ASSESSMENT OF DELAY IN DIAGNOSIS AND TREATMENT OF MULTI-DRUG RESISTANT TUBERCULOSIS: MAGNITUDE AND ASSOCIATED INSTITUTIONAL BARRIERS

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By

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A Dissertation Submitted in (Partial) Fulfillment of the Requirements for the Degree of Master of Arts (Health Policy and Management) of

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CERTIFICATION

The undersigned certifies that he has read and hereby recommends for acceptance by the Muhimbili University of Health and Allied Sciences the dissertation entitled **"*Assessment of delay in diagnosis and treatment of multi-drug resistant tuberculosis: magnitude and associated institutional barriers,"*** in (partial) fulfillment for the Degree of Masters of Art in Health Policy and Management of the Muhimbili University of Health and Allied Sciences.

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Date _____

DECLARATION AND COPYRIGHT

I**, John F. Sijaona,** declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any university for similar or any other degree award.

Signature: _____Date: _____

DEDICATION

This work is dedicated to my lovely wife Esther, my daughter Blandina, and my mother Blandina.

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ABSTRACT

Background: Multi-drug-resistant tuberculosis (MDR-TB) is a serious public health concern in Tanzania. Currently, however, there is a still large gap in management of MDR-TB with respect to detection, laboratory diagnosis and starting treatment. Nonetheless, there has been a substantial increase in the contribution of molecular testing which has reduced the delay in diagnosis dropping to the current 34 days from 269 days in 2013. Yet, TB related mortality attributable to the delay in diagnosis and treatment remains high at an estimated 6.4% (WHO, 2014). Several studies have explored socio-economic and patient related factors that contribute to delays in diagnosis and treatment of MDR-TB. However, little is known on the role of institutional barriers in explaining delays observed in diagnosis and treatment of MDR-TB, particularly in the Tanzanian context.

Objectives: The main objective of this study was to assess the magnitude of MDR-TB diagnosis and treatment delays and associated institutional barriers to diagnosis and treatment.

Methodology: This was a cross sectional study that used both retrospective and explorative designs. Data was obtained by using quantitative and qualitative approaches. On the quantitative part, the MDR-TB patient data was collected from the registers and files kept at KIDH and at CTRL. The qualitative component of the study involved interviewing pre determined health facility superintendents, heads of TB units, laboratory managers and regional TB and Leprosy Coordinators in three regional referral hospitals in Dar es Salaam. Analysis was manually conducted and ethical issues were observed.

Results: The study revealed a serious problem of delay in establishing diagnosis of MDR-TB as well as in initiating treatment to the already confirmed MDR-TB patients. From this study, it was found that 50% (n=192) had their MDR-TB diagnosis delayed. It took an average duration of 94 days (SD = 74.2 days) for the patient to be sent for DST diagnosis and receiving results.

When a sample is sent for Gene Xpert diagnosis, the result is obtained after 11 days (SD = 32 days). Moreover, there was late initiation of treatment for 59 % of confirmed MDR-TB patients. The average duration between MDR-TB laboratory diagnosis by using DST method and starting treatment was about 83 days (SD=122 days). But when diagnosis is done by using Gene Xpert method, treatment was found to start after 40 days (SD=34 days). Institutional barriers such as financial difficulties, shortage of staff, poor clinical and laboratory capacity, poor adherence to guidelines and inadequate managerial and coordination efforts have been found to be associated with these delays.

Conclusion: The magnitude of MDR-TB diagnosis and treatment delay in Tanzania is still high in spite of the increasing number of patients who are tested by using different diagnostic methods. The duration from testing and receiving result and starting treatment has not decreased despite adopting modern techniques like Gene Xpert, Hain or LPA.

Recommendation: There is a need of paying attention to the factors contributing to the delays, including those in the healthcare system. That is, interventions targeting late diagnosis and treatment of MDR-TB should take the identified institutional barriers into account.

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ABBREVIATIONS

AFB	Acid Fast Bacilli
CHMT	Council Health Management Team
CDC	Centre for Disease Control
CTRL	Central Tuberculosis Reference Laboratory
DNA	Deoxyribonucleic Acid
DST	Drug Sensitivity Test
DTLC	District Tuberculosis and Leprosy Coordinator
DOT	Directly Observed Therapy
IC	Infection Control
KIDH	Kibong'oto Infectious Diseases hospital
KNCV	Tuberculosis Foundation of Netherlands
MDR TB	Multi Drug Resistant Tuberculosis
MoHCDGEC	Ministry of Health Community Development, Gender, Elderly and Children
MTB/RIF	Multidrug Tuberculosis/Rifampicin
MUHAS	Muhimbili University of Health and Allied Sciences
NTLP	National Tuberculosis and Leprosy Program
NTP	National Tuberculosis Program
PPM	Planned Preventive Maintenance
PCR	Polymerase Chain Reaction
PI	Principal Investigator
PMO-RALG	Prime Minister's Office-Regional Administration and Local Government
RTLC	Regional Tuberculosis and Leprosy Coordinator
RA	Research Assistant
SOP	Standard Operational Procedure
TB	Tuberculosis
USD	United States Dollar

WHO	World Health Organization
XDR TB	Extensively Drug resistant Tuberculosis

OPERATIONAL DEFINITION OF TERMS

Tuberculosis

According to WHO 2016, Tuberculosis (TB) is caused by bacteria (Mycobacterium tuberculosis) that most often affect the lungs. Tuberculosis is curable and preventable. TB is spread from person to person through the air. When people with lung TB cough, sneeze or spit, they exhume the TB germs into the air.

Multi Drug Resistant Tuberculosis

The bacteria that cause tuberculosis (TB) can develop resistance to the antimicrobial drugs used to cure the disease. Multidrug-resistant TB (MDR-TB) is TB that does not respond to at least isoniazid and rifampicin, the 2 most powerful anti-TB medications.

Extensively Drug Resistant Tuberculosis (XDR-TB)

Is defined as resistance to rifampicin, isoniazid, any fluoroquinolone and resistance to one or more of the following injectable anti-TB drugs: kanamycin, amikacin, and capreomycin.

Diagnostic Delay

This is the time interval between the onset of the symptoms and labeling of the patient as an MDR TB patient. This is a time beyond 48 hours after specimen collection and processed by using Molecular technique. (MDR-TB Operation Guide, 2013).

Treatment Delay

This is the time interval between MDR tuberculosis diagnosis and initiation of treatment. It is a time beyond 14 days after confirmation of MDR TB.

Institutional Barriers

A coordinated series of obstacles designed, employed or originated by the institution that contributes into delay in diagnosis and treatment of MDR-TB. These are usually manmade obstacles.

CHAPTER ONE: INTRODUCTION

1.1 Background

Multi-drug-resistant tuberculosis (MDR-TB) is defined as a form of TB infection caused by bacteria that are resistant to treatment with at least two of the most powerful first-line anti-TB drugs (Green Facts, 2008; 2009) which are isoniazid (INH) and rifampicin (RMP) (Dalton *et al*., 2012). Both MDR-TB and drug susceptible TB exist in the same environment and share the same infection modality of being air-borne diseases. TB bacteria exist in the air, especially when a TB infected person coughs, sneezes, speaks, or sings. These bacteria can float in the air for several hours, depending on the environment. Persons sharing the same airspace with the polluted TB bacteria TB bacteria can in turn become infected.

MDR-TB infection may be classified as either primary or acquired (Fausci *et al*., 2012). Primary MDR-TB occurs in patients who have not previously been infected with TB but who become infected with a strain that is resistant to treatment. Acquired MDR-TB occurs in patients during treatment with a drug regimen that is not effective at killing the particular strain of TB with which they have been infected (Fausci *et al*., 2012).

Most cases of acquired MDR-TB are due to inappropriate treatment with a single anti-TB drug, usually INH. This can either occur due to improper prescription of ineffective treatment, patients not taking the medication as recommended due to expenses, scarcity of medicines, patient forgetfulness, or patients discontinuing treatment early after feeling better (Adams and Woelke, 2014).

According to the World Health Organization (WHO, 2014), early detection of all TB cases, coupled with well administered treatment with first-line anti-TB drugs for susceptible cases, is the best way to prevent development of drug resistance among TB patients. Implementation of appropriate infection control measures at different levels is important to reduce the transmission of both drug susceptible and drug resistant TB.

All patients with confirmed MDR-TB should be treated with second-line drugs according to international standards. Additionally, isolates from all MDR-TB cases should be tested by using susceptibility to second-line agents in order to confirm or exclude a diagnosis of extensively drug resistant tuberculosis (XDR-TB) (Global Fund, 2014).
Essentially, important institutional components that are comprehensive, ensuring elements of MDR-TB timely diagnosis and treatment are discussed here below.

Optimal management of MDR-TB requires both mycobacterial and routine laboratory services. At a minimum, the required mycobacteriology laboratory services include culture, confirmation of *M. tuberculosis* and drug susceptibility test (DST) so as to be able to initiate patients to treatment with at least Isoniazid and Rifampicin. Routine laboratory services include basic hematology, biochemistry, serology and urine analysis for adequate evaluation and monitoring of patients. Currently in Tanzania, the Central TB reference laboratory (CTRL) can perform culture and DST (NTLP, 2013).

The treatment of MDR-TB must be undertaken by a knowledgeable and experienced physician in that particular area. Treatment of MDR-TB must be carried out on the basis of sensitivity testing: it is impossible to treat such patients without this information. (NTLP, 2013). The Xpert® MTB/RIF test (Cepheid Inc., Sunnyvale, CA, USA) is a fully automated nested real-time polymerase chain reaction (PCR) system. It detects MTB complex DNA, as well as MTB with rifampicin resistance (MoHSW, 2015). The GeneXpert purifies and concentrates *Mycobacterium tuberculosis bacilli* from sputum samples, isolates genomic material from the captured bacteria by sonification and subsequently amplifies the genomic DNA by PCR.

By fully integrating and automating all processes required for real-time PCR-based molecular testing, the Xpert MTB/RIF test represents a simple and robust molecular test suitable for use in resource limited settings where the TB burden is high as the automated test is able to provide results directly from sputum within 90 minutes.

The Xpert MTB/RIF test can be used outside of central reference laboratories, and is ideal when placed at district and even sub-district levels (MoHSW, 2015).

The first Gene Xpert instrument was introduced in Tanzania in 2009 for research purposes. Initial rollout for routine patient testing began in 2010. Between 2010 and 2014, Gene Xpert instruments have been placed in 67 sites in 23 regions.

The Xpert MTB/RIF test has the potential to revolutionize TB diagnostic capability for clinicians managing the disease, and to transform the usual lengthy pathway to diagnosis and treatment for individuals with MDR-TB. Since Xpert MTB/RIF detects only rifampicin resistance, conventional culture and DST are required to confirm an MDR-TB diagnosis. All cases of rifampicin resistance will be confirmed by zonal TB referral laboratories (CTRL). Culture and DST (first and second-line DST using phenotypic and/or genotypic methods) will be carried out to confirm the resistance. The zonal TB referral laboratories will release the culture and DST results to the clinician. In addition, rifampicin resistant results will be communicated to the respective RTLC/DTLC and GeneXpert focal person for immediate follow-up (MoHSW, 2015).

There is a human resource consideration (laboratory personnel and clinicians) at all levels of health systems that provide MDR-TB services. Laboratory personnel and treating clinicians have been provided with clear policies and appropriate diagnostic algorithms for screening of patients at risk of MDR-TB and finally interpreting the results. The diagnosis and use of second-line anti-TB drugs for MDR-TB and XDR TB are recorded and reported by the national data management for MDR-TB at the district, regional and national levels. Confirmed simple mono or poly drug resistant TB cases should not be entered in the MDR-TB recording and reporting system, but registered in the standard national TB register. Therefore, NTLP is recommending reporting on and evaluating only MDR TB cases and complicated mono or poly drug resistant TB cases (NTLP, 2013).

The following MDR TB recording forms, cards, and registers are recommended to be used: District DR TB suspect register, MDR TB Patient Identity Card, MDR TB Treatment Card, MDR TB Register, Drug Resistant TB Side-Effect Monitoring Form, Toxicity Monitoring Flow Sheet, Laboratory TB Register for culture and DST and, Drug Resistance TB Referral/Transfer Form. Each DR TB suspect is registered in the district DR TB suspect register; the register is kept at the office of the District Tuberculosis and Leprosy Coordinator (DTLC) office and the DTLC is responsible for entering the DR TB suspects (NTLP, 2013).

1.2. Problem Statement

For Timely diagnosis and treatment of the MDR-TB, case-finding should occur at every level of the healthcare facility. Sputum from MDR-TB suspects should be collected and sent to the district hospitals/DTLCs immediately within 2 days of contact with a suspected MDR-TB patient. The District Tuberculosis and Leprosy Coordinators (DTLC) should immediately send the sputum to CTRL for assays, culture and DST, within 2 days of receipt of the sputum sample. Based on improved rapid diagnostic tests, the turnaround time of not more than 2 working days (from processing the sputum to the feedback to clinician) is recommended. Sending the samples to CTRL is important in order to facilitate rapid and confirmatory diagnosis that will lead to appropriate treatment of drug resistant tuberculosis.

Currently, however, there is a still large detection gap for MDR-TB as well as gaps between the number of cases detected and patients put on treatment. The Global TB Report (WHO, 2014) highlighted that there were 35,923 MDR-TB cases suspected in 2014 among which 516 cases were confirmed positive for MDR-TB. The report further states that only 143 (28%) cases were initiated into treatment. Despite the substantial increase in the contribution of molecular testing rising from 12% in 2013 to 71% 2014 and a significant decrease in delay diagnosis from 269 in 2013 days to 34 days in 2014, the mortality contributed by delay in diagnosis and treatment is high as it is estimated at about 6.4% (WHO, 2014).

Several studies have explored socio-economic and patient related factors that contribute to delays in diagnosis and treatment of MDR-TB. However, little is known on the role of the institutional barriers in explaining delays observed in diagnosis and treatment of MDR-TB, particularly in the Tanzanian context. Therefore, this study was designed to assess the magnitude of diagnosis and treatment delays and the associated institutional barriers to timely diagnosis and treatment of the MDR-TB.

1.3 Rationale for the study

The generated knowledge will inform interventions aimed at bridging the gap between diagnosis and start of treatment for MDR-TB cases. The study results will therefore contribute to the continued improvement efforts towards elimination of MDR-TB as well as addressing policy issues associated with diagnosis and treatment of MDR-TB in Tanzania as it appears in Health policy of 2007,MDR TB Diagnosis and treatment guideline of 2013.

1.4 Objectives

1.4.1 Broad Objective

To assess the magnitude of MDR-TB diagnosis and treatment delays and associated institutional diagnosis and treatment barriers.

1.4.2 Specific objectives

1. To determine the proportion of presumptive MDR-TB cases that were tested by using conventional DST or Gene Xpert.
2. To determine the average duration between the first report of symptoms, sample sent for Gene Xpert or DST tests and receiving of the results.
3. To determine the average duration between MDR-TB laboratory diagnosis and initiation of treatment.
4. To explore the institutional barriers in MDR-TB diagnosis and treatment initiation.

1.5 Research Questions

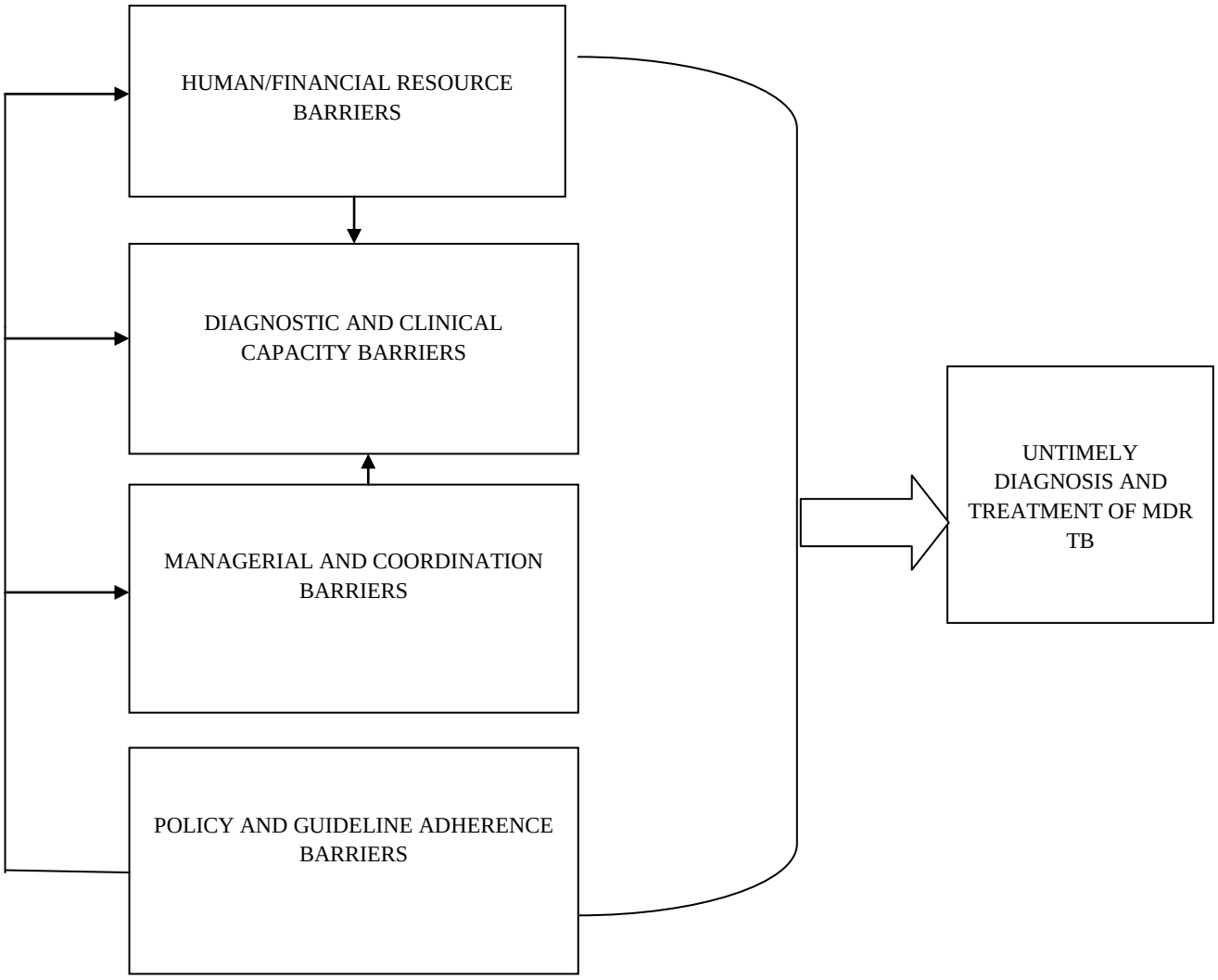
1. What proportion of MDR-TB suspects were tested by using conventional DST or GeneXpert?
2. What is the average duration between the first report of symptoms sent for GeneXpert and DST tests and receiving of the results among MDR-TB cases?
3. What is the average duration between MDR-TB laboratory diagnosis and initiation of treatment?
4. What are the institutional barriers associated with delay in MDR-TB diagnosis and treatment initiation?

1.6. Conceptual Framework

This study was guided by the conceptual framework depicted in Figure 1 below.

The conceptual framework illustrates that institutional barriers to timely diagnosis and treatment MDR-TB may include: **Human and financial resource shortage:** an inadequate number of staff in diagnostic laboratories and treatment clinics with necessary skills will probably lead to delays in diagnosing and treating MDR TB cases. **Managerial and coordination barriers:** this is an important aspect in diagnostic and clinical setup when MDR TB is concerned. Lack of managerial skills and efforts towards solving different challenges in these setups may lead to delays in diagnosis and treatment. **Diagnostic and clinical capacity barrier:** laboratory personnel and clinicians with poor knowledge and skills in diagnosing and treating MDR-TB patients contribute to the ensuing delays. Moreover, less motivated staff may contribute to delays. **Policy and guideline adherence:** most diagnostic and treatment facilities do not properly follow the established national tuberculosis programs (NTPs) policies and guidelines when dealing with MDR-TB cases, and this usually causes in diagnosis and treatment of MDR-TB cases. When these barriers are not removed, then there will be delays in diagnosis and treatment of MDR-TB cases and the consequences will be more devastating to the population.

Figure 1: Conceptual Framework



CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter provides insights on the history, recent findings and information about multi-drug resistant tuberculosis (MDR-TB) based on studies conducted globally. It intends to assess the magnitude of MDR TB Diagnosis and treatment delays and associated institutional diagnosis and treatment barriers. The chapter reviews issues related to specific objectives of the study provided according to available literature.

2.2 Proportion of Presumptive MDR TB Cases Tested Using conventional DST or Gene Xpert

Globally, MDR-TB is emerging at an alarming rate and presents a major challenge for effective clinical management of tuberculosis. MDR-TB is a real threat for global TB control initiatives. Levels of MDR-TB remain worryingly high in some parts of the world, notably countries in Eastern Europe and Central Asia. In several of these countries, 9–32% of new cases have MDR-TB and more than 50% of previously treated cases are found to have MDR-TB. Nonetheless, there has been progress in the detection and treatment of MDR-TB in the last two years. Globally, almost 60 000 cases of MDR-TB were reported to the World Health Organization (WHO) in 2011, mostly by European countries and South Africa. The number of cases reported by the 27 highly burden MDR-TB countries almost doubled between 2009 and 2011 (NTLP, 2013).

In 2013 alone, 5% of all TB cases across the globe were said to be MDR-TB cases. This number includes 3.5% of newly diagnosed TB cases and 20.5% of previously treated TB cases (Green Facts,2008-2009). In the same year, the Mexico–United States border was noted to be "a very hot region for drug resistant TB", although the number of cases remained small (McKay and Betsy, 2013). Countries in the European Union (EU) and European Economic Area (EEA) reported 1,421 patients with multidrug-resistant tuberculosis (MDR TB) in 2012, which is 5% of the 31,004 patients for whom there were drug susceptibility test results (ECDC, 2014).

MDR-TB in Africa may be more prevalent than previously appreciated. The proportion of MDR-TB among all TB cases varies from 5.8% in the Democratic Republic of Congo to virtually 0% in Kenya. The median MDR TB rate is ≈1.9% (Amor *et al*., 2008). Most recent data available on Tanzania indicates that the proportion of MDR-TB among new and retreatment cases is about 1.1% and 3.1 %, respectively (WHO, 2015). The same report highlights that in 2014, Tanzania had tested 35,923 cases for MDR-TB, among which 516 were confirmed cases of MDR-TB and 143 patients were initiated into treatment (WHO, 2015). Recognizing the importance of monitoring the magnitude of MDR-TB in Tanzania, routine surveillance and drug resistance surveys have been undertaken by the National Tuberculosis and Leprosy Program since 1982 (NTLP, 2013). The government of Tanzania embarked on official management of MDR-TB in the year 2009 after the establishment of the National TB Hospital at Kibong'oto, in Kilimanjaro region (NTLP, 2014).

2.3 Average duration between the first report of symptoms, sample sent for Gene Xpert or DST tests and receiving of results

In one study conducted in Zimbabwe it was observed that the methods to diagnose smear samples of TB and MDR-TB are slow and cumbersome. The average turn-around time for smear microscopy is 1-2 days for decentralized sites. Conventional culture techniques used for the diagnosis of drug resistant TB can take 3-8 weeks on solid media and 1-2 weeks in broth media. Drug sensitivity testing following a positive MTB culture takes another 2-4 weeks in solid media and 1 week in broth media. Recent TB diagnostic research has focused on novel molecular technologies for rapid detection of TB, one such example being Xpert MTB/RIF. Xpert MTB/RIF detects *Mycobacterium tuberculosis* as well as rifampicin-resistance conferring mutations directly from sputum, in an assay providing results in 100 minutes[5] (Chemhuru *et al.*, 2011).

The same study on the communication of TB/MDR-TB results showed that the communication of results differs between clinics and hospitals. In clinics, sputa are collected on the day the mobile team is present at the clinic on a once per week basis.

On the day the team is there, the patient brings 2 morning sputum samples or produces 2 on-the-spot samples within the interval of 2 hours. One week later, results are brought back to the clinic. In the 2 hospital sites studied, 2 sputum samples were collected on-the-spot specimens within the interval of 2 hours. The results were communicated to the clinicians on the same day, or latest 1 day later (Chemhuru *et al*., 2011).

A study that assessed delays in the initiation of MDR-TB treatment among patients referred to a specialized drug-resistant treatment facility in KwaZulu-Natal made the observation that culture and drug sensitivity testing (DST) take 8 weeks or longer to obtain results while line probe assays (LPAs) can give results in a matter of hours. These findings make LPAs and the GeneXpert MTB/Rif (GX) be regarded as ground-breaking discoveries for TB diagnosis. However, both LPA and GeneXpert are not easily accessible or available in needy environments, so culture and sensitivity testing remain the standard for TB diagnosis (Narasimooloo and Ross, 2012).

Published literature, data from large multi-centre laboratory validation and demonstration studies, as well as unpublished data from investigator-driven single-centre studies reviewed in late 2010 by the World Health organization (WHO) revealed that the mean time for detection of MDR-TB after report of symptoms was less than 1 day for Xpert MTB/RIF, 1 day for microscopy, 17 days for liquid culture and more than 30 days for solid culture. Rifampicin resistance was detected in less than 1 day with Xpert MTB/RIF compared to an average of 75 days for phenotypic DST (WHO, 2014).

2.4 Average Duration between MDR Laboratory Diagnosis and Initiation of Treatment

A study conducted in Bangladesh made the finding that the time taken for diagnosis of MDR-TB is five days since the introduction of rapid tests in the program. The study further states that it took ten days to initiate patients to treatment after the release of the results.

A recent study on pre-diagnosis and pre-treatment attrition of MDR-TB patients in Bangladesh presented the median time for diagnosis and treatment initiation as four and five days, respectively (Hossain *et al.,* 2015).

Laboratory turnaround time reported by another study conducted in Cape Town, South Africa, was less than one day using Xpert based algorithm and 24 days using Line Probe Assay based algorithm (Naidoo *et al.,* 2014). The study also reported time to initiate treatment after diagnosis as 10 and 14 days in Xpert and Line Probe Assay based algorithms, respectively. Similar results were found in a multicounty study which reported median time to detect rifampicin resistance as one day for Xpert MTB/RIF test and 20 days for LPA-based test (Boehme *et al*., 2014). Another study on the use of MTB-DR Plus for diagnosis showed a reduction in laboratory processing time to a median of 22 days compared to culture-based drug sensitivity testing (DST) which was 55 days, whereas it took 20 days of operational delay to start the treatment (Jacobson *et al.,* 2013). Diagnosis time using MTB-DR Plus was also reported as 4.2 and 11 days in Georgia and India, respectively (Tukvadze *et al.,* 2012).

Delay in treatment initiation of MDR-TB cases was also reported in a few other studies based on conventional DST methods. Two studies using conventional culture and DST for MDR-TB diagnosis reported a total time of 12.4 weeks from diagnosis to treatment initiation and 17 weeks in Kwazulu Natal, South Africa and Cameroon, respectively (Noeske *et al.,* 2012). Time for diagnosis and treatment initiation using conventional culture was 246 to 283 days, respectively among children, if the information of their MDR-TB contact was not one of the criteria for diagnosis (Schaaf *et al.,* 2003). Time taken at different stages of MDR-TB management using conventional culture and DST methods, starting from sample collection to start of treatment, was also reported in another study which presents a total turnaround time of 5 months which was almost double of the bacteriological procedure (Yagui *et al*., 2006). It took 12.8 days in Vietnam to get a patient initiated into treatment after diagnosis (Hoa *et al*., 2014).

2.5 Institutional Barriers in MDR TB Diagnosis and Treatment Initiation

2.5.1 Financial resource barriers

Diagnosis, treatment and care for MDR-TB are demanding, relatively complex, and costly. Ministries of health are quite often relying on models of care that are not suitable to the needs of patients, are not in line with WHO guidelines, reduce the impact of treatment, and are not cost-effective. The major demands come from the length of therapy (two years) and the need to deliver directly observed treatment (DOT) using a patient-centered approach (WHO, 2009).

The 'Stop TB Partnership,' a global plan to stop the spread of TB, has set out interventions that have been implemented from 2006 to 2015 to achieve global targets that have been set against 2015. The initiative also came up with estimates of the funding requirements. The M/XDR-TB component of the plan set a target that 80% of the estimated cases of M/XDR-TB should be diagnosed and treated according to international guidelines by 2015. The total cost of diagnosing and treating the M/XDR-TB patients (including infection control) was estimated at US$ 16.9 billion over seven years, rising from US$ 0.7 billion in 2009 to US$ 4.4 billion in 2015. The funding required in 2015 was 61 times higher than the funding that was made available in 2009. According to WHO (2014), most of the funding quota was required in the European region (US$ 8.9 billion) followed by Asia (US$ 7.1 billion, mostly for China and India).

In one of its many studies, the European Commission for Disease Control and Prevention (ECDC) selected four countries of Austria, Bulgaria, Spain and the United Kingdom as case studies on different factors affecting the management of MDR-TB. All four countries agreed to participate in the study and results showed that all the four countries have a system in place (or are moving towards it) with a centralized and earmarked budget for MDR-TB. Some hospitals reported inadequate funding for in-patient care. These included concerns such as allocating fixed budgets per TB patient/bed without specific arrangements for MDR-TB patients. However, it was reported that this situation does not interrupt services or make them unavailable because the MDR-TB numbers are small (ECDC, 2014).

The major perceived barrier to MDR-TB treatment is the high cost of quality-assured second-line drugs. Additional requirements, adverse effects associated with second-line drugs, low availability of quality-assured second-line drugs, difficulty in ensuring adequate patient support (including DOT) during the long treatment course, and the risk for resistance to second-line drugs are all mentioned as potential hindrances to better provision of healthcare services to MDR patients. Consequently, many national tuberculosis programs (NTPs) focus on achieving high cure rates in their DOTS programs while putting less efforts in diagnosing and treating MDR-TB (Nathanson *et al*., 2006).

2.5.2 Human resource barrier

Not only the scale-up of effective MDR-TB management but also the effective prevention of MDR-TB will depend on sufficient attention being given to human resource development (HRD). DOT has been expanded rapidly in many countries. However, the expansion has not always been accompanied by adequate and continuous efforts to ensure sufficient training of staff, improved supervisory capacity and collection of essential human resource management information. This omission has had a severe effect on the quality of some programs. In a survey of the 22 TB high burden countries (HBC), 17 out of 22 national tuberculosis program (NTP) managers identified inadequate human resources as the most troubling constraint for reaching TB control targets. Evidence from program reviews in many TB HBCs have shown that there is often inadequate central and peripheral level human resource capacity to ensure basic TB service quality, let alone capacity for expanding services into new interventions such as the diagnosis and management of MDR-TB (WHO, 2009).

According to the new Staffing Levels Guidelines of Tanzania (GoT, 2014), the minimum number of health workers required to provide quality healthcare services in 6878 healthcare facilities in the country is 145,454. The actual number of current healthcare workers available is 63,447 and the shortage is 82,007, which is about 56.38%. Moreover, there is the challenge of rapidly aging workforce, which will further exacerbate the crisis. The existing workforce is mal-distributed with the situation being worst in dispensaries. Many individuals prefer to work in urban rather than rural areas due to poor working and living environment.

There is a clear regional disparity with regard to human resource for health (HRH) availability. Kilimanjaro, Dar-es salaam, Iringa, Lindi and Pwani are better off compared to regions such as Kagera, Rukwa, Tabora, Kigoma and Shinyanga. Healthcare workers density ranges from 4/10,000 population to 10/10,000 population (MoHSW, 2016).

2.5.3 Diagnostic and clinical capacity barrier

Laboratory assessment evidence shows that majority of laboratories for culture and drug sensitivity testing (DST) in resource-limited settings do not meet basic standards for laboratory bio-safety or technical proficiency. Standardized operating procedures and quality assurance systems for culture and DST are largely absent or poorly implemented. The high infection risk associated with the manipulation of live (and often drug resistant) cultures of *M. tuberculosis* necessitates renovation, construction and maintenance of laboratories according to bio-safety level 3 standards, including appropriate laboratory design, negative air flow systems, and validation and maintenance of essential bio-safety equipment (WHO, 2009).

One of the main reasons for the precarious state of laboratory services relates to oversight of and budget for laboratories often falling outside the jurisdiction of national TB control programs, thereby aggravating problems relating to laboratory infrastructure, forecasting and planning, and sustainability of their technical competency (WHO, 2009).

In a study conducted in 2014, the European Center for Disease Control and Prevention (ECDC) selected four countries of Austria, Bulgaria, Spain and the United Kingdom being case studies on the factors affecting management of multi-drug resistant tuberculosis (MDR-TB) in which it was observed that the rapid molecular testing (Xpert/MTB or line probe assays) was not available in some hospitals in the four countries. The report states that criteria for rapid molecular testing for drug resistance were not available in most of the countries and testing depended on the decision of the individual clinician. In one country, the time between the initial diagnosis of drug-susceptible TB and MDR-TB diagnosis can be as long as 4–5 months (ECDC, 2014).

2.5.4 Management and co-ordination barriers

A neglected but significant factor fueling the multi-drug resistant tuberculosis (MDR-TB) and extensively drug resistant tuberculosis (XDR-TB) outbreaks in South Africa is the lack of infection control in institutions, including the lack of simple administrative measures such as triaging of patients, as well as more sophisticated expensive environmental control measures such as negative pressure rooms and personal respiratory protection (respirators) (Padayatchi *et al.*, 2007).

The specialized nature of laboratory administration, management, and technical procedures dictate the need for specific knowledge and skills, training and mentoring, and ongoing monitoring of performance. However, experience shows that insufficient time is devoted to the managerial and administrative components of laboratory strengthening, a problem that is deepened by poor accountability mechanisms to ensure sustainable diagnostic quality (WHO, 2009).

2.5.5 Policy and Guideline adherence barriers

Unfortunately, private physicians as well as public sector healthcare service providers outside national tuberculosis programs (NTPs) rarely follow recommended TB treatment regimens. Treatment outcomes are poor in private and public facilities that operate outside NTP, often with a treatment success rate of less than 50%. Many patients thus receive TB treatment that is delayed and of questionable quality both at private and public healthcare facilities. Therefore, prevention of drug-resistance development and amplification needs to include efforts to minimize irrational use of anti-TB medicines across the whole healthcare system (WHO, 2009). Despite the availability of global and localized TB guidelines, clinicians tend to rely on recent literature and/or a mix of professional insights and experience. Many of the clinicians interviewed do not complete the injectable second-line drugs (aminoglycosides/polypeptides) for the full eight months duration that WHO recommends because of frequent adverse effects (ototoxicity) in patients. It has been found that in some countries category five drugs (especially linezolid) are used more widely than it is recommended in the WHO guidelines (ECDC, 2014).

CHAPTER THREE: METHODOLOGY

3.1 Study Area

The study has collected data from five study areas; at Central Tuberculosis Reference Laboratory (CTRL-Muhimbili), Kibong'oto National TB Hospital (Kilimanjaro) and Temeke, Mwananyamala and Muhimbili hospitals. The CTRL and Kibong'oto were selected purposefully for their status of being the national hub of data for MDR TB case diagnosis and treatment.

3.2 Study Design

This was a mixed method study in which the quantitative component was a descriptive cross-sectional study design that involved reviewing multi-drug resistant (MDR-TB) patient data from 2009 to 2015. This quantitative part of the study was complemented by the qualitative component which involved exploring reasons (institutional barriers) that contribute to the delays using in-depth interviews.

3.3 Study Population

The study population included 384 MDR-TB cases diagnosed between 2009 and 2015 whose conventional Culture and Gene Xpert records and results were available at both the Central Tuberculosis Reference Laboratory (CTRL) and Kibong'oto Hospital. Treatment records were obtained from Kibong'oto Hospital. Health facility superintendents, heads of TB units, laboratory managers and regional TB and Leprosy Coordinators were included in the qualitative part of the study.

3.4. Sample size

For the quantitative part, the sample size was intended to find a true underlying proportion of between 45 and 55 % of cases diagnosed by using DST or Xpert.

The sample size was calculated using the following formula: $n= z^2p\ (1-p)/\varepsilon^2$ (Sterne, 2003) whereby;

n =minimum sample size

z =standard deviation (1.96) which corresponds to 95% confidence interval

e = margin of error to be 5%

p =estimated proportion of MDR TB cases diagnosed by DST or xpert from 2009 to 2015 and recorded to be 50% (0.5)

Therefore, sample size was 384 patient records.

For qualitative design: 24 healthcare providers (health facility superintendents, heads of TB units, laboratory managers and Regional TB and Leprosy Coordinators in the three hospitals were interviewed.

3.5. Sampling Techniques and Procedures

3.5.1 For the quantitative component

Central Tuberculosis Reference Laboratory at Muhimbili National Hospital and Kibong'oto Infectious Diseases Hospital (KIDH) were purposively selected in order to obtain the quantitative data. These two centers were selected purposively because they are the centers of excellence for the definitive diagnosis (Muhimbili) and treatment (KIDH) of MDR-TB using the institutionalized care model since 2009 (NTLP, 2015). By selecting these centers purposively, there was a guarantee to reach the targeted sample quickly – that is: *total population purposive sampling*). Data were obtained from the TB and laboratory registers as well as from patient files from these facilities. Sampling of individual files to be reviewed was done using a systematic random sampling technique whereby the total number of MDR-TB patient files in the facility was obtained and then the list of the files was created (sampling frame). Sampling interval "n" was obtained by dividing the total number of files available to the sample size. Finally, the sample was drawn by selecting every n^{th} case, starting with a randomly selected number between one and n.

3.5.2 For the qualitative component

Health facility superintendents, heads of TB units, Laboratory managers and Regional TB and Leprosy Coordinators at Mwananyamala, Temeke and Muhimbili Hospitals were interviewed by using the in-depth interview technique.

Semi-structured interviews were conducted to obtain richer and deeper insights pertaining to institutional barriers towards multi-drug resistant tuberculosis (MDR-TB) diagnosis and treatment. The principle of saturation whereby information the point of self-repeating was used to stop the interviews.

3.6 Eligibility Criteria

3.6.1 Inclusion criteria

Healthcare facilities performing laboratory MDR-TB diagnosis by using Xpert and/or DST methods and provide treatment services to MDR TB patients.

3.6.2 Exclusion criteria

Health facilities that do not perform laboratory MDR-TB diagnosis by using Xpert and/or DST methods and do not provide treatment services to MDR TB patients.

3.7 Data Collection Tools

For the quantitative component, review of TB and laboratory registers and patient files were used to collect data. The following is the algorithm of all activities from patient diagnosis and treatment initiation: After the patient has been registered, an adequate sputum specimen (3–5mls) is collected from him/her essentially for the success of culturing Mycobacterium tuberculosis. The collected sputum collected should be carefully labeled with name facility, TB district number and date of collection. The recommended turnaround time for laboratory results when the specimen is tested by using molecular methods (Gene Xpert) is as follows: positive culture identification should be within 2 hours after primary isolation. Molecular DST reported to clinician should be within 48 hours of specimen collection. Conventional DST should be having results after 14 weeks of specimen collection. After confirmation of MDR-TB, the treatment should be promptly initiated within 7 days. By using this standard guide, the duration from diagnosis to treatment initiation was determined from files. These retrospective data were used in the analysis to establish the proportion of MDR-TB suspects who were tested using drug resistance sensitivity (DST) or Xpert to determine the average duration between the first report of symptoms, testing, receiving of the results, and determining the average duration between MDR-TB laboratory diagnosis and initiation of treatment. A recording tool was designed and used to document all the findings.

In the qualitative design, an interview guide with semi-structured open-ended questions was used. A tape recorder was used to record and store information from the interview.

3.8 Recruitment and Training of Research Assistants

The study recruited four research assistants (RAs) with secondary school education and/or above and with added knowledge on health-related issues and interview experience to cover the estimated sample size. The assistants were trained on the research concept, protocol and interview techniques for one day. Two RAs helped with collecting quantitative data and the remaining two RAs knowledgeable on MDR-TB protocol and hospital settings assisted in collecting qualitative data.

3.9 Pretesting of Data Collection Tools

Piloting for the study was conducted in Kinondoni Municipality at Mwananyamala Hospital. The tools were pretested on a random sample of 50 MDR-TB records and 5 superintendents and managers. This pilot pretest provided a clear indication on the response to interview questions and the estimated time allocated to interview one respondent. The pretest was done on 25th of May 2017.

3.10 Data Collection Procedure

Data was collected using both quantitative and qualitative approaches. The Principal Investigator and one research assistant collected MDR-TB patient data from registers at Kibongoto Hospital. In Dar es Salaam, the PI and two RAs collected data from registers at the Central Tuberculosis Reference Laboratory (CTRL) and the National Institute for Medical Research (NIMR) while two RAs interviewed pre-determined health officers in 3 hospitals in Dar es Salaam. In the qualitative part, the interviewers introduced themselves and handed consent form to the health officers. The interviewees were informed about the aim of the study and were assured of the confidentiality of the information they would provide. The interviews were conducted in privacy in the respondents' own office. Data collection for both approaches was conducted for 25 days from 29th of May to 23rd of June 2017.

3.11 Data Management

The filling of recording tool and the conduct of in-depth interviews were primarily supervised by the Principal Investigator. This was done to ensure that the data collected were accurate and that the responses given were well understood by the interviewer. The filled tools were examined on a daily basis to check for quality of the data collected. Interviews were also checked daily so as to identify any missed items. The data collected using the aforementioned tools were verified for completeness. For qualitative data, clear data file naming was conducted followed by a data tracking system. Then, the transcription and translation of the data was undertaken while ensuring quality control procedures.

3.12 Data Analysis

For the quantitative design: Data analysis was conducted using SPSS version 20. The analysis involved descriptive statistics to describe the sample population and relevant proportions using frequency tables and cross tabulations between independent and dependent variables. Chi square method for showing association between study variables during statistical analysis was also used. Continuous variables were represented by means and standard deviations or median if not normally distributed and categorical data by whole numbers and percentages were also determined. P-value of < 0.05 was considered to be statistically significant. For the qualitative design: Data were analysed using content analysis approach. The process of analysis involved five phases: meaning unit, manual codes, abstracted codes, categories and main categories.

3.14 Dissemination of the Research Findings

The result of this work will be published in academic journals per KNCV and MUHAS requirements. Publishing this work will help to bring findings to the decision and policy makers in the Ministry of Health Community Development, Gender, Elderly and Children through the national Tuberculosis and Leprosy Program (NTLP) together with other partners. This dissertation will also be presented in health-related conferences, including the International Union for TB and in other national health conferences. The final report will also be available in MUHAS achieves for reference purposes.

3.15 Ethical Issues and Consideration

In this study, the researcher sought ethical clearance from Muhimbili University of Health and Allied Sciences (MUHAS) Ethical Review Committee in order to obtain the permission to conduct the study. Permission to conduct the study was sought from the office of District Administrative Secretary of Ilala, Temeke and Kinondoni municipalities where the Muhimbili National Hospital, Temeke Hospital and Mwananyamala Hospital are found.

Permission to conduct the study was also sought from the Kibong'oto Infectious Disease Hospital and Muhimbili National Hospital Directors. All participants and data personnel were informed about the purpose of this study and an informed consent (both verbal and written) to participate was obtained from all respondents who participated in the study. Required measures to maintain human rights, including right to privacy and confidentiality and right to prevention from any type of harm were put into consideration.

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter presents the study findings based on the retrieved data of 384 Multi-drug resistant tuberculosis (MDR-TB) patients recorded from 2009 to 2015 and the lived experience of the healthcare facility superintendents, heads of TB units, laboratory managers and regional coordinators of TB and leprosy regarding institutional barriers that hamper diagnosis and treatment of MDR TB. The chapter is divided into four sections based on the four specific objectives of the study and short introductory section under 4.1. The second section covers characteristics of the study sample and proportion of MDR-TB suspects who were tested using conventional drug sensitivity test (DST) or Gene Xpert. The third section focuses on the average duration between the first report of symptoms, sample sent for Gene Xpert or DST tests and receiving of results. The fourth section explains findings on the average duration between MDR-TB laboratory diagnosis and initiation of treatment while the fifth section will present the results on exploration of institutional barriers in MDR-TB diagnosis and treatment initiation.

4.2 Characteristics of the Study Sample and Proportion of the Patients Tested

4.2.1. Characteristics of the study sample

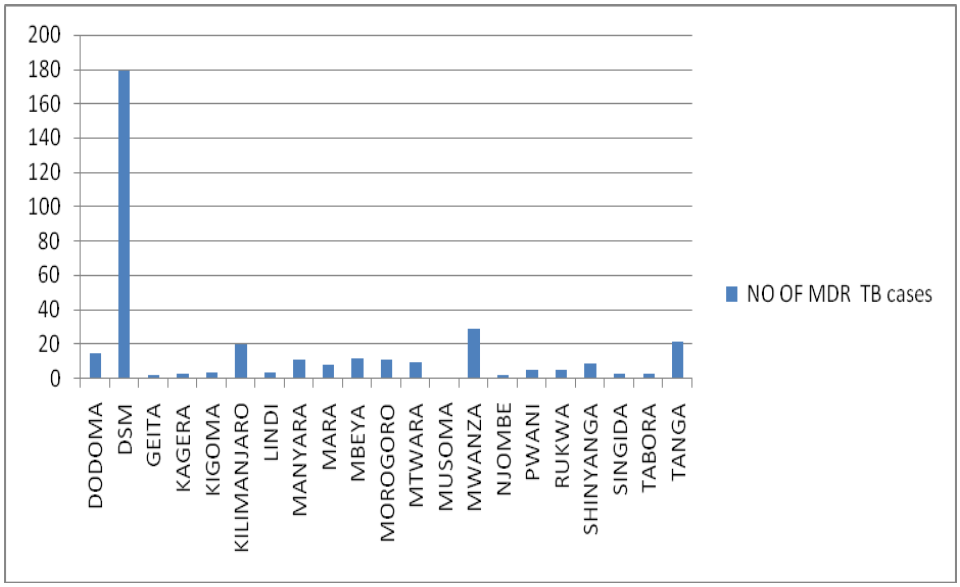
Table 1 above shows the characteristics of the study participants stratified by their sex and age groups. The study has managed to gather data of 384 subjects that were identified randomly from among these 471 patients out of the 471 MDR-TB patients registered in Tanzania since the MDR-TB program started in 2009. The total of 384 participants functioned as the representative sample for this study. Among those, 260 (67.7%) were male and 124 (32.3 %) were female. Majority (n = 207, 53.9%) were in the 21–40 years age group and the minority group was that of 60 years and above (n=18,4.7%). The average age was 36.94 (SD=13.4) years with minimum age of 1 year and a maximum 84 years. Many patients (n=181, 47.1%) were referred to the Kibong'oto Infectious Disease Hospital (KIDH) from Dar es Salaam and the lowest number of patients were from Kigoma, Njombe and Geita (n=2, 0.5%). This is clearly depicted in the Figure 2 below.

Table 1: Characteristics of MDR TB Patients by Age and Sex (2009-2015)

Sex	Age Group of Respondent				
	1-20 years	21-40 years	41-60 years	60> years	Total
Male	15	134	96	15	260
	41.7%	64.7%	78.0%	83.3%	67.7%
Female	21	73	27	3	124
	58.3%	35.3%	22.0%	16.7%	32.3%
Total	36	207	123	18	384
	100.0%	100.0%	100.0%	100.0%	100.0%

Source: Fieldwork, 2017

Figure 2: Distribution of MDR TB Patients by Region of Origin (2009-2015)

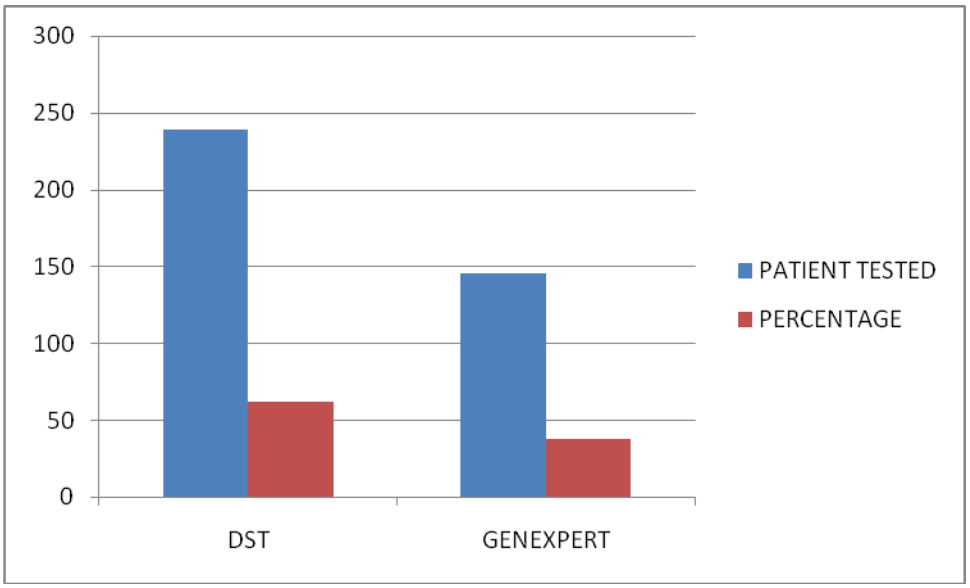


Source: Fieldwork, 2017

4.2.2 Proportion of MDR TB suspects who were tested by using conventional DST or Gene Xpert

Figure 2 above shows that two hundred and thirty-nine patients (n=239, 62.2%) were tested by using the conventional Drug Susceptibility Test (DST) for MDR-TB from the year 2009 to 2012 using first line and second line drugs and one hundred and one forty five patients (n=145, 37.8%) were tested by using Gene Xpert molecular method between 2012 and 2015.

Figure 3: Proportion of Presumptive MDR TB Cases Tested Using Conventional DST or Gene Xpert (2009-2015)



Source: Fieldwork, 2017

4.3 The Average Duration Between First Report of Symptoms, Sample Sent for DST or Gene Xpert Tests and Receiving of the Results

The study did not manage to obtain the first report of symptoms data from the registers at KIDH and the Central tuberculosis Reference Laboratory (CTRL) but the dates for DST and Gene Xpert sample collection, processing and receiving of results were available. It was found that out of 239 patients who were tested by using the DST method, 102 patients (42.7%) received their results within the recommended time of 42 days between sample collection,

processing and receiving the results and 137 patients (57.3%) received their results at later days (more than 42 days). For those recorded to have been tested by using Gene Xpert machine, more patients (n=90, 62.1%) received their results within the recommended time of 2 days or less and 55 patients (37.9%) received their results beyond the prescribed duration of 2 days.

Table 2: Delay in Diagnosis by Method Used

Test	DST		Gene Xpert	
	Recommended time of 42 Days	**More than recommended time of 42 days**	**Recommended time of 2 or Less days**	**More than recommended time of 2 days**
Patient Tested and received results (n)	102	137	90	55
Percentage (%)	42.7	57.3	62.1	37.9

Source: Fieldwork, 2017

From this study, it was found that it took about 94 days (with the Standard Deviation (SD) of 74.2 days) for the patient's sample to be sent for DST diagnosis and receiving results. This average is 54 more days than the recommended days for DST diagnosis and receiving of results. Moreover, results show that the average duration between when a sample is sent for Gene Xpert diagnosis and receiving of the results is 11 days (with the Standard Deviation (SD) of 32 days). This average is 9 more days than the recommended time for Gene Xpert diagnosis and receiving of results.

4.4. The Average Duration Between MDR Laboratory Diagnosis and Initiation of Treatment

Table 3 above shows the results on delay in days from the time that the patient has been confirmed to be MDR-TB until the time he/she is initiated into treatment at KIDH. Out of 239 patients who were tested by using the DST method, 145 patients (60.6%) were initiated into treatments after the recommended 14 days. Only, 94 patients (39.4%) started their treatment within 14 days as prescribed in the guidelines. Furthermore, for those who were tested by using the Gene Xpert method, it was found that 82 patients (56.6%) had a delayed treatment initiation while 63 patients (43.4%) started their treatment on time. (Table 3).

Table 3: Delay from MDR Laboratory Diagnosis to Treatment Initiation

	DST		**Gene Xpert**	
Test	**Recommended time of 14 days or less**	**More than recommended time of 14 or less days**	**Recommended time of 14 days or less**	**More than recommended time of 14 or less days**
Patient Tested and Started treatment (n)	94	145	63	82
Percentage (%)	39.4	60.6	43.4	56.6

Source: Fieldwork, 2017

The average duration between MDR laboratory diagnosis by using DST method and start of treatment was about 83 days (SD=122 days) and the average duration between laboratory diagnosis by using Gene Xpert method and the start of treatment was found to be 40 days (SD=34 days). The earliest time from laboratory diagnosis to the initiation of MDR TB treatment is set at 14 days (NTLP, 2013).

4.4.1. Association Between Delay and Age and Sex of Patients and Method of Diagnosis Used

Table 4 above shows age and sex factors and the type of diagnosis used in relation to delay in diagnosis and treatment initiation. While age and sex showed no significant association with delay, laboratory diagnosis by using the Gene Xpert on the one hand and DST method on the other hand has shown strong association with delays in both diagnosis and treatment initiation.

Table 4: Association Between Delay and Age, Sex and Methods of Laboratory Diagnosis Method

Factor/Characteristic	**Total n (%)**	**Delay n (%)**	**No delay n (%)**	**X^2; p value**
Sex (DST)				
Male	163(68.2)	96 (60.0)	67 (40.0)	
Female	76 (31.8)	51(67.1)	25(32.9)	0.849; 0.654
Sex (GeneXpert)				
Male	97(67.0)	34 (35.1)	63 (64.9)	
Female	48 (33.1)	21 (43.8)	27 (56.2)	1.115 ; 0.573
Age group (DST)				
1- 60 years	169 (70.7)	90 (53.3)	79(46.7)	
Above 60 years	12 (5.0)	7 (58.3)	5 (41.7)	1.78; 0.938
Age group (Xpert)				
1- 60 years	139(95.8)	54 (38.8)	85 (61.2)	
Above 60 years	6 (4.1)	1 (16.7)	5 (83.3)	4.02; 0.674
Diagnosis by DST	239 (62.2)	137(57.3)	102(42.7)	5.920.001
Diagnosis by (Xpert)	145(37.8)	55 (37.9)	90 (62.1)	5.92; 0.001

Source: Fieldwork, 2017

4.5 Institutional Barriers in MDR TB Diagnosis and Treatment Initiation

4.5.1 Financial resource barriers

4.5.1.1 Lack of necessary reagents and/or appropriate medications

The study revealed that generally diagnosis, treatment, and care of MDR-TB are demanding, relatively complex, and costly. The respondents interviewed claimed that their institutions were facing financial difficulties in purchasing laboratory equipment and supplies which are normally expensive. New treatment regimens for MDR-TB, and especially the second line drugs are also expensive and the capacity of these institutions to cover these expenses is very limited. These institutional level financial challenges usually lead to delays in diagnosis and treatment initiation. One interview respondent said the following:

"Sometimes, we have to delay sample processing and even fail to initiate treatment in a timely manner because the necessary reagents or proper drugs are not available, and the institution has no sufficient funds to purchase them from MSD." (Respondent from Temeke Hospital*)*

4 .5.1.2. Concerns over donor dependency

Donor dependency in the provision of MDR-TB services in the country contributes to delay, especially when the donors do not release funds on time for expenses such as purchasing cartridges and maintenance of the machines. Donor dependency causes delays in diagnosis results as most institutions do not have sufficient internal budgetary resources to cover the costs themselves. One respondent had the following to say:

"We have a central diagnosis centre for TB and MDR-TB here, but we do not have a budget of our own to run things in the laboratory. Sometimes, even when a mere door knob is broken, you have to write to donor for replacement. This is a big challenge on our part."

The respondent added that:

"In the event of critical shortage of cartridges and other supplies, we are unable to resort into any alternative of buying from independent vendors because we do not have funds to our disposal. In those occasions, we have to wait for donors to supply us or we have to go back to conventional methods of diagnosis or process only a few selected samples." (Respondent from MNH).

Some hospitals reported inadequate funding for in-patient care: the existing fixed budget system which allocates funds per TB patient/bed does not allow for specific arrangements for accommodating MDR-TB patients. However, so far this has not significantly interrupted services or made them unavailable with the reason being that the MDR-TB.

4.5.1.3 High cost of quality-assured second-line drugs

The other financial barrier leading to treatment delay was revealed to be the high cost of quality-assured second-line drugs. This is a true situation due to frequent stock out of the drugs at the nation's supplier, Medical Store Department (MSD). Therefore, many respondents suggested that the country should put more efforts to strengthen drug procurement services by allocating sufficient budget for TB and MDR-TB management. One respondent said the following during interview:

"It is high time that the government should think about centralizing these services and own them by allocating sufficient budget. It should not leave the uncoordinated donors to own the services and do what they wish for their own benefits, not for the nation." (Respondent from Mwananyamala Hospital).

4.5.2 Human resource barrier

4.5.2.1 Divided attention between service provision and managerial functions

The study also made the finding regarding the existence of an inadequate number of staff working in both diagnosis and treatment centers for multi-drug resistant tuberculosis (MDR-TB). It is a common practice for the small number of staff available to be engaged in other activities like managerial functions, supervisions, outreach visitations, among many others, a situation that leads the bench operations to be paralyzed and hence causing delays in diagnosis and treatment initiation. One respondent said the following during interview:

"Still, the human resource is not enough here, especially on these referral hospitals. We are few and we are required to perform both diagnostic and treatment duties, as well as managerial and leadership functions concurrently. In the laboratories, this situation renders a critical shortage in bench operators." (Respondent from MNH).

4.5.2.2 Inadequacy of training efforts

There has also been a reported inadequate effort at staff training, supervisory capacity and collection of essential human resource management information. This gap creates low skilled personnel and in the situation where the staff lacks skills in testing and treatment of the patients, delays will probably result. According to our respondents, awareness and skills gap is more observed in the laboratory settings than in treatment clinics. One interview respondent said the following:

"There is a lack of sufficient skills and awareness on TB diagnosis and treatment among laboratory staff and clinicians. The gap is more observed in the laboratories than in treatment clinics. Moreover, the tremendous increase of traditional healers in the streets has created more havoc leading to challenges in ensuring early diagnosis and treatment of TB and MDR-TB because people spend much time with traditional healers who usually don't follow proper diagnosis and treatment. By the time they realize that they need to seek medical expertise, the delay has already been created." (Respondent from Mwananyamala Hospital).

4.5.3 Diagnostic and clinical capacity barrier

4.5.3.1 Limited laboratory technical proficiency

The study revealed that the standardized operating procedures and quality assurance systems for culture and drug susceptibility test (DST) were present but poorly observed. At one point, a respondent said the following:

"We have the negative pressure room here to conduct DST but the challenge is that some of the personnel does not follows standardized operating procedures and quality assurance for culture, and results into occasional delays in diagnosis." (Respondent from CTRL).

The rapid molecular testing by using GeneXpert/MTB machine was available at all the institutions surveyed but respondents claimed that they were still having difficulties in testing an adequate number of samples in a timely manner. They revealed that the Xpert machines they have operate with an incomplete number of modules due to mechanical breakdown and the lack of planned preventive maintenance. These mechanical deficiencies result in testing fewer samples and at a delayed time. The frequent unavailability of cartridges and other supplies was another concern that was expressed by all respondents with the situation becoming worse recently due to cut down of donor support in the healthcare sector which comes to further overwhelm the already insufficient government budgetary incapability. One respondent said the following regarding budgetary constraints:

"The frequent stock out of cartridges and operating in less modules per machine is another challenge that the responsible authorities should strive to eliminate if we want to increase TB/MDR case finding rate. At the moment, we are unbale to test enough cases due to these difficulties." (Respondent from Temeke Hospital)

As far as clinical capacity is concerned, most respondents agreed that there is still a challenge on the side of clinicians in conducting their primary role of suspecting and identifying MDR-TB cases through clinical evaluation and in initiating treatment regimen thereafter. One respondent said the following during interview:

"Some of clinicians still struggle on how to discern the risk factors for drug resistance, on strategies for case findings and close contact tracing, as well as on the knowledge of the MDR-TB diagnostic algorithm. This is happening while it is well understood that in order to facilitate the rapid identification of drug resistant TB and its management, clinicians should have a high index of suspicion in certain high-risk groups for MDR-TB, as well as be knowledgeable in diagnostic and treatment requirements." (Respondent from MNH Hospital)

4.5.4 Management and co-ordination barriers

Most respondents reported that there is insufficient time devoted to the managerial, coordination and administrative components of MDR-TB diagnosis and treatment. This is the case for some managers who engage in a lot of ad hoc activities such as routine meetings and travelling for different purposes. The interviewees stated that this results into delays as some of the important decisions about these services usually need the approval of these managers. Otherwise, the respondents said that they have good management, cooperation and coordination in these services from the National Tuberculosis and Leprosy Program (NTLP).

"Our management here is trying very hard to help us work in conducive working conditions but the big challenges is how to get hold of them when we have burning issues needing their authorization, they are always absent in the offices" (Respondent at Temeke Hospital)

4.5.5 Policy and guideline adherence barriers

Many respondents said that they were aware of the availability of provisions about TB in the National Health Policy of 2007 and associated guideline of MDR-TB management of 2013 in the country. However, they admitted that they do not properly adhere to the recommended TB management guidelines because they either do not have the guidelines in their offices or they sometimes fail to clearly interpret the provisions. Therefore, most of them reported to be working according to their prior training on diagnosis and treatment of TB/MDR-TB. The following was said by one respondent during an interview:

"The problem of some practitioners not adhering to the guideline results in late and erroneous diagnosis of presumptive MDR-TB cases. Thereafter, the treatment becomes also questionable." (Respondent from Temeke Hospital)

CHAPTER FIVE: DISCUSSION

5.1 Overview

This five-year retrospective study was conducted to determine the magnitude of MDR-TB diagnosis and treatment delays among patients treated for MDR-TB at Kibong'oto Infectious Disease Hospital, a national referral centre for MDR-TB cases in Tanzania. The research explored lived examples and sought explanation and opinion of the higher officials in the various health provision institutions on barriers leading to these delays. This chapter discusses the findings of the study presented in chapter four.

5.2 Significance of the Demographic Findings

There are several important demographic findings of this study: Over two thirds of all MDR-TB patients in Tanzania are males in their economic reproductive age group. The eastern and the northern regions of the country have a greater number of MDR-TB patients compared to other regions. It is of note that over one quarter of all MDR-TB patients reported in Tanzania are from Dar es Salaam. Moreover, it is reported that, over a quarter of all TB cases diagnosed come from Dar es Salaam (MoHSW, 2016). Possible explanations may include: overcrowding, high population density, presence of diagnostic facilities, and a simplified referral process to Kibong'oto. Similar findings were reported by Boseley (2016) in a study determining rates of TB in cities of West Africa whereby it was found that about 35% of all reported TB cases were coming from major cities of West African countries. The same observation has been made in low incidence countries of Europe whereby, according to Prasad *et al*., (2016), TB notifications were 2.5 times higher in big cities compared to national rates.

5.3. Delay in Diagnosis of MDR-TB

From this study, it was found that 50% of TB patients (n=192) had their MDR-TB diagnosis delayed: One thirty-seven patients (n=137, 57.3%) did not receive their DST results within the recommended time of 42 days. It was further discovered that it took an average duration of 94 days (with the Standard Deviation (SD) of 74.2 days) for the patient to be sent for DST diagnosis and receiving results.

This average is 54 more days than the recommended days for DST diagnosis and receiving results. Moreover, the results show that about 55 patients (37.9%) delayed diagnosis and receiving results when using the Gene Xpert technique. The average duration between the time a sample is sent for Gene Xpert diagnosis and receiving the results is 11 days (with the Standard Deviation (SD) of 32 days). This average is 9 more days than the recommended time for Gene Xpert diagnosis and receiving results.

Overall, these findings indicate a higher magnitude of delay (higher than 42 days for DST and 2 days for Gene Xpert) in establishing diagnosis of MDR-TB. Similar findings were reported by Narasimooloo and Ross (2012) in a study conducted in Kwazulu Natal where it was observed that 56 days or longer were needed to obtain results when using DST, while Gene Xpert gave results in hours. In another study conducted by the World Health Organization (WHO 2014), it was revealed that the mean time detection of MDR-TB after report of symptoms was less that one day for Xpert MTB/Rif and more than 30 days for solid culture.

5.4 Delay in Initiation of Treatment

From the study, there was late initiation of treatment for 59 % (n=227) of confirmed MDR-TB patients. The average duration between MDR laboratory diagnosis by using DST method and starting treatment was about 83 days (SD=122 days) and the average duration between laboratory diagnosis by using Gene Xpert method and start of treatment was found to be 40 days (SD=34 days). These findings suggest that there has been an improvement in the administrative and logistical barriers to getting people on treatment. However, this is still too long of a delay with consequences of onward spread of infection. The earliest time from laboratory diagnosis to the initiation of MDR TB treatment is set at 14 days (NTLP, 2013). This study has demonstrated that to a large extent this standard is not adhered to. Health system related factors such as weak monitoring of care for TB patients and shortage of healthcare workers might explain this failure. These findings are corroborated by findings from studies conducted in South Africa and Cameroon which found that the total time from DST diagnosis to treatment initiation was about 84 days in South Africa and 119 days in Cameroon. (Noeske *et al*. 2012).

In another study conducted in Bangladesh, the average time for diagnosis and treatment initiation was reduced to 4 to 5 days with Gene Xpert technique (Hossain *et al*., 2015).

5.5. Barriers to Early Diagnosis and Treatment

This study has established several barriers to early diagnosis and treatment of MDR-TB. These include:

5.5.1 Financial deficiency

Respondents pointed out that insufficiency of funds constitute a major barrier. This limitation affects the whole infrastructure for diagnosis and treatment – which ranges from low staff motivation to ill-equipped laboratories. This deficiency has been there despite donor support in the area of diagnosis in some healthcare facilities. Donor dependency and sustainability concerns should also be addressed. As a factor, financial barriers in diagnosis and treatment of MDR-TB patients has been documented elsewhere in the world, including revelations from a study conducted to determine the global economic challenges associated with TB diagnosis and treatment (Hanrahan and Shah, 2014). In another study conducted in Vietnam, it was revealed that many TB testing units were unable to test samples using Xpert MTB/Rif as there were no financial mechanism in place for consumable procurement and sputum transportation (Hoang, 2015). It has also been observed globally, and especially in African countries, that many governments lack the funds to cover ordinary costs for case detection and treatment (Raviglione and Sulis, 2016).

The government through NTLP should advocate and solicit funding for these services by developing proposals and submitting them to international funding sources and increase ownership of the services by mobilizing domestic funds from different sources through its annual budgets. Without sustainable fiscal condition, there will always be delays in diagnosis and treatment of patients and this will in turn lead to unhealthy community.

5.5.2 Shortage of staff

Another barrier that was reported was inadequate number of staff working in both diagnosis and treatment institutions for MDR TB. This may be explained due to mal-distribution of the human resource for health which is observed in the country, poor workers emoluments especially in the public health sector, high attrition rates due to various reasons, as well as presence of ad hoc activities among the few staff. This combination results in a decrease in the number of bench operators and clinicians in healthcare facilities leading to delays in diagnosis and treatment, respectively. In these institutions, it has been reported that the level of burn out is very high, as it can be the case that one referral laboratory may be having 10 staff assuming the role of both bench operators and managers. The skills and awareness of updated TB/MDR-TB diagnosis and treatment is another gridlock and the scenario is more in the laboratory settings than in the treatment clinics. This finding concurs with the one observed in one study conducted in South Africa to determine the human resource crisis in diagnosis and treatment of MDR-TB (Wilson *et al.*, 2011).

Therefore, the Ministry of Health in collaboration with the regional and district authorities should ensure sufficient deployment of skilled personnel for TB/MDR TB diagnosis and treatment and strengthen capacity building to these staff to equip them with updated information on the ever-changing diagnostic protocols, technology and treatment regimes.

5.5.3 Failure to meet basic standards for laboratory bio safety

Respondents identified failure to meet basic standards for laboratory bio safety as another barrier. To date, sites for culture and DST are non-operational because of lacking necessary standards and bio safety measures. Only CTRL remains as the single institution where culture and DST are conducted at the required quality standards in the country. The rapid molecular testing by using GeneXpert machine was available in all 4 hospitals visited during the research but the challenge was that they were few in number and were having only some modules working while others were non-functional due to mechanical reasons and PPM was infrequent and unreliable. This situation has resulted into testing only a few samples and a delay in the testing protest.

The frequent unavailability of cartridges was another concern that was raised by all respondents during data collection for the study with the situation worsening amidst reduction in donor support in healthcare sector. Other difficulties facing the optimal use of Xpert machine in diagnosis of the TB/ MDR TB in most healthcare facilities include unreliable power supply, inadequate storage of test kits and improper calibration of modules. These facility-level institutional weaknesses in the diagnosis of MDR TB using the Xpert machine have been observed elsewhere around the globe. This barrier has been clearly elaborated in studies conducted by Hanrahan and Shah (2014) and Kirwan and others (2012) with both investigations suggesting that the implementation of this technology should be slowed down especially in resource-constrained countries like Tanzania. Poor ordering and forecasting of the reagents and drugs is another area which results into delays of both diagnosis and treatment initiation for MDR TB. This has been quantified by another study carried out in South Africa where inadequate ordering and forecasting skills led to more frequent testing stoppage and overstock wastage (Peters, 2015).

The government in collaboration with the institutions should seek the means of strengthening capacity for conventional culture and DST as the two still remain the most reliable – a gold standard – in confirming MDR TB status. This capacity building in MDR TB diagnosis can be possible by strengthening inventory and supply chain management while ensuring that there is budget support for the initial investment in machines and its infrastructures as well as supporting cost for cartridges and calibration.

5.5.4 Poor adherence to guidelines

The study also made the finding that there is a poor health workers' adherence to the guidelines for diagnosis and treatment of MDR TB. Many of the institutions visited had no readily available editions of the MDR TB guidelines released in 2013; they had the old version and even the use of the available guidelines was minimal. Some respondents said that they were using their prior knowledge from various training opportunities they have attended to diagnose and treat the patients and did not rely on the guidelines.

Such respondents justified their defense by stating that they were automatically following the guideline even if they did not read them because the patients were continuously diagnosed and treated, and that the treatment outcome was satisfactory. This non-observance of clinical guidelines in dealing with TB cases is further corroborated by a survey by the World Health Organization (WHO), among other studies, which concluded that clinicians often deviate from standards and internationally recommended TB management practices. These deviations include underutilization of the smear microscopy for diagnosis-generally associated with over reliance on radiography; use of non-recommended drug regimen with incorrect combinations of drugs and mistakes in both drug dosage and delaying duration of initiating treatment (Hopewell, 2014).

In another study conducted in Nigeria, it was observed that adherence of healthcare workers to the country's National Tuberculosis Program (NTP) guidelines for diagnosis and treatment of TB/MDR TB was apparently sub optimal and needed improvement (Oshi *et al*., 2014). There is a need for the government to make sure that the guidelines and policy on diagnosis and treatment are made available in the diagnosis and treatment institutions and efforts should be made to ensure that healthcare workers use them in the quest to fast track diagnosis and treatment of MDR TB.

5.5.5 Managerial constraints

The study has found no big challenge in terms of the institution effort in managing diagnosis and treatment initiation of MDR TB because most managers have specific knowledge, skills and proper training in monitoring performance of their institutions to this endeavor. The only constraint is the availability and devotion of these managers to the managerial and administrative components of the services which can guarantee timely decision making in issues of diagnosis and treatment of MDR TB to reduce delays.

5.6 Limitations of the Study

This study had the following limitations:

1. The quantitative component of this study used secondary data that was available in major hospitals handling MDR TB patients. The challenges in using this data were: poor recording of patients' information; and inappropriate and delay in transferring of information by healthcare workers from patients' case report forms to registers. Sometimes, laboratory results especially culture results are missing due to frequent breakdown of laboratory equipment. There are no quality control protocols in place to ensure all the information is filled in correctly and accurately. To minimize the impact of these challenges, the routinely collected data from the MDR-TB patients register at the Kibong'oto Infectious Disease Hospital (KIDH) was compared with those from CTRL laboratory registers maintained at the Muhimbili National Hospital (MNH). Moreover, information that was missing from the MDR-TB patient registers was collected from the MDR-TB Treatment cards and files as the way to obtain data triangulation.

2. The qualitative part of the study used the in-depth interviews to capture information from the key informants. The challenge was the occurrence of a *social desirability response bias* – that is the tendency of the respondents to answer questions in a manner that will be viewed favorably by the interviewers. It took the form of over-reporting or under-reporting institutional barriers which may have happened to compromise the interpretation of the institutional barriers as well as individual differences. This challenge was minimized by explaining to respondents that the study was not meant to be a witch hunt for the wrong doers and that their confidentiality was maintained throughout the interview.

CHAPTER 6: CONCLUSION AND RECOMMENDATION

6.1 Conclusion

From the study, it has been evident that the magnitude of MDR-TB diagnosis and treatment delay in Tanzania is still high regardless of the increasing number of patients who are tested by using different diagnostic methods. The duration from testing and receiving result to starting treatment has not decreased despite the adoption and use of modern techniques like Gene Xpert, Hain or LPA. Therefore, this study suggests that there need of paying attention to the factors contributing to the delays including those in the healthcare system. That is, interventions targeting late diagnosis and treatment of MDR TB should take the identified institutional barriers into account.

6.2 Recommendations

From the study findings and analysis, the following recommendations are made: -

1. **On diagnosis and treatment of MDR-TB:** More investment in improving laboratory capacity for rapid DST and for operational research into factors that can improve patient diagnosis and treatment are urgently required. Therefore, major fiscal deliberations from domestic sources and donor support is required in efforts to improve the staffing, data management and laboratory and hospital infrastructure in the country for effective implementation for optimal results towards the elimination of TB/MDR-TB.

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2. **On drugs, equipment and supplies:** The observed frequent stock out of drugs tends to affect the timing for initiating patients into treatment. The government should ensure constant supply of recommended standard MDR-TB regimen at treatment facilities in order to achieve early treatment initiation. Furthermore, the available diagnostic equipment and machines, such as Gene Xpert, prove inadequate to cater for the increasing number of TB suspects. Therefore, the government should scale-up the GeneXpert distribution to cover all regions and districts as this will help to increase TB/MDR-TB case detection rate and early treatment initiation. The frequent stock out of cartridges and other supplies hinders the early detection of the MDR TB cases.

3. **On human resource for health:** The government through the Ministry of Health should recruit enough healthcare staff so as to improve the provision of healthcare services to MDR TB patients. There is a critical shortage of healthcare personnel in diagnostic institutions as well as in treatment clinics. Recruitment of staff should go hand in hand with their development especially in the areas of new technological advancement like Gene Xpert and new treatment regimes.
4. **On financial capacity:** Tanzania's healthcare sector has been facing financial challenges for several years. There is a need for the government its annual budgetary allocations to the health sector. The diagnostic laboratories and treatment centers for TB/MDR-TB require enough financial resources to be able to provide quality services to the people. Currently, the sustainability of the available tuberculosis and other healthcare programs is at stake because of the existing high donor dependence. The government should strive to own these services and therefore support them from its domestic fiscal system. But until then, these developing partners like KNCV, PATH, Management Development for Health (MDH) and the United States Agency for International Development (USAID) should be encouraged to support these services for the betterment of the people.
5. **On policy and guidelines:** Many patients receive substandard TB diagnosis and treatment at delayed circumstances due to providers in the facilities not observing the established policies and guidelines. The efforts to minimize erratic diagnosis and treatment should be emphasized on the correct use and adherence to these guidelines. Laboratory technicians and clinicians should be prepared to rely on these guidelines in their day to day dealings with TB/MDR-TB suspects and patients. The government should be innovative in ensuring that there is constant availability of guidelines to the healthcare workers such as converting the paper based guidelines into electronic form where they can access it through the web portal or mobile applications because the traditional way of providing paper based guidelines is not working very well.

6. **Future research:** Operational research for improvement of MDR-TB management – like the one that will determine factors that can improve facility level institutional capacity to early diagnosis and treatment of MDR-TB – is one area for as future research.

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8.0 APPENDICES

APPENDIX I: CONSENT FORM ENGLISH VERSION

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES(MUHAS)
DIRECTORATE OF RESEARCH AND PUBLICATIONS.

STUDY ON ASSESSMENT OF DELAY IN DIAGNOSIS AND TREATMENT OF MULTI-DRUG TUBERCULOSIS: MAGNITUDE AND ASSOCIATED INSTITUTIONAL BARRIERS

Dear Sir/Madam

You are hereby invited to participate in a study conducted by John Sijaona who is a student at Muhimbili University of Health and Allied Sciences. John Sijaona is conducting this study for his Masters Dissertation.

Your participation in this study is entirely voluntary. You should read the information below and ask questions about anything you do not understand, before deciding whether or not to participate in the study. You are being asked to participate in this study because you are …….. working at Dar es Salaam/ Mbeya / Mwanza /Kilimanjaro at…….. hospital.

PURPOSE OF THE STUDY

The purpose of the study is to explore institutional barriers contributing to the delay in diagnosis and treatment of Multidrug resistant Tuberculosis patients. We hope to use all the information from this study to understand these barriers contributing to delay in diagnosis and

treatment of Multidrug resistant Tuberculosis patients. You will be informed of the findings through the planned means of results dissemination through publication and thesis for academic purpose.

VOLUNTARY PARTICIPATION

Please note that your participation in this study is voluntary and you have the right to refuse to consent. If you agree to join this study, you will be required to sign this consent form and answer the question that you will be asked by the interviewer.

BENEFITS

There are no direct benefits for participating in the study. However the findings from the study will derive key factors leading to delay in diagnosis and treatment of Multidrug resistant Tuberculosis patients. This will help the administration, policy makers and health system in general to put in place the best system to improve diagnosis and treatment of multidrug resistant patients.

RISKS AND DISCOMFORT

There are no risks or discomforts involved in this study. Participants will be asked questions through in depth interviews that they will be able to give their views and ideas concerning the study.

COMPESATION FOR TIME

You will not receive any payment or other compensation for participation in this study. There is also no cost to you to participate in the study.

CONFIDENTIALITY

Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or as required by law. We will not use your name in any of the information we get from this study in any way we think is best for publication or education. Any information we use for publication will not identify your name.

CONSENT FORM

I confirm that I have read carefully and I have understood the information provided and consent to participate in the study. I am aware that I can freely withdraw from this study anytime I wish to do so.

Whom to contact if you have any question about the study

If you ever have questions about this study, you should contact the Principal Investigator John Sijaona, from Muhimbili University of Health and Allied Sciences, P.O .Box 65001, Dar-es-salaam. If you ever have questions about your rights as a participant, you may call Prof. Said Aboud Chairman of the Research and Publications Committee, P.O. Box 65001, Dar es Salaam. Tel: 2150302-6.

Do you agree? Yes…….. No……

Participant agrees ……..... Participants does not Agree. ……...…

I, …… Have read the contents of this consent form and my questions have been adequately answered. I therefore agree to participate in this study.

Signature of the participant ……. Date ……

Signature of the interviewer ……..... Date ……

APPENDIX 2: RIDHAA YA KUSHIRIKI KATIKA UTAFITI (KISWAHILI VERSION)

CHUO KIKUU CHA SAYANSI ZA AFYA MUHIMBILI

KURUGENZI YA UTAFITI NA MACHAPISHO

Habari,

Nakukaribisha kushiriki katika Utafiti unaofanywa na John Sijaona mwanafunzi kutoka katika Chuo kikuu cha Sayansi za Afya cha Muhimbili. John Sijaona anafanya utafiti huu kwa ajili ya Stashahada yake ya pili.

Kushiriki kwako katika utafiti huu ni kwa hiari; Unatakiwa kusoma taarifa zote katika fomu hii na kama kuna swali kuhusu jambo lolote ambalo halikueleweka unaweza kuuliza kabla hujaamua kushiriki au kutokushiriki katika utafiti huu. Umeombwa kushiriki katika utafiti huu kwa kuwa ni mmoja wa wafanyakazi ambao wanafanya kazi kama……..katika hospitali ya mkoa/kanda ya Dar es Salaam/ Mbeya / Mwanza /Kilimanjaro.

MADHUMUNI YA UTAFITI

Dhumuni la utafiti huu ni kuangalia vikwazo mbali mbali vya kitaasisi zinazotoa huduma za afya vinayopelekea wagonjwa wa kifua kikuu sugu kuchelewa kufanyiwa uchunguzi na kuanzishiwa matibabu mapema.

USHIRIKI

Ushiriki wako katika utafiti huu ni wa hiari na una haki ya kukataa kushiriki katika utafiti. Kama umekubali kushiriki utatakiwa kuweka sahihi yako katika fomu hii na kujibu maswali utakayokuwa unaulizwa na msahili.

FAIDA

Hamna faida ya moja kwa moja kwa wewe kushiriki katika utafiti huu. Ila matokeo ya utafiti huu yatasaidia watawala katika sekta ya afya,watunga sera na mfumo mzima wa afya kuweza kutafuta njia mbadala za kuwezesha kuwafanyia vipimo na kuwapatia dawa bila kuchelewa wagonjwa wataokuwa wanahisiwa kuwa na kifua kikuu sugu.

HASARA

Hakuna hasara za moja kwa moja zitakazotokana na utafiti huu.Washiriki wataulizwa maswali kwa mahojiano na msahili ambapo watakuwa na uhuru wa kutoa majibu na mawazo yao kutokana na maswali watakayoulizwa.

MALIPO

Hakutakuwa na malipo yoyote kutokana na ushiriki wa utafiti huu na pia kama mshiriki hutakuwa na gharama zozote za yeye kushiriki katika utafiti huu.

USIRI

Taarifa zote zitakazokusanywa zitashughulikiwa kwa usiri wa hali ya juu na pia zinatolewa kwa ruhusa yako maalum kutokana na taratibu na sheria. Jina lako halitatumika mahali popote katika utafiti huu.

FOMU YA UTAFITI

Nakiri kwamba nimesoma maelezo yote kwa umakini na nimeelewa kila kilichoandikwa katika fomu hii. Ninaelewa kwamba ninaweza kujitoa muda wowote nitakaotaka kujitoa.

MAWASILIANO

Kwa mawasiliano zaidi kuhusu utafiti huu Unaweza kuwasiliana na mtafiti, John Sijaona kutoka chuo kikuu Muhimbili, S.L.P 65001,Dar es Salaam au kama kuna maswali kuhusu haki zako kama mshiriki unaweza kuwasiliana na Profesa Said Aboud, Mwenyekiti wa Idara ya Utafiti na Machapisho ,S.L.P 65001, Dar es Salaam. Namba ya simu 2150302-6.

Je Unakubali Kushiriki? Ndio..... Hapana.....

Mshiriki amekubali..... Mashiriki amekataa.....

Mimi, …… Nimesoma maelezo yote katika fomu hii na maswali yangu yameweza kujibiwa.Nakubali kushiriki katika utafiti huu.

Sahihi ya Mshiriki..... Tarehe ……

Sahihi ya Msahili ……..... Tarehe ……

APPENDIX 3 – DATA RECORDING TOOL

RESEARCH TO ASSESS DELAY IN DIAGNOSIS AND TREATMENT OF MULTI-DRUG TUBERCULOSIS: MAGNITUDE AND ASSOCIATED INSTITUTIONAL BARRIERS

Checklist number: .....

Name of Organization: .....

Type of Organization: .....

Service: ……..

Date of Review: ..... Name of Reviewer: …….

Data recording tool (Laboratory Registers, MDR TB registers, Patients files)

Instruction: Enter the dates in the parameter asks about dates and YES or NO in other parameters. Enter the patient serial numbers starting from 1.

Patient Identifier	Date of reporting first symptom	Date of MDR TB suspicion	Sample sent for DST	Sample sent for Xpert	Date sample sent for DST/Xpert	Date received results	Date initiated into Treatment

APPENDIX 4: KEY INFORMANT INTERVIEW GUIDE

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES (MUHAS) DIRECTORATE OF RESEARCH AND PUBLICATIONS

RESEARCH TO ASSESS DELAY IN DIAGNOSIS AND TREATMENT OF MULTI-DRUG TUBERCULOSIS: MAGNITUDE AND ASSOCIATED INSTITUTIONAL BARRIERS

IDENTIFICATION

NAME OF THE DEPARTMENT ……..

Serial No.…….

Date; ……

Age ……years…….

Sex……

Education Level ……..

Job Title …….

INSTRUCTIONS TO INTERVIEWER

1. The interview will be conducted in Privacy.
2. Introduce yourself and assign an ID number to the interviewee.
3. The interview will take approximately 25 to 30 minutes.
4. Every bit of the interview should be clearly tape recorded and notes will also be taken to compliment recorded interviews.

INTERVIEW GUIDE.

1. How long have you worked in TB department?

- *Probe on satisfaction of working place.*
- *Probe on day to day roles and responsibility as far as TB diagnosis and treatment is concerned.*

2. Testing Capacity(Understanding, Knowledge and experience)

- *Have you ever receive any training on diagnosis and treatment of MDR TB patient*
- *Probe when and for how long?*
- *What is your experience in MDR TB diagnosis and treatment?*
- *Can you explain are little bit on the diagnosis and treatment of MDR TB cases according to the available guidelines?*

3. We understand that as an institution you might have been facing several barriers during diagnosing and treating MDR TB cases, what are your views on this?

- *Probe about Resources (Availability of health workers, Funding, Sample transportation, availability of reagents, and drugs)*
- *Probe about the Capacity of the institution in terms of diagnostic equipments especially availability and condition of Gene Xpert machine, LPA, Hain Test.*
- *Probe on the Managerial efforts, responsiveness and accountability towards diagnosis and treatment of MDR TB cases*
- *Probe on the MDR TB data management (Registration of cases, record keeping, use of available computerized databases)*
- *Probe on any other institution barrier*.

4. What is your suggestion to overcome those barriers?

5. What do you think are perceived benefits of timely diagnosis and treatment of MDR TB cases to your institution?

6. Can you suggest any policy recommendation as far as the diagnosis and treatment of the MDR-TB is concerned?