pressure				
Normal pressure	210 (83)	140 (93.3)	70 (68)	
Hypertension	43 (17)	10(6.7)	33 (32)	<0.001
RBG				
Hypoglycemia	65 (25.7)	48 (32)	17 (16.5)	
Normal glucose	174 (68.8)	100 (66.7)	74 (71.8)	
Hyperglycemia	14 (5.5)	2 (1.3)	12 (11.7)	<0.001
Hemoglobin				
<12g/dL	196 (80)	116 (80.6)	80 (79.2)	
>12g/dL	49 (20)	28 (19.4)	21 (20.8)	0.795
MCV				
< 80 fL	81 (43.7)	55 (50.9)	26 (33.8)	
80 – 100 fL	95 (51.4)	48 (44.4)	47 (61)	
>100 fL	9 (4.9)	5 (4.6)	4 (5.2)	0.065
MCH				
< 25 pg/cell	48 (26.5)	28 (25.7)	20 (27.8)	
25-35pg/cell	123 (68)	75 (68.8)	48 (66.7)	
>35pg/cell	10 (5.5)	6 (5.5)	4 (5.6)	0.951
GFR				
< 60	120 (47.4)	43 (28.7)	77 (74.8)	
≥60	133 (52.6)	107 (71.3)	26 (25.2)	<0.001

The physical and laboratory findings at baseline for the two study groups, adults and elderly TB patients, were as shown in Table 2. More than a half of all the study subjects had a normal BMI; but a larger proportion of adults (40%) were underweight or severely underweight compared to (28.2%) among the elderly ($p< 0.001$). On the other hand a greater proportion of elderly (17.4%) had BMI greater than normal compared to 9.3% among the adults ($p<0.001$).

Majority (83%) of all our study subjects were normotensive (BP<140/90mmHg). However a larger proportion (32%) of elderly patients had hypertension (BP≥140/90mmHg) compared to 6.7% among the adult group ($p< 0.001$).

Random blood glucose (RBG) was within normal range in 68.8% of the study subjects; however a larger proportion (11.7%) of elderly had hyperglycemia compared to (1.3%) among the adult group ($p<0.001$).

With respect to the level of hemoglobin 80 percent of all our study subjects had anemia (Hb <13g/dL for male and Hb< 12g/dL for female) and it was not related to age.

Reduced glomerular filtration rate (GFR), at enrolment, was found in 74.8% and 28.7% among the elderly and adult groups respectively ($p< 0.001$).

3.1.0 Factors Associated With Tuberculosis among Adults and Elderly TB Patients.

Table 3.Risk Factors for Developing Tuberculosis among Adults and Elderly TB patients.

Variable	Adult (n, %)	Elderly (n, %)	p-value
Active Cigarette smoking			
Never	104 (69.4)	65 (63.1)	
Quit	23 (15.3)	32 (31.1)	
Current smoking	23 (15.3)	6 (5.8)	0.006
Passive cigarette smoking			
Yes	34 (26.2)	34 (33.1)	
No	116 (77.3)	69 (66.9)	0.028
Alcohol consumption			
Never	93 (62)	64 (62.1)	
Past drinker	34 (22.7)	34 (33)	
Current drinker	23 (15.3)	5 (4.9)	0.014
Illicit drug use			
Yes	6 (4)	3 (2.9)	
Never	139 (92.7)	98 (95.1)	
Quit	2 (1.3)	2 (2)	0.483
Current use	3 (2)	0 (0)	

We also found that over 60% of patients in both study arms had never smoked; 31.1% Vs 15.3% of adults and elderly patients respectively reported to have quit smoking more than a month prior to enrollment ($p< 0.006$). At enrolment 23/150 (15.3%) of adults were still smoking compared to 6/103 (5.8%) from the elderly group ($p=0.006$)

Over 60% of subjects from either arm reported they had never taken alcohol; however a 15.3% of adults compared to 4.9% of elderly patients were still consuming alcohol ($p=0.02$). With respect to illicit drug use more than ninety percent of our subjects had no such history and there was no difference between the two groups. [Table 3 above]

3.1.1 Baseline Clinical Characteristics of TB among Adults and Elderly TB Patients.

Table 4: Baseline Clinical characteristics of TB among Adults Compared to Elderly TB patients.

Symptom	Total N =253	Adults (n, %) N=150	Elderly (n, %) N =103	*p*-value
Cough	236 (93.3)	142 (94.7)	94 (91.3)	0.288
Sputum Production	188 (74.3)	116 (77.3)	72 (69.9)	0.184
Hemoptysis	46 (18.2)	30 (20)	16 (15.5)	0.366
Evening Fevers	159 (62.8)	94 (62.7)	65 (63.1)	0.943
Profuse Night Sweats	167 (66)	97 (64.7)	70 (68)	0.587
Weight Loss	202 (79.8)	123 (82)	79 (76.7)	0.302
Anorexia	145 (57.3)	86 (57.3)	59 (57.3)	0.993
Chest Pain	143 (56.5)	82 (54.7)	61 (59.2)	0.473
DIB	121 (47.8)	65 (43.3)	56 (54.4)	0.084
GBM	140 (55.3)	62 (41.3)	78 (75.7)	< 0.001

Table 5: Baseline Clinical characteristics of TB among Smear Positive Adults Compared to Elderly TB Patients.

Symptom	Total N =101	Adults (n, %) (N= 77)	Elderly (n, %) (N= 24)	*p*-value
Cough	100 (99)	76 (98.7)	24 (100)	0.575
Sputum Production	92 (91.1)	70 (90.9)	22 (91.7)	0.909
Hemoptysis	20 (19.8)	18 (23.4)	2 (8.3)	0.006
Evening Fevers	69 (68.3)	51 (66.2)	18 (75)	0.42
Profuse Night Sweats	65 (64.4)	48 (62.3)	17 (70.8)	0.448
Weight Loss	86 (85.1)	67 (87)	19 (79.2)	0.345
Anorexia	61 (60.4)	47 (61)	14 (58.3)	0.813
Chest Pain	49 (48.5)	35 (45.5)	14 (58.3)	0.27
DIB	43 (42.6)	33 (42.9)	10 (41.7)	0.918
GBM	49 (48.5)	35 (45.5)	14 (58.3)	0.27

The first objective of this study was to describe and compare clinical characteristics of TB in the elderly and adults. The findings were as summarized in Table 3 above.

Of the ten (10) clinical characteristics elicited (Table 4), general body malaise was reported by 75.6% (78/103) of the elderly compared to 41.3% (62/150) in the adult group ($p<0.001$). There was no difference between the two study groups with regards to the other characteristics.

Among smear positive TB patients; hemoptysis was found in 23.4% (18/77) of the adults compared to 8.3% (2/24) among the elderly (p= 0.006). There was no significant difference in the frequency of the other characteristics (Table 5).

In patients with smear negative pulmonary tuberculosis, GBM was reported by 37% (27/73) of adults compared to 81% (64/79) of elderly patients (p<0.001). There was no significant difference between the two study groups with regards to other nine (9) characteristics assessed.

There was no statistically significant difference in the clinical presentation between adults and elderly with extra pulmonary tuberculosis. (EPTB)

3.1.2 Baseline Sputum Examination

Table 6: Baseline Sputum Microscopy Yield for *Mycobacterium tuberculosis* among Adults Compared to Elderly TB Patients.

Variable	Total (N, %)	Adults (n, %)	Elderly (n, %)	*p*-value
Sputum for AFB results				
Positive	101(39.9)	77 (51.3)	24 (23.3)	< 0.001
Negative	152 (60.1)	73 (48.7)	79 (76.7)	< 0.001

The second study objective was to determine and compare the sputum microscopy yield for *Mycobacterium tuberculosis* in elderly and adults with pulmonary tuberculosis. Microscopic examination of sputum for AFB yielded positive results in 51.3% (77/150) and 23.3% (24/103) of patients from the adult and elderly study arms respectively (p< 0.001).

3.1.3 Chest Radiological Findings

Table 7: Baseline Radiological Findings for Adults Compared to Elderly TB patients

Radiological Findings	Total (n, %)	Adults (n, %)	Elderly (n, %)	*p*-value
Site of Lesion				
Unilateral	101 (47.4)	55 (44)	46 (52.3)	
Bilateral	112 (52.6)	70 (56)	42 (47.7)	0.234
Zonal Involvement				
Upper	38 (17.8)	27 (21.6)	11 (12.5)	
Lower	56 (26.3)	23 (18.4)	33 (37.5)	0.005
Multiple	119 (55.9)	75 (60)	44 (50)	
Cavity Formation				
Yes	87 (40.8)	65 (52)	22 (25)	
No	126 (59.2)	60 (48)	66 (75)	<0.001
Pleural Effusion				
Yes	62 (29.1)	37 (29.6)	25 (28.4)	
No	151 (70.9)	88 (70.4)	63 (71.6)	0.851
Radiological Diagnosis				
Pulmonary TB	213 (87.3)	125 (88.7)	88 (85.4)	
Extra pulmonary TB	17 (7)	7 (4.9)	10 (9.7)	0.327
Normal chest X-ray	14 (5.7)	9 (6.4)	5 (4.9)	

Our third objective was to compare the chest radiological findings in elderly and adults with TB. These were as summarized in table 7. The baseline CXR findings for the two study groups showed that majority 87.3% (213/244) of all the study subjects had PTB; but a larger proportion of elderly 9.7% (10/103) had EPTB compared to 4.9% (7/141) adults (p=0.327). On the other hand a greater proportion of adults 6.4% (9/141) had normal CXR findings compared to elderly 4.9% (5/103).Nine adult subjects did not do CXR.

In more than a half of all the study subjects with PTB 52% (112/213) the lesion was bilateral. However a larger proportion 52.3% (46/88) of elderly patients had a unilateral involvement compared to 44% (55/125) among the adult group (p=0.234).

Nearly sixty percent 55.9% (119/213) of all the study subjects with PTB had a multiple zonal involvement. However, elderly 37.5% (33/88) as compared to adults 18.4% (23/125) displayed a lower zone involvement. (p=0.005).On the other hand, adults 52% (65/125) as compared to elderly 25% (22/88) had a more likelihood to form cavities. ($p<0.001$).

The difference was not very significant between adults (29.6%) as compared to elderly (28.4%) with respect to pleural effusion.(p=0.851).

Table 8: Predictors of Lower Zone Involvement and Cavity Formation by Univariate and Multivariate Analysis.

Characteristic	Univariate OR(95% CI)	*p*-value	Multivariate AOR(95% CI)	*p*-value
Lower Zone Involvement				
Age (Years)				
≥60	Reference			
<60	0.23(0.10 – 0.54)	0.001	0.21(0.08 – 0.54)	0.001
Sex				
Female	Reference			
Male	0.36(0.15 – 0.91)	0.03	0.53(0.19 – 1.47)	0.23
RBG(mmol/L)				
7 – 11.1	Reference			
>11.1	1.35(0.23 – 8.03)	0.74		
HIV				
Positive	Reference			
Negative	0.16(0.05 – 0.59)	0.006	0.14(0.04 – 0.54)	0.004
Cavity Formation				
Age (Years)				
<60	Reference			
≥60	0.31(0.17 – 0.55)	<0.001		
Sex				
Female	Reference			
Male	1.57(0.88 – 2.81)	0.13		
RBG(mmol/L)				
7 – 11.1	Reference			
>11.1	0.71(0.17 – 2.90)	0.63		
HIV				
Positive	Reference			
Negative	1.19(0.66 – 2.13)	0.57		

Lower zone involvement was found in 37.5% and 18.4% among the elderly and adult groups respectively (p=0.005). On the other hand Cavity formation was found in 52%

and 25% among adults and elderly groups respectively. ($p<0.001$).Multivariate analysis in relation to age, sex, hyperglycemia and HIV found older age ($p=0.001$) and HIV ($p=0.004$) to be the only predictors of Lower zone involvement. On the other hand a similar analysis on cavity formation found young age to be the only predictor. ($p<0.001$) [Table 8]

3.1.4 Treatment Outcomes at Two Months.

3.1.4.1. Physical and Laboratory Findings after Two Months of TB Treatment.

Table 9: Physical Examination and Laboratory Investigation Findings at Two Months of Treatment among Adults Compared to Elderly TB Patients.

Variable	Total (n, %)	Adults (n, %)	Elderly (n, %)	*p*-value
BMI category				
Severely underweight	71 (28.1)	44 (29.3)	27 (28.1)	
Underweight	30 (11.9)	23 (15.3)	7 (6.8)	
Normal weight	119 (47)	70 (46.7)	49 (47.6)	
Overweight	19 (7.5)	8 (5.3)	11 (10.7)	
Obese	12 (4.7)	3 (2)	9 (8.7)	
Severely obese	2 (0.8)	2 (1.3)	0 (0)	0.019
Hemoglobin				
<12g/dL	113 (60.8)	66 (59.5)	47 (62.7)	
>12g/dL	73 (39.2)	45 (40.5)	28 (37.3)	0.66
MCV				
< 80 fL	33 (30.6)	20 (31.7)	13 (28.9)	
80 – 100 fL	66 (61.1)	38 (60.3)	28 (62.2)	
>100 fL	9 (8.3)	5 (7.9)	4 (8.9)	0.944
MCH				
< 25 pg/cell	15 (14.6)	7 (11.5)	8 (19)	
25-35pg/cell	77 (74.8)	46 (75.4)	31 (73.8)	
>35pg/cell	11 (10.7)	8 (13.1)	3 (7.1)	0.403
GFR				
< 60	113 (44.7)	59 (39.3)	54 (52.4)	
≥ 60	140 (55.3)	91 (60.7)	49 (47.6)	0.04

The physical and laboratory findings after two months of treatment for the two study groups, adults and elderly TB patients, were as shown in Table 9. Less than a half of all the study subjects had a normal BMI; A much larger proportion of adults (44.6%) were still underweight or severely underweight compared to (34.9%) among the elderly (p=0.019). On the other hand a greater proportion of elderly (19.4%) had BMI greater than normal compared to 8.6% among the adults (p=0.019).

With respect to the level of hemoglobin the proportion of all study subjects who had anemia before treatment (80%) had decreased to 60.8% after treatment.

The GFR of less than 60 was found in 52.4% and 39.3% among the elderly and adult groups respectively (p=0.04).

3.1.4.2. Clinical findings After Two Months of TB Treatment.

Table 10: Clinical Findings after Two Months of TB Treatment among Adults Compared to Elderly Patients.

Symptom	Total N=253	Adults N=150	Elderly N=103	*p*-value
Cough	72 (28.5)	31 (20.7)	41 (39.8)	0.001
Sputum Production	19 (7.5)	9 (6)	10 (9.7)	0.271
Hemoptysis	2 (0.8)	0 (0)	2 (1.9)	0.087
Evening Fevers	3 (1.2)	0 (0)	3 (2.9)	0.035
Profuse Night Sweats	5 (2)	0 (0)	5 (4.9)	0.006
Weight Loss	10 (4)	4 (2.7)	6 (5.8)	0.205
Anorexia	14 (5.5)	7 (4.7)	7 (6.8)	0.467
Chest Pain	30 (11.9)	12(8)	18 (17.5)	0.022
DIB	21 (8.3)	4 (2.7)	17 (16.5)	<0.001
GBM	28 (11.1)	5 (3.3)	23 (22.3)	<0.001

Table 11: Clinical Findings after Two Months of Treatment among Smear Positive Adults Compared to Elderly TB Patients.

Symptom	Total N=16	Adults (n, %) (N= 13)	Elderly (n, %) (N= 3)	*p*-value
Cough	8 (50)	6 (46.2)	2 (66.7)	0.522
Sputum production	3 (18.8)	2 (15.4)	1 (33.3)	0.473
Profuse night sweat	1 (6.2)	0 (0)	1 (33.3)	0.032
Weight loss	1 (6.2)	1 (7.7)	0 (0)	0.62
Anorexia	2 (12.5)	1 (7.7)	1 (33.3)	0.226
Chest pain	5 (31.2)	2 (15.4)	3 (100)	0.004
DIB	2 (12.5)	1 (7.7)	1 (33.3)	0.226
GBM	1 (6.2)	0 (0)	1 (33.3)	0.032

None of the sputum positive subjects presented with hemoptysis and evening fevers at two months.

Ten (10) clinical findings were assessed after 2 months of treatment; these are as elicited in table 10.Cough was reported by 38.9% (41/103) of the elderly compared to 20.7% (31/150) in the adult group (p=0.001).Evening fevers was reported by 2.9% (3/103) of the elderly compared to none in the adult group (p=0.04).Profuse night sweats was reported by 4.9% (5/103) of the elderly compared to none in the adult group (p=0.006).Chest pain was reported by 17.5% (18/103) of the elderly compared to 8%(12/150) in the adult group (p=0.02).Difficulty in breathing was reported by 16.5% (17/103) of the elderly compared to 2.7% (4/150) in the adult group (p<0.001).General body malaise was reported by 22.3% (23/103) of the elderly compared to 3.3% (5/150) in the adult group (p<0.001). There was no difference between the two study groups with regards to the other characteristics.

Among TB patients who were still smear positive after two months of treatment profuse night sweats was reported by 33.3% (1/3) of the elderly as compared to none in adult group (p=0.03).Chest pain was reported by 100% (3/3) of the elderly as compared to 15.4% (2/13) in the adult group (p=0.004).General body malaise was reported by 33.3% (1/3) of the elderly as compared to none in adult group (p=0.03). There was no significant difference in the frequency of the other characteristics (Table 10).

In patients with smear negative pulmonary tuberculosis after two months, Cough was reported by 50% (10/20) of the elderly compared to 18.8% (9/48) in the adult group (p=0.009).Sputum production was reported by 20% (4/20) of the elderly compared to 4.2% (2/48) in the adult group (p=0.04). Hemoptysis was reported by 10% (2/20) of the elderly compared to none in the adult group (p=0.03)Weight loss was reported by 15% (3/20) of the elderly compared to none in the adult group (p=0.006)Difficulty in breathing was reported by 10% (2/20) of the elderly compared to none in the adult group (p=0.03)General body malaise was reported by 15% (3/20) of the elderly compared to none in the adult group (p=0.006)There was no difference between the two study groups with regards to the other four characteristics assessed.

There was no statistically significant difference in the clinical presentation between adults and elderly with extra pulmonary tuberculosis. (EPTB)

3.1.4.3 Sputum Conversion Rate after Two Months of TB Treatment.

After two months of intensive TB treatment microscopic examination of sputum for AFB yielded positive results in 16.9% (13/77) and 12.5% (3/24) of patients from the adult and elderly study arms respectively (p=0.88). The conversion rates were 83.1% and 87.5% among adults and elderly groups respectively.

3.1.4.4 Chest Radiological Findings after Two Months of TB Treatment.

Nearly sixty percent (58.6%) 143/244 of all the study subjects showed the improvement in chest radiological findings after two months of intensive phase of TB treatment. However, elderly 22.5% (23/103) as compared to adults 14.1% (20/141) displayed no

improvement radiologically (p=0.114). Nevertheless elderly 2.9% (3/103) as compared to adults 0.7% (1/141) had worsened radiologically (p=0.114).

3.1.4.5 Encountered Drug Side Effects After Two Months of TB Treatment.

Of the six (6) side effects that were assessed, peripheral neuropathy was reported by 52.4% (54/103) of the elderly compared to 38.7% (58/150) in the adult group (p=0.03). There was no difference between the two study groups with regards to the other side effects.

3.1.4.6 Mortality Rates and Loss of Follow up After Two Months of TB Treatment.

The mortality rate was significantly higher among [17.5% (18/103)] of elderly as compared to [6.7 % (10/150)] in adults (p<0.01). Loss of follow up was higher among adults (16%) compared to (5.8%) in the elderly group. [Table 11]

3.1.5 Co morbidities Associated with Tuberculosis among Adults and Elderly TB Patients

Our last objective was to describe and compare the co morbidities associated with TB among adults and elderly patients. These were as shown in table 12 below.

Past history of TB treatment was reported by 32% (33/103) of the elderly compared to 16.7% (25/150) in the adult group (p=0.04).Diabetes mellitus was reported by 9.8% (11/103) of the elderly compared to 2% (3/150) in the adult group (p<0.01).Hypertension was reported by 14.7% (15/103) of the elderly compared to 2% (3/150) in the adult group (p<0.001) Reduced glomerular filtration rate (GFR was reported by 52.4% (54/103) of the elderly compared to 39.3% (59/150) in the adult group (p=0.04). On the other hand HIV was reported by 34% (51/150) of the adults compared to 27.2% (28/103) in the elderly group (p=0.25).The overall prevalence of HIV was 31.2% (79/253).

Table 12: Co morbidities Associated with Tuberculosis among Adults Compared to Elderly TB Patients

Co morbidity	Total (N, %)	Adults (n, %)	Elderly (n, %)	*p*-value
Past History of TB Treatment				
Yes	58 (22.9)	25 (16.7)	33 (32)	
No	195 (77.1)	125 (83.3)	70 (68)	0.004
HIV Status				
Reactive	79 (31.2)	51 (34)	28 (27.2)	
Non reactive	174 (68.8)	99 (66)	75 (72.8)	0.25
Chronic Illness				
Diabetes	14 (5.2)	3 (2)	11 (9.8)	< 0.01
Hypertension	18 (7.1)	3 (2)	15 (14.7)	<0.001
Asthma	8 (3.2)	5 (3.3)	3 (2.9)	0.86
Chronic kidney disease	1 (0.4)	1 (0.7)	0 (0)	0.39
No Chronic Illness	212 (84.1)	138 (92)	74(72.5)	<0.001
GFR at Baseline				
< 60	120 (47.4)	43 (28.7)	77 (74.8)	
≥60	133 (52.6)	107 (71.3)	26 (25.2)	<0.001
GFR After Two Months				
< 60	113 (44.7)	59 (39.3)	54 (52.4)	
≥ 60	140 (55.3)	91 (60.7)	49 (47.6)	0.04
Overall Outcome				
Dead	28 (11.1)	10 (6.7)	18 (17.5)	<0.01
Alive	195 (77)	116 (77.3)	79 (76.7)	0.91
Treatment default	7 (2.8)	7 (4.7)	0 (0)	0.03
Transferred out	13 (5.1)	9 (6)	4 (3.9)	0.46
Not reachable	10 (4)	8 (5.3)	2 (1.9)	0.17

CHAPTER FOUR

4.0 DISCUSSION

This was a comparative study in which we aimed at assessing the clinical, radiological, and laboratory features of tuberculosis and its associated factors in elderly patients and adults newly diagnosed with TB. But we also assessed their differences with respect to co morbidities, different treatment outcomes and mortality.

4.1 Sociodemographic Characteristics.

Socio demographically, we found that there was male predominance in both adults and elderly patients. This was not a surprising finding as male predominance in active tuberculosis is widely known globally. Gender inequalities in socio-cultural factor, effect of sex hormones on immunological factors and access to health care have been reported to be contributing factors to the reported disparities in sex in active TB **[104,105,115 – 118]**

But not all studies in the world have reported male predominance in active TB. Female predominance have been reported in a study done in Pakistan **[123]** and the argument is that in many societies with low SES women are often very socially and economically marginalized and they are prone to malnutrition including Vitamin D deficiency which has been reported in association with TB **[124 – 126]** But another reason for women predominance could be due to the fact that they are often the care takers for the family including the sick, children and elderly and they are therefore more exposed to the transmission of TB than men.

In our study however, it is difficult to conclude if male predominance was due to socio cultural or hormonal factors.

4.2. Physical and Laboratory Findings

A larger proportion of young adults were underweight and severely underweight compared to elderly while the latter were more likely to be overweight, obese and severely obese. TB is associated with weight loss but elderly are more prone to a lot of co morbidities and overweight is one of them. So these findings are very consistent with that fact.

Anemia is a common feature in almost all chronic infections and TB is one of them [133] Several mechanisms of TB associated anemia have been suggested but most studies have shown that suppression of erythropoiesis by inflammatory mediators [127,128,134,135] nutritional deficiency [136] and malabsorption syndrome [137] could be the reason behind. But iron deficiency has also been implicated in the cause of anemia in TB because the absence of iron in the bone marrow have been observed in some studies [129,132] This explains why we also had patients with microcytic hypochromic anemia in this study.

But our patients showed an improvement in hemoglobin after two months intensive treatment. The proportion of subjects with anemia dropped from 80% to 60.8% across the board and the difference between adults and elderly was not statistically significant. ($p=0.66$).This is in line with other studies which have seen the same trend. And the reason is that iron retention, erythropoietin response, nutritional status and malabsorption can improve as the burden of the mycobacteria and the inflammatory process are resolved by medication [147]

We also observed that a significantly greater proportion of elderly had an GFR less than 60mL/min/1.73m^2 at baseline compared to young adults and this difference was statistically significant ($p<0.001$). This observation was not unexpected since as it is known physiologically that renal capacity declines with age because the latter is associated with a loss of renal mass by about 20–25% from 30 to 80 years of age [149] Microscopically, the aging human kidney is characterized by increased fibrosis, tubular atrophy, and arteriosclerosis [151,152] All these factors are possible attributes of significant low GFR that we observed among elderly.

4.3.2 Clinical Characteristics of TB among Adults and Elderly TB Patients

In this study cough was a predominant clinical characteristic and was present in more than 90% of all study subjects. Hemoptysis was found to occur less frequently among the elderly compared to adults ($p<0.001$). The findings of this study also showed that cavitary lung lesions were reported more frequently among adults than the elderly ($p<0.001$). Published studies that have compared the spectrum of clinical presentation of TB among the elderly and adult by en large have found that adults were more likely to

present with cough, hemoptysis, cavities and fever compared to the elderly patients [51, 60, 153 – 166] Hemoptysis and/or cavity formation in the lung seen significantly more frequent among adults than elderly patients is thought in part to be a product of a relatively more intense immunological response to M. tuberculosis. Formation of small "Rassmusen's aneurysms" along the walls of these cavities has been described [71 – 73] and it is thought that the rupture of these aneurysms may be manifested by hemoptysis- at times severe.
On the other hand the findings of this study show that general body malaise (GBM) was reported more frequently among the elderly compared to adults ($p<0.001$). These findings are similar to those reported elsewhere [51,60,153 – 166] GBM is a non-specific complaint that may be thought to be due to old age or may indeed be due to co-morbidities such as hypertension, diabetes mellitus and other age related conditions. Indeed it has been reported to be an underlying factor to misdiagnosis of TB among the elderly. Our study was based in a TB outpatient clinic and therefore we are not able to determine the effect- if any-GBM caused delayed diagnosis of TB.

In most studies the presentation has been documented to be different and even atypical among elderly and this has further led to a suggestion that TB in elderly should even be classified as a separate entity [162]

In this study we observed during follow up that a relatively larger proportion of elderly as compared to adults were still presenting with the same clinical features even after two months of intensive treatment. This could be attributed to a number of factors and one of them being the pre existing co morbidities which we also encountered among the significant larger proportion of elderly patients .Poor treatment outcomes among elderly however, have been reported in several studies [154,158 – 160] But there is a study in which the treatment outcome was reported to be not different between young and elderly [166]

4.3.2 Sputum Microscopy Yield for *Mycobacterium Tuberculosis* in Elderly and Adults

It was not surprising also to have a significantly larger proportion of young adults who were smear positive compared to elderly($p<0.001$).This went in hand with a high bacillary density which was also the case among young adults as compared to elderly.($p<0.001$). This finding can be explained by the fact that elderly are more likely to fail to produce sputum samples by spontaneous expectoration. This might be attributed by their weakness in coughing and as a result the quality of sputum sample they provide is poor as it contains more saliva than pulmonary secretion. This observation has also been documented in various studies. [167 – 171]

4.3.3 Chest Radiological Findings in Elderly and Adults with TB

In this study elderly patients were more likely to present with Lower zone involvement compared to adults while young adults were more likely to present with Cavity formation and the differences in both cases were statistically highly significant. ($p<0.001$).These findings have also been documented in various studies [87, 97,156] [167 – 174] But since most cases of pulmonary TB in the elderly are a result of reactivation of primary infection, classically, reactivation of TB is expected to involve the upper lobes of the lungs [168] This atypical radiological finding is what poses a serious diagnostic challenge in this group of people. However there are some few studies that have argued differently that lower zone involvement can occur at any age. [175]

4.3.4 Treatment Outcomes after Two Months.

This study had a follow up component in which all the study subjects were re assessed at the end of the second month of treatment. This forms the basis of our fourth objective which was to document the treatment outcomes at the end of two month intensive phase in the two groups. In this case we again looked into the following aspects:

1. Physical and laboratory findings
2. Clinical findings
3. Sputum conversion rate
4. Chest radiological findings for PTB and Pleural effusion
5. Encountered drug side effects
6. Mortality rates and loss of follow up

Our aim was to assess the effectiveness of treatment and the extent of repercussions the latter could have possibly imparted on young adults and elderly patients.

4.3.4.1 Physical and Laboratory Findings after Two Months of TB Treatment.

We used BMI and hemoglobin levels as parameters of nutritional status in our study subjects and we found that weight loss was featured in both groups irrespective of age. But adults were more likely to have had BMI below average as compared to elderly. This can be explained by their high propensity to present with gastrointestinal drug side effects as it was observed. But it is very early to draw a conclusion with respect to BMI at this juncture as we do not expect drastic changes in terms of weight within only two months of treatment.

The changes that were observed in the level of hemoglobin and GFR have been discussed in detail above.

4.3.4.2 Clinical Findings after Two Months of TB Treatment.

The changes in clinical presentation after two months of intensive treatment have also been discussed above.

4.3.4.3 Sputum Conversion Rate after Two Months of TB Treatment.

After two months of intensive TB treatment a relatively larger proportion of adults were still smear positive compared to elderly [Adult: 13/77 =16.9%; Elderly: 3/24= 12.5%] but Fisher's exact test did not reveal any statistically significant difference between the two groups (p=0.88) possibly because the proportion of smear positive subjects after two months was very small. However the conversion rate was relatively higher among elderly compared to adults. (87.5% Vs 83.1%) This is because the bacillary density was low among elderly as compared to adults.(p<0.001).The sputum conversion rate is the percentage of smear-positive pulmonary TB (PTB+) cases enrolled in a specified period that converted to smear negative status after the standard two months of the intensive phase of treatment. WHO recommends its use as a useful indicator for TB control programs in monitoring the TB program performance, and as a trigger for rigorous assessment in patients with still positive smears [176] It has been suggested that even in well functioning national TB programs 25% of initially PTB + patients may still be smear-positive at the end of the intensive phase of treatment, despite good adherence to medication [177] In our study however, this proportion is very low in both groups and this is a reflection of the effectiveness of the drugs and good performance of the NTLP.

4.3.4.4 Chest Radiological Findings after Two Months of TB Treatment.

Nearly sixty percent (58.6%) of all the study subjects showed the improvement in chest radiological findings after two months of intensive phase of TB treatment. However elderly patients were more likely to deteriorate radiologically compared to adults but the difference was not statistically significant (p=0.114).

4.3.4.5 Encountered Drug Side Effects after Two Months of TB Treatment.

The side effects that we assessed in this study were peripheral neuropathy, skin rash, anorexia, nausea, vomiting, diarrhea and jaundice. Elderly patients were more likely to present with peripheral neuropathy compared to adults (52.4% Vs 38.7%) and this difference was statistically significant. (p=0.03) This can be explained by the fact that, dietary intake of vitamin B6 is lower in elderly than adults.[81] This makes the elderly patients more prone to isoniazid induced peripheral neuropathy. Except for peripheral neuropathy, in this study however, all other side effects were more or less similar in both groups, something that is contrary to other studies in which increased susceptibility to adverse drug reactions among elderly have been documented [46,65,83,84] [158,159,178,179] High susceptibility to adverse drug reactions among elderly could possibly due to decreased drugs absorption secondary to some age related physiological changes that occur in the stomach, including altered gastric pH, modified gastric emptying rates, slower intestinal transient time and drug intolerance associated with the likelihood of polypharmacy [85,86]

4.3.4.6 Mortality Rates and Loss of Follow up after Two Months of TB Treatment.

The mortality rate was significantly higher among elderly compared to adults. (17.5% Vs 6.7 %,) and this difference was statistically significant (p<0.01). But other studies have also shown that even after timely diagnosis and completion of treatment mortality is three times higher among elderly than adults with TB. [46, 71] This is again due to high rates of co morbidities and poor treatment outcomes with consequent suspension of treatment [65]

Other similar comparative studies also revealed a higher mortality rates among elderly as compared to adults. For example in a study done by Pratt et al in the US the mortality rate was (21% vs. 7%, P < 0.001) among elderly compared to adults.[180] A similar observation was reported in another study in Taiwan by Wang et al. (27% vs. 4%, P = 0.001). [167] All these differences were statistically highly significant and their observation does not differ much from ours. This high mortality rate among elderly can be due to pre existing co morbidities, organ dysfunctions and immunological changes that occur with aging .But there is one study that suggested that despite higher mortality

rate among elderly, if diagnosed early and adequately treated, elderly patients with TB do not have greater mortality than those without [181]

In our study however, loss to follow up was more frequent among adults compared to the elderly (5.8% Vs 16%).This was because almost each elderly had a family member who was taking care of them, mainly their children and grand children. This means those elderly without care takers are more likely to die at homes before reaching to the health facility.

4.3.5 Co morbidities Associated with Tuberculosis among Adults and Elderly TB Patients

Elderly were more likely to have a history of being treated for TB before compared to adults. (32% Vs 16.7%) and this difference was statistically significant. (p=0.004).Previous history of TB treatment has been documented as a potential risk factor for developing TB [182,183]

The overall HIV prevalence among the study population was 31.2% and adults were more likely to be HIV positive compared to elderly.(34% Vs 27.2%) but the difference was not statistically significant (p=0.25).The Tanzania national HIV prevalence is 5.3% and for Dar es salaam is 6.9% [184] The 3-5 fold higher HIV prevalence among TB patients (elderly and adults)is in keeping with the fact that HIV infection is one of the strongest risk factor for developing clinical disease due to M. tuberculosis [26,42,43] [185 - 189] Hence, a co-disease due to HIV and Tuberculosis as the findings of this study and others have demonstrated [190 - 194] Our findings lend support to the recommendation that ANY patient with TB should be screened for HIV and that ANY HIV infected person should be investigated for TB.

In this study a significantly larger proportion of elderly as compared to adults were found to have other clinical entities namely Obesity, Hypertension ($p<0.001$), Diabetes ($p<0.001$) and reduced glomerular filtration rate ($GFR<60mL/min/1.73m^{2)}$ Diabetes mellitus is a known risk factor to developing TB; however we were not able to determine the contribution of any of the co-morbid conditions to the development of TB among our patients for the study was not designed for that purpose. The presence of these co-morbidities however, is likely to impact on patient management and outcome.

CHAPTER FIVE

5.0 STRENGTHS AND LIMITATIONS

5.1 STRENGTH

1) The study was conducted based on a well organized clinical service for patients with tuberculosis through the NTLP which ensured controlled availability and uninterrupted drug supply and low dropout rates of 16% and 5.8% for adults and elderly respectively.

5.2 LIMITATIONS

1) The diagnosis of TB was based on "program definition"; sputum cultures (the gold standard) for AFB were not done. It is quite possible that some patients labeled as sputum negative would actually have grown AFB.
2) The study subjects were not followed up beyond two months, thus our comment on kidney function is wanting as the definition requires measurements done 3 months apart.
3) Some of the study subjects never made it to follow up [6.7% of young adults and 17.5% of elderly], so survivor bias was inevitable in this case.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSIONS

In this study the following conclusions can be drawn:

1. TB in the elderly often presents with atypical clinical features which may be confused with age related illnesses and this may lead to delay in TB diagnosis and treatment.
2. Elderly patients are more likely to fail to produce adequate sputum samples by spontaneous expectoration.
3. Elderly patients with TB often present with atypical chest radiological findings and this can pose a great challenge in diagnosis.
4. Elderly patients with TB are more susceptible to isoniazid induced peripheral neuropathy.
5. Elderly patients with tuberculosis are more likely to die even after initiation of TB treatment.
6. Old age is associated with increased risk of co-morbidities such as diabetes mellitus, impaired renal function and poor nutritional status.
7. HIV is an important risk factor for TB for both adults and elderly.

6.2 RECOMMENDATIONS

From what we have observed in this study, we recommend the following things to be done:

1. All elderly patients presenting with cough and other non specific symptoms like GBM should be screened for TB.
2. All elderly patients attending TB clinics across the country should be screened for HIV.
3. All elderly patients attending TB clinics across the country should also be screened for co morbidities such as hypertension, diabetes and renal insufficiency and be treated accordingly.
4. There is need to determine the causes of the high associated mortality among elderly patients with TB and how to reduce it.

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APPENDICES

Appendix I: Consent Form (English Version)

Consent to participate in a study of The Clinical Characteristics of Tuberculosis and Associated Co-Morbidities in the Elderly Compared to Adults in Dar Es Salaam, Tanzania.

Introduction

Greetings madam/ Sir,

My name is Dr Riemann Ray, a resident in the department of Internal Medicine at MUHAS and I am conducting a study on The Clinical Characteristics of Tuberculosis and Associated Co-Morbidities in the Elderly in Dar Es Salaam, Tanzania. In a few minutes, I will tell you about this research and will ask for your consent to participate. I will be delighted to respond in case you have any questions.

Purpose of the study

The aim of this study is to describe and compare the clinical characteristics of tuberculosis and associated factors among patients aged 18-59 and those aged 60 years or more (elderly) attending TB clinics in the city of Dar es salaam. The results of this study are expected to improve the quality of healthcare particularly in elderly whom we strongly believe they are being misdiagnosed and therefore mistreated with respect to Pulmonary Tuberculosis.

What participation involves

If you agree to participate you will be asked some questions related to the research then you will undergo physical examination in which your height and weight will also be measured. Furthermore venopuncture will be performed where 5 mls of blood will be drawn for Full blood picture, Random blood glucose, Serum creatinine and HIV . You will also be required to provide sputum for analysis and a chest x ray will be performed on you. You will be treated accordingly in case we encounter any other condition. We will also need to see you in two months from now to see how you are progressing; the same tests will be repeated except for HIV. Before we begin this process you will be required to sign a form to indicate your willingness to participate.

Confidentiality

Your name will only appear on one form to create an Identification number. Only the created number will be used in the laboratory forms and in the computer where all the information will be stored. The information we obtain from you will be confidential and will only be used for the purpose of this research and better care and treatment. No one else other than the people involved in the research and health personnel involved in your care will have access to this information.

Benefits and Risks

You will benefit from the study by knowing your HIV status and other diseases which you at the moment are not aware of. This will enable you to get medical intervention early before you develop any further complications. The information you provide will also be very useful in improving the quality of health care for many other Tanzanians with similar problems. The only risk you will have to take is a mild pain which you will feel when the blood is drawn.

Voluntary participation & rights to withdraw

Your participation is voluntary and you have all the rights to discontinue from participating in our study at any time. However your decision may be it will not in any way affect your rights to care and treatment in this hospital or anywhere in the country.

In case of injury

We do not anticipate any harm as a result of taking part in this research. However, should

physical injury occur, we shall provide you with treatment according to the current standard of care in Tanzania.

Contact persons

If you have questions about this study or please do not hesitate to contact:

Professor M. Moshi, The Chairman of the Research and Publications Committee, MUHAS, P.O. Box 65001, Dar-es-Salaam. Office Tel: 022 2152489. E-mail: drp@muhas.ac.tz.

In case of any information about your rights as a participant in this study please contact:

1. The Principal Investigator: Dr. Riemann Ray, Department of Internal Medicine
Tel: +255 784 466 663. E-mail: riemannray@gmail.com.

2. Supervisor: Professor K. Pallangyo, Department of Internal Medicine.
Tel: +255 783 176 464. E- mail: kpallangyo@gmail.com

I _____

Have understood the above information and my questions have been answered to my satisfaction. I agree to take part in this research.

Signature of the participant: _____

Name of the Witness (if participant can't read) _____

Signature of the Witness: _____

Date of signed consent: _____

Appendix II: Consent form (Swahili Version)

Utangulizi:

Fomu ya ridhaa katika utafiti wa ugonjwa wa kifua kikuu kwa wazee na vijana jijini Dar es Salaam.

Utambulisho:

Habari za saa hizi,

Majina yangu ni Riemann Ray, daktari mwanafunzi wa stashahada ya magonjwa ya ndani katika Chuo Kikuu cha Sayansi ya Tiba Muhimbili.Ninafanya utafiti kuhusu ugonjwa wa kifua kikuu na athari zake kwa wazee na vijana jijini Dar es Salaam.Sasa nitakupa maelezo ya kina kuhusu utafiti huu na kisha nitakuomba ridhaa yako ya kushiriki. Endapo utakuwa na maswali yoyote nitafurahi kukujibu.

Malengo ya utafiti:

Malengo ya utafiti huu ni kufafanua na kulinganisha dalili za ugonjwa huu kwa vijana kati ya umri wa miaka 18 mpaka 59 na wazee wa miaka 60 na kuendelea wanaoudhuria katika kliniki za kifua kikuu jijini hapa.Matokeo ya utafiti huu yanategemewa kutumika katika uboreshaji wa huduma ya afya hasa kwa wazee ambao inasadikika kwamba dalili za kifua kikuu kwao zimefichika kutokana na magonjwa nyemelezi ya uzeeni na hivyo kusababisha vifo kutokana ucheleweshwaji wa tiba.

Ushiriki unahusisha nini?

Ukiridhia kushiriki katika utafiti huu,kwanza utaulizwa maswali kadhaa yanayohusiana na ugonjwa wa kifua kikuu halafu nitakupima kifua, uzito na urefu na nitachukua damu kidogo(mililita 5) kwa ajili ya kukupima vipimo vifuatavyo: Wingi wa damu,Kisukari,hali ya figo na virusi vya ukimwi(VVU).Nitaagiza pia upige picha ya kifua leo ili tuangalie mapafu yako na utahitajika kutoa makohozi kama utakavyoelekezwa kwa uchunguzi zaidi. Yamkini ukipatikana na magonjwa mengineyo yote utatibiwa kikamilifu. Utahitajika kurudi tena baada ya miezi miwili tangu kuanza dawa za kifua kikuu ili tuangalie maendeleo yako.Vipimo vitarudiwa tena isipokuwa VVU.Kabla ya kuanza zoezi hili nitakuomba usaini fomu hii.

Usiri:

Taarifa zote utakazotupa ni siri na zitatumika tu kwa ajili ya utafiti huu na kuboresha huduma ya afya kwa mtoto. Hakuna mtu mwingine zaidi ya wanaohusika wa utafiti huu atakayesoma/kupata maelezo yako.

Faida:

Utafaidika na utafiti huu kwanza kwa kujua hali yako ya kiafya pamoja na mgonjwa mengine yaliyojificha.Hii itakusaidia kupata tiba muafaka kwa haraka kabla hujaathirika zaidi.Pia maelezo yako yatatumika kuunda mfumo bora wa huduma ya afya ambao utawasaidia watanzania wengine wenye tatizo linalofanana na lako.Lakini utahisi maumivu kidogo tu wakati unachomwa ili kutolewa damu kwa ajili ya vipimo.

Uhuru wa kushiriki na haki ya kujitoa:

Ushiriki wako katika utafiti huu ni kwa hiari kabisa na pia unayo haki ya kukubali kushiriki au kukataa. Uamuzi wako wa kushiriki katika utafiti huu au la, hautaathiri hata kidogo haki yako ya kupata huduma unayostahili hospitalini hapa au popote nchini.

Kukitokea madhara:

Hatutarajii madhara yoyote katika kushiriki kwako kwenye utafiti huu, lakini endapo utapata madhara yeyote kutokana na ushiriki wako tutakupa huduma zote za matibabu ya afya kama inavyotakiwa kwa kiwango cha Tanzania.

Kwa maswali zaidi:

Iwapo utakuwa na swali lolote kuhusu utafiti huu , unaweza kuwasiliana na

Profesa M. Moshi, Mwenyekiti wa Kamati ya Utafiti na Uchapishaji, chuo kikuu cha Tiba na Sayansi za Afya Muhimbili, S.L.P 65001, Dar-es-Salaam. Simu: 022 2152489.

Barua pepe: drp@muhas.ac.tz.

Kukiwa na tatizo lolote wasiliana na wafuatao:

1. Mtafiti mkuu: Dk. Riemann Ray, Idara ya magonjwa ya ndani.
   Simu: +255 784 466 663. Barua pepe: riemannray@gmail.com.

2. Msimamizi mkuu : Profesa K. Pallangyo, Idara ya magonjwa ya ndani.
   Simu: +255 783 176 464. Barua pepe: kpallangyo@gmail.com

Mimi _____

Nimeelewa maelezo yaliyoandikwa hapo juu na kuridhika na majibu niliyopewa kwa maswali

yangu yote. Ninakubali kushiriki katika utafiti huu.

Sahihi ya mshiriki: _____

Jina la mshahidi(kama mshiriki hawezi kusoma)_____

Sahihi ya mshahidi_____

Tarehe ya kusaini ridhaa: _____

Appendix III: Study Questionnaire

TO BE FILLED IN BY THE PI OR ASSISTANT [MEDICAL PERSONEL] ONLY

i. Study Number……
ii. Patient's File Number……
iii. Patient's name……
iv. Patients Cell phone number……..
v. Next of kin/confidant cell phone number……

Section I: Socio-demographic Information.

1) Date of Birth…….. (Age……Years

2).Ward:…….

3).Gender:

a) Male
b) Female

4). Marital status:

a) Single
b) Married
c) Cohabiting
d) Divorced
e) Widowed

5). How many years did you study/spend in school?.....

a) Std VII = 7
b) Form IV = 11
c) Form six = 14
d) College = >14….Quantify……years.

6). Working status:

a) Employed
b) Unemployed
c) Retired

7). Cigarette smoking status:

a) Never

b) Quit

c) Currently smoking

8). If you do not smoke, does anyone in your family smoke?

a) Yes

b) No

9). Alcohol consumption habits:

a) Never drink

b) Past drinker- when did you stop?.....(No of months)

c) Current drinker: ……..bottles per day

10). Illicit drug use:

a) Yes

b) Never

c) Quit

d) Current

e) If the answer above is Yes, specify……

Section II: Present chief complaints.

11). Do you have any of these symptoms for the past two weeks or more?

	Symptom	Duration (wks)
1	Cough	
2	Sputum production.	
3	Hemoptysis	
4	Evening fever	
5	Profuse night sweats	
6	Weight loss	
7	Anorexia	
8	Chest pain	
9	Difficulty in breathing while at rest	
10	Generalized body malaise and fatigue.	
	Other Symptoms	Duration (wks)
11		
12		
13		
14		
15		

Section III: Past Medical History.

12). Have you been treated for TB before?

a) Yes

b) No

13). What is your HIV status?

a) Positive

b) Negative

c) Not tested

14). If HIV positive, when did you start ARV treatment?

a) ……..months ago.

b) Not started

15). If No, why? Specify……

16). Have you been diagnosed to have any of the following diseases?

a) Diabetes mellitus

b) Hypertension

c) Asthma

d) Malignancy

e) Chronic kidney disease

17). Have you been diagnosed to have any other chronic disease apart from the ones mentioned above?

a) ……

b) ……

c) ……

d) ……

18). Are you currently on any medication?

a) Yes

b) No

19). If Yes, Specify……

Section III: Specific physical examination and investigation findings.

20). Weight(Kg)……Height(M)……BMI……Kg/M^2

LABORATORY INVESTIGATION RESULTS:

21). Sputum microscopy for AFB:

a) +1

b) +2

c) +3

d) Negative

22). Hemoglobin level (baseline)……g/dL.

23). Random blood glucose……mmol/L

24). Serum creatinine……...mg/dL

25). HIV status (from the TB card)……

Chest x ray findings.

26). Site of the lesion:

a) Unilateral

b) Bilateral

27). Zonal involvement:

a) Upper

b) Lower

c) Multiple

28). Cavity formation:

a) Yes

b) No.

29). Pleural effusion:

a) Yes

b) No

30). Other encountered radiological findings:

a) ……

b) ……

c) ……

d) ……

31). Final diagnosis.

a) Pulmonary TB

b) Extra pulmonary TB.

32). Tb drugs given:

a) ……

b) ……

c) ……

d) ……

Section IV: Follow-up at two Months.

33). Symptoms:

	Symptom	Present	Absent
1	Cough		
2	Sputum production.		
3	Hemoptysis		
4	Evening fever		
5	Profuse night sweats		
6	Weight loss		
7	Anorexia		
8	Chest pain		
9	Difficulty in breathing while at rest		
10	Generalized body malaise and fatigue.		
	Other Symptoms	Present	Absent
11			

12			
13			
14			
15			

34). Side effects:

	Side Effect	Yes	No
1	Burning sensation of the feet		
2	Skin rash		
3	Nausea		
4	Vomiting		
5	Diarrhea		
6	Jaundice		
	Others	Yes	No
7			
8			
9			
10			

35). Other parameters.

Weight at 2 months……Kg

Hemoglobin……g/dL.

Serum Creatinine……mg/dL

36). Sputum microscopy at two months for those who were sputum smear positive

a) Positive
b) Negative
c) Not performed

37). CHEST X RAY (For PTB and Pleural Effusion only)

a) Improvement

b) No improvement.

c) Worsening

38). Outcome at two months of TB treatment.

a) Dead

b) Alive

c) Treatment default

d) Transferred out

39). If yes: Date of death……

40). Any other additional information:

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