PREVALENCE AND RISK FACTORS ASSOCIATED WITH TUBERCULOSIS AND DRUG RESISTANCE-TUBERCULOSIS AMONG ILLICIT DRUG USERS IN TEMEKE, DAR ES SALAM, TANZANIA

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ABSTRACT

Tuberculosis (TB) is among ancient diseases which for over 4000 years has been affecting mankind. Tanzania is among the 22 TB high burden countries despite government's efforts to fight the disease. Illicit drug users (IDU) constitute the population at high risk of harboring TB infection in the community. A cross sectional study was conducted between April and August 2020 to investigate the prevalence and risk factors associated with TB and drug-resistant TB amongst illicit drug users in Temeke district, Dar es Salaam. A total of 384 IDUs were recruited, each consenting participant providing spot sputum sample which was analyzed using GeneXpert, smear microscopy and LJ culture at Central TB reference laboratory (CTRL) in Dar es Salaam. Information on IDUs was obtained through structured Questionnaires and analyzed using univariate analysis in General Linear Model, variables with *p*-value < 0.2 were further analyzed using Binary Logistic Regression using IBM SPSS Version 20, variables with *p*-values < 0.05 were considered statistically significant. Overall, TB prevalence among IDUs was 9.89% which was significantly high compared to the reported TB prevalence of 0.25% in Tanzanian general population in 2018. Prevalence of TB among active IDUs was 16.15% and IDUs under methadone was 3.6%. Prevalence of Drug Resistance TB was found to be 2.43% for overall IDUs, among active IDUs was 3.23% and 0% for IDUs under methadone treatment. Previous TB treatment interference, HIV positivity and active illicit drug use were the risk factors significantly associated with TB infection, with (*p*=0.001, OR=140. 6, 95% CI=17.4-1129.9), (*p*=0.024; OR=2.2, 95% CI=1.4-3.3) and (*p*=0.004, OR=5.1, 95% CI=2.2-11.9) respectively. These findings call for immediate intervention strategies specifically focusing amongst population at high risk of acquiring and spreading TB, through ensuring early diagnosis and proper treatment to avoid long transmission time of the disease in communities.

DECLARATION

I, Aziza Ahmed Said, declare to the Senate of Sokoine University of Agriculture that, this dissertation is my own original work done within the period of registration and that it has neither been submitted nor being concurrently submitted in any other institution.

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DEDICATION

I would like to dedicate this thesis to my mother Ms. Awena Mohammed for the support and taking good care of my children for all years I had been pursuing my MSc. Studies.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

LIST OF ABREVIATIONS AND ACRONYMS

χ^2	Chi- square
CDC	Centre of Disease Control and Prevention
CTRL	Central tuberculosis reference laboratory
EMCDDA	The European Monitoring Centre for Drugs and Drug Addiction
HBC	High burden country
HIV	Human Immunodeficiency Virus
IDUs	Illicit Drug Users
IgG	Immunoglobin G
IgM	Immunoglobin M
MDR-TB	Multi Drug Resistance-Tuberculosis
MTB	*Mycobacterium tuberculosis*
MTC	*Mycobacterium tuberculosis* complex
MUKIKUTE	Mapambano ya Kifua Kikuu na Ukimwi_Temeke
SACIDS-ACE	Southern African Centre for Infectious Disease Surveillance - Africa Centre of Excellence in Infectious Diseases of Humans and Animals
Std	Standard deviation
TB	Tuberculosis
URT	United Republic of Tanzania
WHO	World Health Organization
XDR-TB	Extensive Drug Resistance- Tuberculosis

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background Information

Tuberculosis (TB) is one of the ancient diseases which for over 4000 years has been affecting mankind (Thapa *et al.,* 2016). It is a chronic airborne disease caused by the acid fast bacilli bacteria, members of *Mycobacterium tuberculosis* complex (MTC). Commonly, TB affects lungs particularly (pulmonary TB) but may also affect other organs in the body such as brain, intestines, kidneys or the spine (miliary TB) (Thapa *et al.,* 2016). Although TB treatment had been developed and used for decades but researches show that globally about one million people are still dying each year due to TB, with majority being from low and middle income countries especially in sub-Saharan Africa which has a high incidence of TB (Otokunefor *et al.,* 2018). In 2014 there were about 9.4 million TB new cases reported and 1.5 million deaths related to the disease worldwide (Navarro *et al.,* 2016).

Illicit drug users (IDU) have been associated with high prevalence of TB and HIV, and emergence of multi drug-resistance TB (MDR-TB) which is the result of human related factors and poor life style (Gobena *et al*., 2018). Tanzania Ministry of Health and Social Welfare reported TB incidence of 253 per 100 000 in 2018 (URT, 2019).

Therefore, this study was conducted to establish the prevalence of TB and risk factors associated with TB among IDUs in Temeke district. Results from this study will serve as a base-line data in designing and developing effective TB control programs particularly among the IDUs and hence help to achieve Tanzania's five years development plan strategy on improving TB and infectious diseases control URT, 2016).

1.2 Problem Statement and Study Justification

Tuberculosis is the 9th leading cause of high mortality worldwide (Glasauer *et al*., 2019). Reports indicate that deaths related to TB worldwide stood at 1.5 million in 2014 (Navarro *et al*., 2016) with Tanzania being among the 22 high burden countries (HBCs) with respect to the number of TB cases. The burden of TB in Tanzania during 2017 was 69 623 notified cases (URT, 2019) and IDUs are among the high risk population for TB disease due to physiological effects of drug use, environmental factors and risk behaviors conducted by illicit drug users. IDUs are associated with numbers of epidemiological factors which offer additional risk factors for TB transmission such as tobacco use, homelessness, alcohol abuse and incarceration (Deiss *et al.*,2009). Emergence of MDR-TB strains is a major challenge in developing effective measures for TB control and treatment in Tanzania and worldwide, because drug resistance TB requires prolonged treatment which is costly and with more adverse effects. An effective TB control program requires early diagnosis, immediate and effective drug initiation to reduce transmission time to the community. Hence, this study was designed to determine the prevalence of TB, drug resistance TB and risk factors associated with TB among illicit drug users in Temeke district, Dar es Salaam, in order to generate data that might be useful to generating or making of TB control strategies, particularly among IDUs in Tanzania.

1.3 Research Objectives

1.3.1 Main objective

This study was conducted with the general objective of establishing the status of TB and risk factors among Illicit Drug Users in Temeke district, Dar es Salaam.

1.3.2 Specific objectives

i. To determine the prevalence of TB and DR- TB among illicit drug users in Temeke district, Dar es Salaam.

ii. To assess possible risk factors associated with TB infection among illicit drug users in Temeke district, Dar es Salaam.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Tuberculosis (TB) and Causative Agent

TB is a chronic airborne disease caused by acid fast bacilli known as *Mycobacterium Tuberculosis. Mycobacterium tuberculosis* is carried in air droplets (aerosols) 1– 5 microns in diameter which are generated when a person who has pulmonary or laryngeal TB disease cough, sneeze or shout, these droplets can remain suspended in the air for several hours (URT, 2019). *M. tuberculosis, M. bovis, M. africanum, M. microti, M. caprae, M. pinnipedii, M. canetti* and *M. mungi and Bacille Calmette-Gueri* (BCG) together comprise what is known as the *Mycobacterium tuberculosis* complex (MTC). All members of MTC can cause human TB and they differ in their host ranges, epidemiology and clinical manifestation in humans. However, studies show that they are 99% DNA homologous (CDC, 2013; Hoza *et al*., 2016). *M. tuberculosis* strains are presumed to have coevolved with ancient hominids and continue to evolve even today (Yimer *et al*., 2015) and *M. tuberculosis* strains cluster into seven lineages, each associated with specific global geographical locations which are; lineage 1 is Indo-Oceanic, lineage 2 is East Asian, including "Beijing", lineage 3 is Central Asian (CAS)/Delhi, lineage 4 is Euro-American including Latin American-Mediterranean (LAM), Haarlem, X type and T families, lineage 5 and lineage 6 are West African 1 and West African 2 respectively and lineage 7 (Comas *et al*., 2014).

2.2 Drug Resistance Tuberculosis (DR-TB)

TB treatment regime loses its effectiveness due to emergence of drug-resistance TB strains posing a huge challenge worldwide (Glasauer *et al*., 2019). Drug resistance TB requires prolonged treatment with more "toxic" drugs which are in turn costful and with

more adverse effects (Hoza *et al*., 2015). MDR-TB is a major public health concern in third world countries attributed by poor diagnostic capacity, delayed diagnosis and poor adherence to effective TB treatment which attribute to unsuccessful TB control programs (Mesfin *et al*., 2018). MDR-TB Multi-drug resistant tuberculosis is mainly a man-made crisis related to multiple factors such as poor drug supply management, inappropriate guideline, none adherence, meager infection control practice, improper drug storage conditions, wrong dose or combination, lack of information and monitoring of treatment (Gobena *et al*., 2018).

The first-line anti-TB drugs include ethambutol (E), rifampicin (R), isoniazid (H), pyrazinamide (Z) while anti-TB injectable drugs consist of capreomycin, kanamycin, amikacin) and fluoroquinolones (e g; ofloxacin) (Frontieres Medecins Sans, 2015). Drug resistance TB can be mono-resistant TB which is resistance to one of the first-line anti-TB drugs, poly drug-resistant (PDR) which is resistance to two or more of the first-line drugs but not R and H together, multidrug-resistant (MDR) TB which is resistance to at least R and H and extensively drug-resistant (XDR) which resistance to R, H in parallel with resistance of one or more of the anti-TB injectable drugs (WHO, 2018). *Mycobacterium tuberculosis* Complex (MTC) strains differ in their drug sensitivity as some strains are more resistant than others to anti-TB drugs, “Beijing” strain is an example resistance strains as it frequently acquires drug resistance (Hanekom *et al*., 2011). Strains of MTC circulating in Tanzania might be are of different lineages as a study conducted in 2016 showed that in Northern parts of Tanzania alone there were 18 distinct spoligotype MTC strains among TB patients where by 70% were from “modern” strains and 30% were ancestral lineage (Hoza *et al*., 2016).

2.3 Illicit Drugs

The term “illicit drugs” refers to highly addictive and illegal substances such as heroin, marijuana and meth (Juergens, 2020). Illicit drugs can occur naturally (marijuana and cocaine) or prepared from naturally occurring substances (heroin) also can be totally synthetic like amphetamines (Houck and Siegel, 2015). Illicit drugs fall into four categories by the way they affect bodies including depressants, narcotics, hallucinogens and stimulants. Depressants drugs slow down the function of the central nervous system, hallucinogens affect senses and change the way user see, hear, taste, smell or feel things while stimulants speed up the function of the central nervous system (Houck and Siegel, 2015) and one drug can fall into all categories such as opioids. Illicit drugs can be applied orally, through injections, smoking or sniffing and same body effect is achieved, cannabis is the most widely used illicit drug with an estimation of about 192 million users worldwide while opioids are the most harmful which accounts for 76% of drug use disorder-related deaths globally (Ryan *et al*., 2019). Use of illicit drugs has been associated with an increased overall rate of mortality and with an elevated rate of a number of individual causes of death attributed by illicit drug addiction which is AIDS, overdose, suicide and trauma. For example in 2000, the median number of global deaths attributed to illicit drugs estimated was 194058 (Degenhardt *et al*., 2004).

2.4 Behaviors of Illicit Drug Users

Many illicit drugs pose serious health risks even when taken in small dose furthermore some drugs can cause an addiction after a single use. Commonly the decision to use one of these drugs for the first time is usually a voluntary but unexpected addiction can make the decision to quit later significantly harder. An addiction to illicit drugs changes the way a person’s brain works and consequently the way they think and act. The beginning of an illicit substance abuse disorder is marked by a physical dependence which recognized by

a tolerance to and withdrawal symptoms from the drug of abuse. Tolerance occurs when you need more of the substance to get the same effects as when you started and when a tolerance is established, a person may experience withdrawal when they stop using the substance. Withdrawal symptoms are severe and can include heart palpitations and seizures depending on the type of drug used.

The second part of an abuse disorder involves a psychological dependence on the substance. This is characterized by a subjective feeling that the user needs the drug to feel normal. There is often a desire to stop using the drug as well as prioritization of its use over social and familial responsibilities. Nevertheless, a person suffering from an illicit substance abuse disorder recognizes the negative consequences of their drug use but they feel unable to stop on their own. Illicit drug use disorders can lead to multiple behavioral problems which are both in the short - and long-term such as paranoia, aggressiveness, hallucinations, addiction, impaired judgment, impulsiveness and loss of self-control. Excessive illicit drug use causes dramatic changes in the brain which can disrupt a person’s psychological well-being and may drive a person to behave differently than they would normally, causing them to make self-destructive decisions such as driving under the influence and suicide. Negative impact on IDUs life include damages to relationships with family, friends and romantic partners, trouble staying on top of daily responsibilities and social obligations and financial hardships due to spending large amounts of money to maintain a drug habit.

2.5 Methadone Treatment

Methadone is an opioid like heroin or opium which has been used to treat opioid dependence since the 1950 (WHO, 2009). The opioid dependent patient takes a daily dose of methadone as a liquid or pill which reduces their withdrawal symptoms and cravings for opioids. Researches show that methadone treatment reduces crime rates, improves employment and family relationships (Sheerin, 2004). Methadone is administered orally and is absorbed slowly through the gastro intestinal tract (GIT), it has ideal properties for the long-term treatment as opioid agonist medication (Moran *et al*., 2018).

Currently, methadone treatment is highly used in treatment of Illicit drug addiction globally and example is the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, 2016) reported that "In Europe, 61% of clients who were IDUs receive methadone resulting in it being the most frequently administered agonist therapy". Methadone treatment program reduces criminal activity and improves social well-being of drug users in China as well as quality of life (Teoh, 2016).

2.6 TB and DR-TB among Illicit Drug Users

Illicit drug addiction is a chronic relapsing brain disease that causes compulsive illicit drug seeking and use, despite the harmful consequences to the addicted individual and to the society (Saeed *et al*., 2018). Although the initial decision towards illicit drug use is voluntary for most addicts, the brain changes that occur over time challenge the self-control and hamper the ability to resist intense impulses to take the drugs (Saeed *et al*., 2018). IDUs have been associated with higher prevalence of TB disease due to physiological effects of illicit drug use along with the environment and risk behaviors of IDUs (Friedman *et al*., 2003). In vitro studies have demonstrated the deleterious effects of drug use on the immune system (Friedman *et al*., 2003). Studies demonstrated biological

evidences supporting direct impairment of cell-mediated immunity due to opiates (Wei *et al*., 2003). Thus impaired immune system may result into high risk of TB infection and other opportunistic diseases among IDUs.

2.7 Diagnosis of TB and MDR-TB

TB diagnosis can be achieved by either direct or indirect methods. Direct methods include smear microscopy, culture, Mycobacterium speciation by biochemical assays, Mycobacterium antigen detection by monoclonal sera, analysis of lipid composition by chromatograph and detection of DNA of Mycobacterium origin (CDC, 2013). Detection of IgG or IgM antibodies against Mycobacterium and Cellular immunity via skin tests are indirect diagnostic methods (CDC, 2013). The GeneXpert assay is an innovative tool for prompt detection of MTB and drug resistance and is definitely an attractive point of care test with high sensitivity and specificity with low turn round time of two hours which facilitates timely diagnosis and appropriate management of TB (Saeed *et al*., 2017).

2.8 Risk Factors Associated with TB Infection

The presence of an infected person in a community increases chances of TB spread to the population. Prolonged exposure to infection may be due to either health system-related factors such as delay in diagnosis or host-related factors such as diabetes, alcohol, malnutrition and indoor air pollution (Narasimhan *et al*., 2013; Kalonji *et al*., 2016).

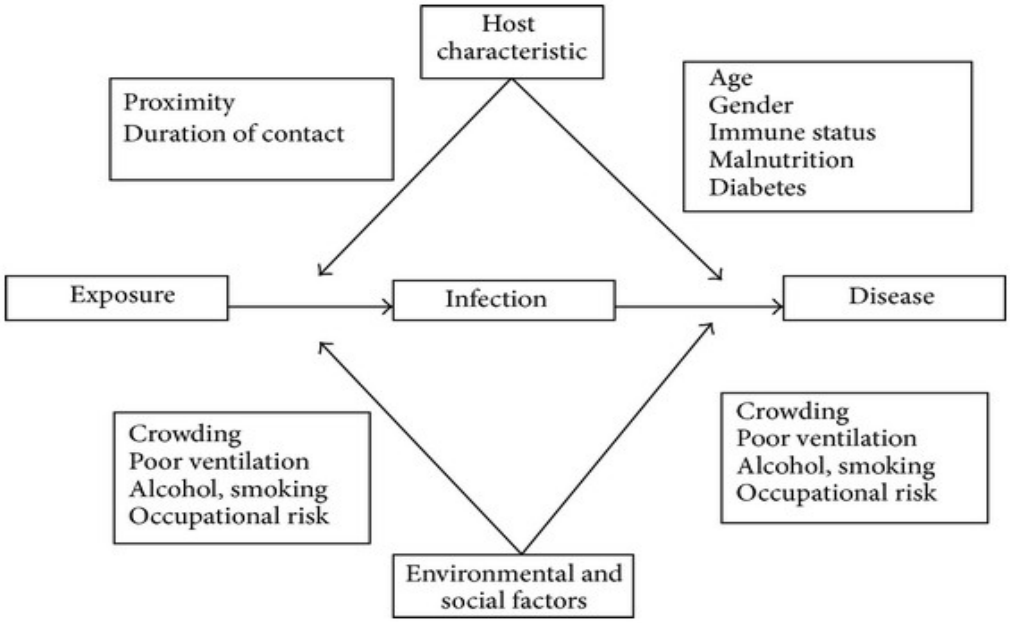

Figure 1: Summary of risk factors associated with TB

Source: Narasimhan *et al*. (2013).

2.9 Risk Factors Associated with TB among IDUS

Illicit drug users are at high risk for TB infection an account of their daily risk behaviors and the evidence from contact investigations and molecular epidemiologic studies demonstrates that a disproportionate incidence of TB disease among drug users results from TB transmission, with the presence of identical DNA patterns ("clusters") between TB isolates implying recent transmission among them (Deiss *et al*., 2009). In the study conducted in U S showed that an outbreak occurred at a methadone treatment program with one patient subsequently becoming the source case for a hospital outbreak of MDR-TB (Deiss *et al*., 2009). "Shot-gunning," a practice of inhaling then exhaling smoke directly into another's mouth, has been reported among of drug users which was implicated in a South Dakota TB outbreak (Mcelroy *et al*., 2003) which may attribute into TB transmission among themselves.

2.9.1 Cigarette smoking

Cigarette smoking and illicit drug use association had been well documented for over decades example is the study conducted in Hispanic country (Colombia, South America) 2003 showed a strong association between earlier daily cigarette smoking and later marijuana use, other illicit drug use and problems with drug use (Siqueira *et al*., 2003). Several studies have been conducted to examine the progression of drug use in youth including a cross-sectional study (Bailey, 1992) and a longitudinal study (Lai *et al*., 2000) and their results support the idea of a general pattern of progression from non-use to tobacco and alcohol use, to marijuana and finally to the use of illicit drugs (Kandel *et al*., 1992). A similar pattern of drug use has been found in various cultures in cross-sectional study (Adler and Kandel, 1981).

Besides cigarette smoking being able progress into illicit drug users but also is almost inescapable among illicit drug users although it had been strongly associated with lung diseases such as TB. A prospective cohort study conducted between 1992-2006 (14 years) in South Korea revealed evidences that smoking increases the incidence of TB, the mortality rates from TB disease and TB recurrence (Jee *et al*., 2009). In 2018, WHO reported that cigarette smoking increases the risk of contracting TB, recurrent TB and impairs the response to treatment of the disease (WHO, 2018). Smoking substantially increases the risk of TB and death from TB and more than 20% of global TB incidence may be attributable to smoking (WHO, 2009). A study conducted 2007 to 2012 in Northern Iran demonstrated that cigarette smoking was three times more frequent in TB patients, compared to healthy individuals (Alavi-Naini *et al*., 2012). Wen *et al*. (2010) reported that “smokers had very high TB mortality as much as nine times more than those who had never smoked, but once they quit, the risk reduced substantially and was similar with those who never smoked” and the same study showed that the 65% reduction of TB

mortality risk as the result of smoking cessation was substantial and statistically significant (Wen *et al*., 2010). Another study showed that TB risk could be reduced by nearly two-third if one quits smoking is a compelling evidence in highlighting the important role of smoking in TB control (Lin *et al*., 2008).

2.9.2 Homelessness

Homelessness is the condition whereby persons do not have customary or regular access to a conventional dwelling or residence (Rossi, 1987). Homeless person can be defined as a person living in the streets without a shelter or a person with no place of usual residence (Dias *et al*., 2017). Research conducted in Portugal 2017 showed that TB incidence among homeless persons was five times higher than among the non-homeless and even higher in regions with greater TB incidence among non- homeless persons (Bamrah *et al*., 2013; Dias *et al*., 2017).

Nevertheless, homeless people tend to sleep in overcrowding areas such as bus stands ghetto and ferry which increases high risk for TB transmission but also may sometimes end up under low ventilated places and impose a great risk of TB transmission. A study conducted in United States between 1994 and 2010 showed that the number of TB cases among persons experiencing homelessness decreased between 1994 and 2010 but the proportion of total TB cases that occurred among homeless persons remained stable 6%, and they were disproportionately represented in genotype clusters that suggested local transmission of TB which empirically supports the perception that homeless individuals had a higher TB burden (Bamrah *et al*., 2013).

2.9.3 Incarceration

Prison is a term used for any place of detention including centers for pre-trial and convicted prisoners as well as centers for juvenile offenders and illegal immigrants. On any day, it is estimated that the world's prisons hold 8-10 million prisoners, however 4-6 times this number passes through prisons each year and because of the high turnover of the population (WHO, 2018). Illicit drug users are very common in committing crimes hence makes a large population in incarceration and re- incarceration. Illicit drug users offenders are likelier to recidivate than those who are not, over half of substance-involved inmates have one or more previous incarcerations compared with inmates who are not illicit drug users (NASA, 2010). In order to break the cycle of re-arrests and re-incarceration requires breaking the cycle of illicit drugs addiction (NASA, 2010).

The level of Tuberculosis in prisons has been reported to be up to 100 times higher than that of the civilian population and tuberculosis cases in prisons may account for up to 25% of a country's burden of Tuberculosis (WHO, 2018). Occurrence of active tuberculosis (TB) in prisons is usually reported to be much higher than the average levels reported for the corresponding general population (Dara *et al*., 2009). Prisons which are located in developing countries, TB has been reported as the most common cause of death (Reyesa, 1997) because prisons conditions and set ups facilitate TB infection due to overcrowding, late case detection, inadequate treatment of infectious cases, high turnover of prisoners and poor implementation of TB infection control measures are all known factors contributing to transmission of *Mycobacterium tuberculosis*.

Prisons represent a reservoir for disease transmission to the community because the TB infection may spread into the general population through prison staff, visitors and close contacts of released prisoners (Niveau, 2006). The transmission dynamics between

prisoners and the general population has been hypothesized to play a key role in driving overall population-level TB incidence, prevalence and mortality rates (Stuckler *et al*., 2008).

2.9.4 Previous TB history

Previously treated patients with TB represent >15% of all patients with TB in large countries, such as India, China, and the Russian Federation, and in all areas with the highest TB burden (Zignol *et al*., 2015). A study conducted in Georgia Atlanta described that illicit drug use was one of the factors for TB re-currency in US born patients (Kim *et al*., 2017) and another study conducted in eight provinces of Vietnam showed that patients completing treatment for tuberculosis (TB) in high-prevalence settings face a risk of developing recurrent disease (Rutledge *et al*., 2018). The high prevalence of TB and longer periods of infectivity may further contribute to increased rates of TB transmission among drug users and may attribute into recurrence of TB among illicit drug users as most of them live in common areas.

2.9.5 HIV Seropositivity

Due to risk behavior conducted by illicit drug users as the psychological effect of illicit drug use are in high risk of HIV infection, such behavior include needle sharing and un protected sex activities. Example is the study conducted in Spain showed that almost half of HIV patients who participated in the study had used illicit drugs in the last 12 months, with cannabis and cocaine being the most frequent drugs used (Fuster-ruizdeapodaca *et al*., 2019). Someone infected with both HIV and TB is at least 10 times more likely to develop active TB, especially when their CD4 count is under 200. HIV infection is the most important risk factor for developing active TB, which increases the susceptibility to primary infection or reinfection and also the risk of TB reactivation for patients with

latent TB (Bruchfeld *et al*., 2015). AIDS patient the main feature of immunosuppression in AIDS patients is the manifest loss of CD4+ T cells in increased risk of developing active TB disease (Moir *et al*., 2011).

2.9.6 Alcoholism

Substance abuse involves the chronic use of alcohol and drugs and commonly a person who abuses alcohol has a greater risk of using at least one illicit drug such as marijuana, cocaine and heroin, a prolonged consumption of drugs and alcohol increases tolerance therefore requiring more of the substance to achieve the same desirable effects (Galbicsek, 2020). The association between alcohol use and TB has long been known, even before the discovering its etiological agent (Rehm *et al*., 2004). A book published by Benjamin Rush in 2018 showed established association between TB and alcoholism, the book stated that “TB and pneumonia as infectious sequel of sustained heavy drinking” (Rush, 2018).

2.9.7 TB treatment interference

Illicit drug use, homelessness and imprisonment affect the ability of patients to access health care and to take treatment (Story *et al.,* 2007) inconsequence may ensue interference of TB dosage treatment. Incomplete adherence to treatment showed significant association with TB recurrence, in the study conducted in eight provinces of Vietnam (Rutledge *et al*., 2018) Risk factors which have been identified for failure to complete TB treatment include lack of compliance to long treatment regimens, illicit drug use, homelessness and alcoholism (Friedman *et al.,* 2003).

Furthermore, non-adherence to TB treatment has been associated with drug resistance TB like shown by the study conducted in Arba Ethiopia which stated that failure of complete

TB treatment increases the risk of development of drug-resistant strains and spread of TB in the community which in turn increases morbidity and mortality rates of TB disease (Addisu *et al*., 2018). Another study shows that prior but ineffective treatment is a strong predictor of drug resistance TB (Wells *et al*., 2007). One of the factors known of emerging of MDR-TB is known to be a previous history of TB treatment and interruption of first-line treatment (Elduma *et al*., 2019).

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Area

Temeke district is one of three districts of Dar es Salaam city located in the southern part of Dar es Salaam covering an area of 786.5 km². The district is bordered by an Indian Ocean in the eastern part of Temeke and Coast region in the south and west. According to the United Republic of Tanzania National Census Temeke district has a population size of 1 368 881, with males being 669056 and female being 699825 (URT, 2012). Administratively Temeke District is divided into 24 wards.

3.2 Study Design and Sample Collection

A cross sectional study was conducted between April and August 2020 where a total of 384 illicit drug users were recruited. Spot sputum samples were collected from each consenting individual and all samples were kept in a cool box before transported to the Central TB Reference Laboratory (CTRL), at Muhimbili, Dar es Salaam for analysis. The morning sputum samples could not be collected due to ill behaviors of illicit drug addicts.

A structured questionnaire (Appendix 1) was used to collect demographic information of the study participants and to assess the risk factors associated with TB and drug-resistant TB amongst illicit drug users amongst the study population. Consenting candidates were asked to provide information on demographic bio data, risk factors such as cigarette smoking, previous TB history, residence type, number of individuals sharing a sleeping area, HIV status, method of illicit drug administration, status of drug use whether active or under methadone treatment and whether has been in incarceration places or not were included.

3.3 Sample Size

The sample size was calculated based on the Cochran formula: $\left[n=\frac{Z^2\,pq}{l^2}\right]$

Where: Z is standard (1.96), P is the unknown prevalence (50%) and q is $[1-p]$and L is the desired level of precision (i.e. the margin of error) 0.05. A of 50% prevalence was used since the prevalence of TB among IDUs in Tanzania and in this study population is unknown. From formula above: $\left[n=\frac{\left(1.96^2\right)\left(\frac{50}{100}\right)\left(1-\left(\frac{50}{100}\right)\right)}{0.05^2}\right]$ Therefore, the numbers of IDUs recruited for the study was 384.

3.4 Detection of MTB by GeneXpert

Sputum samples were first analyzed for detection of MTB and drug-resistance TB by using GeneXpert as per manufacturer's instructions. Briefly, each sample was placed into a separate well labeled, leak proof, 50 ml falcon tube then the sample reagent (SR) containing NaOH and isopropanol was added to each sample in the falcon tube in 2:1 ratio and shaken vigorously for 10-15 minutes to allow inactivation of MTB and liquefaction of sputum samples. After that the samples were incubated for 15 minutes at room temperature and finally, the samples were loaded into labeled cartridges and GeneXpert machine is allowed for to run automated assay which takes 90 minutes. Within GeneXpert machine double automated washing and filtration is done followed by ultrasonic lysis of captured microorganisms to release DNA molecules which are mixed with PCR dry reagents and finally hemi nested PCR amplification and detection occurs under which machine gives out the printable results (Negi and Das, 2015). Printable

results output were then recorded as per manufacturer's instructions as MTB detected or not detection for Rifampicin Resistance (RR) detection or not detected.

3.5 Sample Decontamination

Sputum samples were processed using Modified Petroff method as per WHO guidelines (WHO, 2014b) where by an equal volume of 4% NaOH was added to each sample and the screw cap tighted followed by vortexing for 30 seconds until a homogenous mixture was obtained and allowed to stand at room temperature for 15 minutes. Thereafter, samples were filled with distilled water up to 50 ml and mixed by shaking the tubes gently and the mixtures centrifuged at 3000g for 15 minutes. The supernatants were poured off and the pellets were vortexed vigorously to get a homogenized suspension. The suspensions were used 1ml for smear microscopy and 1ml for culture.

3.6 MTB Detection by Smear Microscopy

Auramine-Rhodamine staining method was used for smear microscopy where by each test sample was prepared by taking a drop of sample to prepare a small smear at the center of a microscope slide and heat fixed. Auramine stain was flooded on the smears and allowed to stand for 15 minutes, then rinsed with distilled water until no color remained. The smears were flooded again with 0.5% hydrochloric acid for about two minutes followed by washing with distilled water then counterstained by flooding the slides with potassium permanganate for about two minutes. Then slides were rinsed with distilled water and air dried before observation under the florescence microscope at 400X magnification and results were recorded as AFB positive or AFB negative.

3.7 Detection of MTB by LJ Medium Culture

All samples were cultured onto egg based Lowenstein-Jensen (LJ) pyruvate solid medium by putting about three drops of decontaminated test sample onto the media using a Pasteur pipette and incubated at 35-37^{o}C horizontally for 72 hours to get a uniform inoculum, thus was then incubated in vertical position for the eight weeks. Cultures were observed daily in the first week for signs of contamination and then once a week from the second week to eighth week as described in WHO guidelines (WHO, 2014a). Each sputum sample was inoculated into two slunt media.

3.8 Data Analysis

The software used to analyze data was IBM Statistical Package for the Social Sciences (SPSS) Version 20. Socio-demographic data were filled in Microsoft Excel 2010 spreadsheet before being analyzed using SPSS. Descriptive analysis in SPSS was used to analyse socio- demographic factors and prevalence of TB in each factor was obtained. The univariate analysis in General Linear Model used to check for associations between risk factors and TB positive diagnosis, cut-point to include variables in the multivariate models was set at p-value<0.2 and the variables selected were entered into the Binary Logistic Regression Model. Variables with p-value > 0.2 were not recruited in the Binary Logistic Regression Models. Binary logistic regressions were used to control the confounding effect of different variables while assessing the effect of each variable on the likelihood of TB positivity occurrence. To determine the model fitness of risk factors associated with TB infection Hosmer–Lemeshow statistic was used and variables with p-values < 0.05 were considered as statistically significant. During statistical analysis (binary logistic regression) both independent and dependent variables were used. Dependent variables was TB status while independent variables used were TB treatment

interference, previous TB history, incarceration, education level, IDU status and HIV status.

3.9 Ethical Consideration

Prior to this study ethical clearance was sought from the National Institute for Medical Research (NIMR), Dar es Salaam, Tanzania and the protocol for this study was reviewed and approved by the Ethical Committee of NIMR, Reference Number NIMR/HQ/R.8a/Vol. IX/3410. All participants gave their written consent to participate by signing or put thumb print on the consent form before being recruited in the study. In Minors under 17, non IDUs and patients under TB treatment for more than one month were excluded from the study.

CHAPTER FOUR

4.0 RESULTS

4.1 Demographic Characteristics among IDUs

A total of 384 participants including 192 active IDUs and 192 individuals under methadone treatment were recruited in this study. Overall males were 74.4% (n=286) and females were 25.6% (n=98) of all the participants. A total of 125 out of 286 males were under methadone treatment and 179 out of 286 were active IDUs, while 71 out of 98 females were under methadone treatment and 27 out of 98 were active IDUs. The median age in this study was 34 years, ranging from 17 to 55 years old with majority (50.0%) of the IDUs being at the age range of 31to 45 years old (Figure 2).

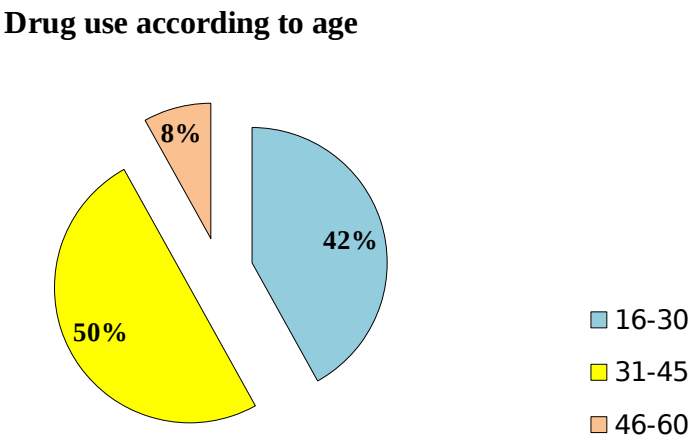

Figure 2: Distribution of IDUs according to age

4.2 Prevalence of MTB among IDUs at Temeke District

GenExpert results showed that MTB detected in 38 samples out of the 384 and one of them was Rifampicin resistance (RR). Smear microscopy showed that 35 samples were MTB positive and through culture method 38 samples were found to be MTB positive.
All samples which were MTB detected by GeneXpert also showed MTB positive growth in culture method. Hence total TB positive samples were 38 with seven being from IDUs under methadone treatment and 31 from active IDUs.

The overall TB prevalence among IDUs in this study was 9.9%$\left(n=\frac{38}{384}\right)$ at 95% confidence interval limits 0.071 - 0.133. Prevalence of TB among IDUs under methadone being 3.7% $\left(n=\frac{7}{192}\right)$ at 95% confidence interval limits 0.01 - 0.06 and for active illicit drug users being 16.2%$\left(n=\frac{31}{192}\right)$ at 95% confidence interval limits of 0.11-0.21.

About 71.1% (n=27) of the total MTB positive were new TB cases while 28.9% (n=11) had history of TB (recurrence cases). Among the active drug users' 57.9% (n=22) were new TB cases and 23.7% (n=9) had history of TB, whereby for IDUs under methadone treatment 13.1% (n=5) were new cases and 5.2% (n=2) had history of TB (Table 1). GeneXpert results for the DR-TB showed that one case was detected as RR out of the 38 positive cases among IDUs, hence prevalence of Drug resistance TB among IDUs (n=1) was 2.6%. RR detected sample was from active IDUs and hence active IDUs had drug-resistance TB prevalence (n=1) of 3.2%. Prevalence of DR-TB among IDUs under

methadone treatment was found to be 0% because none of the IDUs under methadone treatment showed DR-TB (n=0).

Table 1: Prevalence of TB in IDUs in Temeke Dar es Salaam, Tanzania.

Variable Category	TB positive	TB negative	Total (n)	Prevalence (%)
Age				
17-30	14	147	161	8.7
31-45	22	170	192	11.5
46-60	2	29	31	6.5
Gender				
Male	32	254	286	11.2
Female	6	92	98	6.1
Marriage status				
Single	25	225	250	10.0
Married	11	98	109	10.1
Divorced	2	23	25	8.0
Education				
Primary	29	284	313	9.3
Secondary	6	42	48	12.6
Illiterates	3	20	23	1.2
Residence				
Family house		65	71	8.4
Room renting	10	115	125	8.0
Non- specific	16	121	137	11.7
Ghetto	6	45	51	11.8
Shelter sharing				
1-10	24	242	266	9.0
11-20	14	97	111	12.6
21-30	0	6	6	0.0
Cigarettes smoking				
No	0	2	2	0.0
Yes	38	344	382	10
Incarceration				
No	4	23	27	14.8
Yes	34	323	357	9.5
TB history				
No	27	297	324	8.3
Yes	11	49	60	18.3
Previous TB-treatment interference				
Yes	11	1	12	91.7
No	27	345	372	7.3
Duration of illicit drug use (years)				
1-10	6	84	90	6.7
11-20	29	230	259	11.1
21-30	2	13	15	13.3

Duration of Methadone (months)				
0	31	161	192	16.1
1-12	5	121	126	4.0
13-24	2	64	66	3.0
Drug administration				
Smoking	3	46	49	6.1
Injection	1	35	36	2.8
Both	34	265	299	11.3
HIV status				
Negative	16	264	283	5.7
Positive	12	57	69	17.4
No answer	7	25	32	21.9
IDUs status				
Methadone	7	185	192	3.7
Active	31	161	192	16.2

KEY:
TB-Tuberculosis
IDUs -illicit drug users

4.3 Risk Factors Associated with TB among IDUs in Temeke District

The most socio-demographic factors analyzed among IDUs in this study showed no significant association with TB infection. Univariate analysis in General Linear Model factors with *p*-value<0.2 including TB history, previous TB treatment interference, education level, active illicit drug use and HIV positivity were further analyzed by a Binary Logistic Regression (Table 2) using references as follows;

i. For the TB treatment interference, the reference category was no history of TB treatment interference.

ii. For the previous TB history, the reference category was no history of TB.

iii. For incarceration, the reference category was no (never been incarceration).

iv. For education level, the reference category was primary education level.

v. For IDU status, the reference category was under methadone treatment

vi. For HIV status, the reference category was HIV negative.

A preliminary analysis suggested that the assumption of multicollinearity was met (tolerance). An inspection of standardized residual values revealed that there was only one outlier which was kept in dataset (Std residual =.2.9). The logistic regression model was statistically significant, χ^2 (7) = 70.43, $p < 0.0005$. The model explained between

16.8% (Cox and Snell R^2) and 35.3% (Nagelkerke R^2) of the variance in TB infection correctly classified 92.7% of cases. As shown in Table 2 previous TB treatment interference, active illicit drug use and HIV positivity contributed to the model while TB history and education level did not contributed to the model. Among IDUs the factors which were found to have statistical significance association with TB infection were previous TB treatment interference (p=0.001, OR=140. 6, 95% CI=17.4-1129.9), HIV positivity (p=0.024; OR=2.2, 95% CI=1.4-3.3) and active illicit drug use (p=0.004, OR=5.1, 95% CI=2.2-11.9). Other risk factors among IDUS investigated in this study showed no significant association TB infection.

Furthermore, incarceration of IDUs was found to have risk of one times more chance likely to have TB and lack of education was found to have the risk of two times more for TB infection among IDUs. In binary logistic regression the “Previous TB history” was the only risk factor which showed characteristics of confounder and it affected both the outcome of TB positivity and the risk of previous TB treatment interference.

Table 2: Selected risk factors associated with MTB infection among Illicit Drug Users in Temeke district Dar es Salaam, Tanzania

Variables	*p*-value	Odds ratio	Confidence interval (CI)	
			Lower limit	Upper limit
TB treatment interference	0.001*	140.6	17.4	1129.9
Previous TB history	0.314	2. 5	1.2	5.3
Incarceration	0.379	1.7	0.2	5.1
Education primary	0.073	-	-	-
Education secondary	0.834	0.8	0.2	4.0
Education none	0.235	2.9	0.5	17.0
Active IDUs	0.004*	5.1	2.2	11.9

HIV positive	0.024*	2.1	1.4	3.3

P value is statistically significant at $P < 0.05$

* Statistical significance

CHAPTER FIVE

5.0 DISCUSSION

Through this study it was found that majority of IDUs were males comparing to females, this might be the reason of males being more prone to drug and alcohol abuse due to social behaviours that give males more opportunity to start drugs use than females as it was explained by National Institute of Drug Abuse (NIDA) of USA journal (Van Etten *et al.,* 1999). The finding that majority of IDUs in this study were males compared to females is comparable to findings from another study conducted in Tanzania which suggested that males were far more numerous in IDU by both report and observation than their female counter parts (Ndayongeje *et al.*, 2019).

With regards to residence amongst IDUs in this population, the results showed that most of drug addicts had no specific residence, with some sleeping in market places, ferry and bus stations. Not only behavioral effects of drug use may result into one being run out of fund to pay rent and end up in street but also homeless are more likely to abuse alcohol and drugs than normal population. This finding is supporting the study conducted in - Rotterdam which indicated that that most of homeless suffered addiction of either illicit drugs or alcohol (Vries *et al*., 2007).

In this study, IDUs were found to be more prevalent among the middle-aged than in the younger generation. This finding might be because most of IDUs start the use of illicit drugs during adolescent age, also most of IDUs don't live long to reach an old age due to different health effects and ill behaviors which can cause death at young age. A similar finding has also been reported elsewhere that the percentage of drug use was far higher among the population aging 16 to 49 years old (HHS, 2013).

While prevalence of TB in the general population of Tanzania is well documented, the status of TB in high risk population like prisoners, IDUs and the homeless currently are not available. This might be because more of TB studies conducted in Tanzania were based in general population comparing to the population at high risk.

Although strategies to end TB are well established in Tanzania, chances of population at high risk for MTB infection acting as reservoir of TB in the communities are high and hence may contribute to increase the burden of TB diseases. The overall prevalence of TB among IDUs in this study was found to be high compared to that of general population in Tanzania with TB incidence of 253 per 100 000 in 2018 and prevalence of about 0.25% (URT, 2019). This proves that IDUs are not only at high risk of contacting TB and spread it among each other, but also can act as reservoir to general population.

Findings from this study are in agreement with researches conducted in other countries. For example a study conducted in Rotterdam showed that 1/6 of all TB cases are either drug addict or homeless at the time of diagnosis (Vries and Hest, 2005). Researchers suggested that illicit drug use is associated increases additional risk for TB infection (Dorbniewski, 2002; Altet-Gómez *et al*., 2005) which is equivalent to observed outcome of high TB prevalence among IDUs in Temeke district in Dar es salaam, Tanzania. IDUs

drug-resistance TB prevalence in this study was found to be low compared to that of general population in a study performed by Hoza *et al.* (2015) at northern Tanzania, which found that the prevalence of any drug-resistance to new cases of TB to be 11.4% in general population (Hoza *et al*., 2015). But WHO reported that drug resistance TB have different ranges in different geographical locations and examples are prevalence of resistance to at least one drug of TB treatment was 2.9% in New York, 40.8% in Estonia, 0% in Finland and 18.1% in New Caledonia (WHO, 2000). Due to different ranges of drug resistance TB in different geographical locations further studies should be directed to other parts of Tanzania especially among populations at high risk for TB.

In Africa, prevalence of drug resistance TB among IDUs is less documented but data on the prevalence of drug resistance TB in general population is well documented. A study of meta-analysis derived a pooled MDR-TB based on culture of samples from 34 056 individuals of general population, spanning 20 years (1997-2017) showed a prevalence of 2.0% for new cases of TB in Sub Saharan Africa (Musa *et al*., 2017). This study showed low prevalence of DR-TB might be due to limited number of IDUs participants and short duration. Henceforth, further studies on the prevalence of drug resistance TB among population at high risk such as IDUs in Africa are required.

This study found that prevalence of TB was higher among active IDUs than among IDUs under Methadone treatments (Table 1), this can be explained that IDUs under Methadone treatment are required to attend hospital daily for methadone dosage and consequently access to early diagnosis and proper treatment of TB. The principal researcher of this study witnessed periodic TB screening of IDUs under Methadone treatment at Temeke Hospital, health education and consultation was being provided by health practitioners at Temeke Hospital and at the harm reduction center (MUKIKUTE).

On the other hand, active IDUs are known to be health care avoiders hence result in a delayed diagnosis, treatment and increased transmission period of TB to fellows. This finding is in agreement with the study performed by Pérez-Perdomo which showed that illicit drug use has been associated with a high prevalence of TB disease and HIV (Deiss *et al*., 2009; Pérez-Perdomo and Pérez-Cardona, 1999). Most social-demographic and risk factors which were analyzed in this study at 95% confidence interval (CI) showed no statistical significance association with TB infection. However, factors which showed statistical significance associations with TB infection were previous TB treatment interference, HIV and TB co-infection and active drug abuse rather than under methadone treatment as shown in Table 2.

In this study, previous TB treatment interference showed statistical significance association with TB infection, IDU with previous TB treatment interference was 140 times more likely to have TB infection. This can be explained as the result of active drug users being health service avoiders and have lower tendency of compliance to TB recommended treatment. Examples of studies that support these findings are the study conducted in eight provinces of Vietnam which showed that incomplete adherence to treatment showed a significant association with TB recurrence (Rutledge *et al*., 2018) and the study performed by Lan which suggested that poor treatment adherence to TB treatment is an important predictor of TB recurrence (Lan *et al*., 2003). Different studies showed an association between illicit drug use and TB treatment interference like the study performed in South Africa 1999-2001 concluded that failure to comply with TB treatment is highly associated with the use of illicit drugs (Holtz *et al*., 2006) and is one of the factors resulting in TB recurrence.

Another study performed in New York showed crack cocaine users and illicit drug injection users had the highest rates of both regulatory intervention and detention for TB treatment completion (De Mattos *et al*., 2006) which may result in TB recurrence. A study conducted in Florida showed that illicit drug use, homelessness and alcoholism are risk factors that have been identified for failure to complete TB treatment (Friedman *et al*., 2003) which may attribute to TB recurrence. Active illicit drug use showed statistical significance association with TB infection with five times more chances of TB infection. This can be explained as most of active IDUs health care avoiders and increases transmission time when contact a transmissible diseases. Illicit drugs users TB patients are more contagious and remain contagious longer because of treatment failure, presumably extends periods of infectiousness and are more likely to be involved in a localized genotype cluster which can represent recent transmission (Oeltmann *et al*., 2009). This finding is in -agreement with findings of another study by Deiss *et al*. (2009) which showed that illicit drug use is associated with high prevalence of TB and HIV (Deiss *et al*., 2009). This may be due to euphoria feeling which is the effect of illicit drugs use as a study conducted in Washington during a TB outbreak investigation among long-term marijuana users showed that despite feeling ill and reporting increased coughing, IDUs patients delayed seeking health care until their cases of TB were advanced and primarily cavitary (Oeltmann *et al*., 2006). Another study with similar results was conducted in Wichita, Kansas (USA) at 2001 showed that TB incidence were more common among illicit drug users and illicit drug sharing (Mcelroy *et al*., 2003).

This study showed that HIV positivity has statistical significance association with TB infection and chances HIV positive IDUs to TB infection was two times more than HIV negative IDUs. This might be due to HIV being known to cause low immunity and TB being one of the common co-morbidity. HIV infection is important risk factor for

developing TB because it increases the susceptibility to primary infection or reinfection due to low immunity (Bruchfeld *et al*., 2015). AIDS patient experience immunosuppression which manifest loss of CD4+ T cells in the blood, lymphoid tissues and mucosa, which is an important contributor to the increased risk of TB infection and re- infection (Moir *et al*., 2011). The finding of this study supports the Tanzania National Tuberculosis and Leprosy program report which indicates that people with TB/HIV co-infection have an annual risk of 5-10% and a lifetime risk 20-30 times higher for developing TB disease (URT, 2020).

This finding is in agreement with the high prevalence of TB infection commonly reported among HIV-positive IDUs (Pérez-Perdomo and Pérez-Cardona, 1999). Another study suggested that HIV induces immunosuppression which it is the most important reason for high TB incidence among HIV positive IDUs (Moreno *et al*., 1993). Another study which supports our findings states that TB is among the most common opportunistic infection in endemic areas and it is also seen among HIV positive IDUs even in low prevalence areas (Baalwa *et al*., 2008). A study conducted in Guangxi showed that prevalence of TB among people living with HIV/AIDS was 173 times higher than general population in Guangxi (Cui *et al*., 2017).

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

Key findings of this study indicated high TB prevalence among IDUs and hence proper target interventions are needed for TB control among IDUs in Temeke district. Previous TB treatment interference, HIV positivity and active illicit drug use among IDUs were the important risk factors found to have strong association with TB.

I would like to recommend additional research towards populations at high risk of contacting TB such as prisoners and homeless and IDUs with better tools for data collection and a better designed study.

i. Further studies on population structure of MTB are required so as to know the exact MTB strains circulating among IDUs and homeless, which will aid in understand the pattern of infection if its clusters and hence proper strategies can be set.

ii. Follow-up to default TB patients should be more emphasized to ensure that patient takes the right drugs in the right doses at the right intervals and for the right duration, especially among patients with ill behaviors such as illicit drug users so as to achieve successful treatment and reduce risk of recurrence TB.

iii. The fight against TB should be directed more towards population at high risk such as IDUs, which can be achieved by periodic screening, effective and appropriate

counseling be directed to population at high risk so as to reduce period of infection among them. This may aid in setting proper control strategies of TB so as to achieve Tanzania five year development plan strategy which is to improve TB and infectious diseases control (URT, 2016).

iv. The fight against illicit drug use among youth in Tanzania should be strongly intensified by increasing awareness through provision of more education on effects of illicit drug use from primary schools to universities.

6.2 Limitations

i. Sampling technique used was purposive as only convenient subjects were used and may attribute to bias samples which might be affected the results of this study.

ii. Unfaithfulness behaviors of respondents (illicit drug users) might result into wrong interpretation of results especially on the risk factors. Unreadiness of subjects to answer some questions (such as HIV status) also might affect the results and interpretation.

iii. Failure to collect early morning sputum sample because of poor cooperation from subject and only spot sputum samples were collected might interfere with results of this study especially culture and smear results.

iv. Few subjects had history of disease and all previous TB treated patients who interfered with TB treatment were diagnosed TB positive, and this led to previous TB treatment interference risk to have high odds ratio (140.0) number and a wide range at 95% confidence interval (17.4-1129.9). This finding may not be reliable in other conditions.

v. Limited number of subjects and short duration might affect the results and miss the real picture of TB among IDUs at Temeke district.

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APPENDICES

Appendix 1: Questionnaire

Sokoine University Of Agriculture

(SUA)

SACIDS Foundation for One Health

College of Veterinary Medicine and Biomedical Sciences

P.O Box 3297, Chuo Kikuu, Morogoro,

Tanzania

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Patient Bio Data

Patient name:_____

Age:_____

Sex:_____

Nationality _____

Educational level:_____

Period of Drug use _____

Occupation _____

Residential area: _____

Type of residents: family house/ ghetto/rented a room/sober hostel/ others

If others mention:_____

Number of people in a room:_____

Marital status:_____

Number of children:_____

Associate Conditions

Cycle appropriate answer

Have you ever been tested for TB? YES/NO

If yes 2(a) above, what was the results POSITIVE/NEGATIVE/ I DON'T KNOW

If yes 2(a) above were you given any medication? YES/NO

What happened with the medication _____

Have you been smoking? YES/NO

Are you drinking Alcohol? YES/NO

If yes 2(f) above, How often are you drinking?_____

Can you describe yourself as heavy drinker? YES/NO

How many are you living in a room:_____

Have you been prisoned? YES/NO

If yes (j) For how long?_____

Do you understand AIDS/HIV? YES/NO

Have you ever been tested for HIV/AIDS? YES/NO

What were your results? POSITIVE/NEGATIVE/ I DON'T KNOW

Do you get information about AIDS/HIV in your area? YES/NO

Have you ever had a relative with TB? YES/NO

If yes 2(p) above, were you living with him/her in the same house?

YES/NO

In your house is there any one known with TB? YES/NO

If yes 2(r) above, how many are they? _____

In your room is there any one with Persistence coughing for more than two weeks?

YES/NO

If yes (t) above, how many?_____

Are you under Methadone? YES/NO

If yes (v) for how long?

Type of Illicit Drug which you were/are using? INJECTABLES/ NON-INJECTABLES/ COCKTAILS

For how long have you been using Illicit drugs?

Suggestive Symptoms

Do you experience any of the following symptoms?

Chronic cough for 2 weeks or more? YES/NO

Coughing sputum streaking with blood? YES/NO

Feeling Fever YES/NO

Fatigue YES/NO

Night sweating YES/NO

Unexpected weight loss YES/NO

Loss of appetite YES/NO

Laboratory Results

Smear results:_____

GeneXperresults:

MTB:_____

Rifampicilin: _____

Culture results:_____

Spligotyping:_____

Appendix 2: Maelezo ya Mgonjwa

Sokoine University of Agriculture (SUA)
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Maelezo Binafsi

Jina la mgonjwa:_____

Umri:_____

Jinsia:_____ _____

Uraia_____

Kiwango cha elimu:_____

Muda wa matumizi ya madawa ya kulevya:_____

Kazi:_____

Mahala anapoishi:_____

Aina ya makazi: nyumba ya familia/ geto/chumba cha kupanga/ nyumba za matibabu ya madawa ya kulevya/nyengine

Kwa nyengine elezea:_____

Hali ya ndoa:_____

Idadi ya watoto:_____

HALI

Zungushia duara jibu sahihi

Umeshawahi kupima ugonjwa kifua kikuu? NDIO/HAPANA

Kama ndio(a), majibu yalikuwaje? NINA UGONJWA/SINA UGONJWA/ SIJUI

Kama majibu (a)yalionyesha una ugonjwa, ulipatiwa matibabu? NDIO/HAPANA

Nini kilitokea kwa matibabu uliyopewa_____

Umewahi kuvuta sigara? NDIO/HAPANA

Unakunywa pombe? NDIO/HAPANA

Kama ndio(f), unakunywa kila baada ya muda gani?_____

Je wewe ni mnywaji pombe sana? NDIO/HAPANA

Mnaishi wangapi katika chumba:_____

Umewahi kukaa jela? NDIO/HAPANA

Kama ndio (j), kwa muda gani?_____

Unaelewa chochote kuhusu UKIMWI/ VVU? NDIO/HAPANA

Umeshawahi kupima UKIMWI/VVU? NDIO/HAPANA

Kama ndio, majibu yalikuwaje? NINA UGONJWA/SINA UGONJWA/ SIJUI

Je mnapewa elimu juu ya UKIMWI/VVU katika eneo lako? DIO/HAPANA

Umewahi kuwa na ndugu anaeumwa Kifua kikuu? NDIO/HAPANA

Kama ndio(p), ulikuwa unaishi nae nyumba moja? NDIO/HAPANA

Katika nyumba unayoishi kuna yeyote anaejulikana kama mgonjwa wa TB? NDIO/HAPANA

Kama ndio(r), ni wangapi?_____

Je katika chumba unachoishi kuna yeyote mwenye kukohoa kwa muda wa zaidi ya wiki mbili?

Kama ndio(t), Ni wangapi?_____

Je upo katika matibabu ya Methadone? NDIO/HAPANA

Kama ndio(v), kwa muda gani?_____

Aina ya madawa ya kulevya uliyokuwa/ ambayo unatumia: SINDANO/ZISIZO SINDANO/MCHANGANYIKO

Kwa muda gani uliwahi/ umekuwa ukitumia madawa ya kulevya._____

Dalili

Unapata dalili yeyote katika hizi?

Kikohozi kilichodumu zaidi ya wiki mbili?	NDIO/HAPANA
Kutoa makohozi yenye damu?	NDIO/HAPANA
Unapata homa?	NDIO/HAPANA
Uchovu	NDIO/HAPANA
Kutoka jasho sana usiku?	NDIO/HAPANA
Kupungua uzito bila sababu.	NDIO/HAPANA
Kukosa hamu ya kula.	NDIO/HAPANA

LABORATORY RESULTS

Smear results:_____

GeneXpert results:

MTB:_____

Rifampicilin: _____

Culture results:_____

Spligotyping:_____

Appendix 3: Consent Form

Sokoine University of Agriculture (SUA)
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This Consent form is for Illicit Drug Users (IDU) in Temeke district in Dar es Salaam invited to participate in research for Tuberculosis, Drug Resistance Tuberculosis and Population structure of *Mycobacterium tuberculosis* from Temeke district.

Researcher: Aziza Ahmed Said

Contact: 0672179400

Email: azzysa@gmail.com

Institute: Sokoine University of Agriculture (SUA)

Sponsor: SACIDS

Study: Tuberculosis amongst IDU

Supervisors: Dr. Hoza, A.S (SUA), Prof. Mfinanga, S (NIMR). and Prof. Matee, M. (MUHAS)

This consent Form has two parts:

Information Sheet (gives you information about the study)

Certificate of Assent (this is where you sign if you agree to participate)

Part I: Information Sheet

Introduction

My name is Aziza Ahmed Said, I am a student from Sokoine University of Agriculture taking MSc. One Health and Molecular Biology. As part of my studies requirement I have to conduct research on Tuberculosis and IDU are at high risk to

TB disease due to physiological effects of drug use, environment factors and risk behavior conducted by them.

I am inviting you to be part of this research study. You can choose whether or not you want to participate. We have discussed this research with Temeke hospital Authority and have accepted but I would like your permission to participate voluntarily.

Purpose of the research: To determine drug resistance Tuberculosis and population structure of *Mycobacterium tuberculosis* among Illicit Drug Users at Temeke district in Dar es Salaam.

Choice of participants:

We would like to know status of Tuberculosis and *Mycobacterium tuberculosis* isolates circulating in amongst IDU in Temeke district. All IDU and former IDU who are under Methadone Treatment are invited to participate in this study. IDU who have been in TB treatment for more than 10weeks with improved symptoms will not be included.

Participation is voluntary:

To participate in this research is voluntary, you are allowed to accept or decline your participation and your decision will have no effect in your livelihood.

Procedures:

Once you accept to participate in this research you will be required to sign this consent form then two sputum samples will be collected from you in two consecutive days, the first day at a visiting time and second day early morning sputum will be required.

During sample collection you will be given special container with a lid. You will be required to open lid and gag or cough to get sputum from deep of your chest then spit in that given container then tightly cover the container with a lid. Then give back the sample to the one who gave you container and sample collection procedure is done for the day.

You will also be asked for some information to be filled in a form. The information form will go together with you sample. Including your age, name, any signs or symptoms suggesting Tuberculosis experiencing such as persistence coughing.

This sample will be tested for Tuberculosis infection and if positive Temeke hospital authority will be informed and you will have to start your treatment immediately.

Risks:

There are no any risks, pain, ill effects or discomfort expected to happen to you following this research.

Benefits:

Benefits of this research are IDU who will be Tuberculosis positive will be referred to Temeke hospitals and start his/her medication immediately. Also this study will help us understand population structure of *Mycobacterium tuberculosis* and hence contribute national goal of improving TB and infectious diseases control.

Reimbursements:

By participation in this research you will not be given any gifts or payments in return.

Confidentiality:

Only researcher and Temeke hospital authority will know your participation and so your health status after sample analysis. Your fellow will not access your information or whether you agreed to participate or not in this research.

Compensation:

As we expect no ill effect to happen to you due to this study then there is no need for compensation. Only those Tuberculosis positive will be directed to health facility and receive proper treatment.

Sharing the Findings:

All information about you will be confidential and your test results will be given to Temeke hospital authority and you will be able to know your results and if you are positive proper treatment will be given to you at Temeke hospital.

Right to Refuse:

You have a right to accept or decline participation in this research and you will suffer no consequence for your choice. No one will be mad or disappointed with your choice.

Part 2: Certificate of consent

I have read this information (or had the information read to me) I have had my questions answered and know that I can ask questions later if I have them.

I agree to take part in the research.

Name: _____

Signature: _____

Date:_____

Day/month/year

If illiterate:

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the assent form to my fellow and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness: _____

Right Thumb print of participant

Signature of witness _____

Date _____

Day/month/year

Received by: _____

Date: _____

Day/month/year

Name of researcher:_____

Signature of researcher:_____

Date:_____

Day/month/year

Appendix 4: Fomu ya Idhini

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Fomu ya idhini hii ni kwa ajili ya kuwakaribisha waathirika wa madawa ya kulevya (IDU) kushiriki katika utafiti dhidi ya ugonjwa wa Kifua kikuu, usugu dhidi ya dawa za kifua kikuu na aina za vimelea vinavyosababisha Kifua kikuu katika wilaya ya Temeke mkoani Dar es Salaam.

Mtafiti:Aziza Ahmed Said

Taasisi: Chuo Kikuu cha Kilimo Sokoine

Mdhamini: SACIDS

Somo la utafiti: kifua kikuu kwa waathirika wa madawa ya kulevya

Wasimamizi: Dr. Hoza, A.S (SUA) and Prof. Mfinanga, S (NIMR)

Fomu hii ina sehemu kuu mbili:

Sehemu ya maelezo (kukupa maelezo juu ya utafuta)

Cheti cha idhini (sehemu ya kuweka sahihi kama unakubali kushiriki katika utafiti)

Sehemu I: Maelezo

Utangulizi

Jina langu ni Aziza Ahmed Said, ni mwanafunzi wa Chuo kikuu cha kilimo Sokoine wa shahada ya umahiri. Kama sehemu ya matakwa ya masomo yangu ninahitajika kufanya utafiti kuhusu ugonjwa wa Kifua kikuu na waathirika wa madawa ya kulevya wapo katika

hatari kubwa ya kuugua kifua kikuu kutokana na athari za kisaikologia zitokanazo na madawa ya kulevya, mazingira na tabia hatarishi zinafanywa na waathirika wa madawa ya kulevya.

Napenda kuwakaribisha kushiriki katika utafiti huu. Ni chaguo lako kukubali au kukataa kushiriki. Tumeshaongea na uongozi wa Hospitali ya Temeke na tumekubaliana lakini pia nahitaji ridhaa ya ushiriki wenu kwa hiari.

Kusudi la utafiti:

Kujua uwepo wa Kifua kikuu sugu dhidi ya dawa na aina za vimelea vinavyosababisha ugonjwa wa Kifua kikuu miongoni mwa waathirika wa madawa ya kulevya katika wilaya Temeke mkoani Dar es Salaam.

Chaguo la washiriki:

Tungependa kujua hali ya ugonjwa wa Kifua kikuu na aina za vimelea vya Mycobacterium tuberculosis vilivyopo miongoni mwa waathirika wa madawa ya kulevya katika wilaya ya Temeke. Waathirika wote wa madawa ya kulevya ambao bado wanatumia madawa ya kulevya pamoja na waathirika wa madawa ya kulevya waliopo katika matibabu ya methadone wana karibishwa kushiriki katika utafiti huu. Waathirika wa madawa ya kulevya ambao wapo katika matibabu ya TB kwa zaidi ya wiki 10 na wanaonekana kupona kifua kikuu hawatoruhusiwa kushiriki katika utafiti huu.

Ushiriki ni hiari:

Kushiriki katika utafiti huu ni hiari, unaruhusiwa kukubali au kukataa kushiriki katika utafiti huu na maamuzi yako hayato athiri maisha yako.

Utaratibu:

Iwapo utakubali kushiriki katika utafiti huu utatakiwa kutia sahihi katika fomu hii halafu utapewa vikopo viwili kwa ajili ya kuekea makohozi yako ambapo kimoja utaweka makohozi mara baada ya sahihi na kikopo cha pili utawekea makohozi ya asubuhi mapema kabla kula chochote wala kusafisha kinywa.

Utapewa vikopo vyenye mifuniko na utatakiwa kufungua mfuniko halafu ukohoe kutoa makohozi yaliyo ndani ya kifua na uyateme katika kikopo kisha ukifunike kwa mfuniko wake. Sampli utamkabidhi aliyekupa kikopo na hapo zoezi la utoaji sampuli litakuwa limeisha kwa siku hiyo.

Utaulizwa baadhi ya taarifa zako na kujazwa katika fomu maalumu ambayo itakwenda pamoja na sampuli zako maabara. Maelezo yatakayohitajika ni pamoja na umri, jina, na dalili zozote za Kifua kikuu unazozipata kama kukohoa zaidi ya wiki mbili.

Sampuli zako zitapimwa maambukizi ya Kifua kikuu na iwapo umeathirika na ugonjwa huo uongozi wa Hospitali ya Temeke utataarifiwa na utahitajika kuanza matibabu mara moja.

Athari

Hakuna hatari yeyote, athari mbaya au usumbufu unaotegemewa kujitokeza kwako kutokana na utafiti huu.

Faida:

Faida ya utafuti huu ni waathirika wa madawa ya kulevya watakaogundulika wana maambukizi ya ugonjwa Kifua kikuu itajulishwa uongozi wa hospitali ili kupewa

matibabu mapema. Pia faida ya utafuti huu utatuwezesha kujua aina za vimelea *Mycobacterium tuberculosis* hivyo itachangia lengo la kitaifa la kuboresha udhibiti dhidi ugonjwa wa Kifua kikuu na magonjwa ya kuambukiza.

Malimbikizo:

Kushiriki katika utafiti huu hakutakupelekea kupewa zawadi au malipo yeyote.

Usiri:

Mtafiti pekee na uongozi wa hospitali ya Temeke utakuwa na taarifa za ushiriki wako pia afya yako baada ya upimwaji wa sampuli. Watu wengine na hata marafiki zako hawatopata taarifa za ushiriki au kutoshiriki kwako.

Fidia: Kwa sababu tunatarajia hakuna athari mbaya itakayojitokeza kwako kutokana na utafiti huu basi hakuna haja ya fidia. Uongozi wa hospitali ya Temeke utapewa taarifa za watakao gundulika ni waathirka wa Kifua Kikuu ili waweze matibabu sahihi.

Ushirikishi wa matokeo:

Maelezo yote kuhusu wewe na majibu ya vipimo vyako yatakuwa siri isipokuwa kwa uongozi wa hospitali ya Temeke kwa ajili ya kuweza kukupatia matibabu iwapo umeathirika na Kifua kikuu.

Haki ya kukataa:

Unayo haki ya kukubali au kukataa kushiriki katika utafiti huu na hutapata madhara yeyote kwa chaguo lako. Hakuna mtu atakayechukizwa au kufadhaika na chaguo lako.

Sehemu 2: Hati ya idhini

Nimesoma maelezo haya (au nimesomewa). Maswaali yangu yamejibiwaa na naweza kuuliza maswali baada ya hapa.

Nimekubali kushiriki katika utafiti huu.

Jina :_____

Sahihi:_____

Tarehe_____

siku/mwezi/mwaka

Iwapo hajui kusoma na kuandika

Shahidi ajuae kusoma lazima asaini (ikiwezekana, mtu huyu anapaswa kuchaguliwa na mshiriki na haipaswi kuwa na uhusiano na timu ya utafiti). Washiriki ambao hawajui kusoma na kuandika wanapaswa kujumuisha kuchapishwa kwa kidole pia Nimeshuhudia usomewaji sahihi wa fomu ya uhiari hii na amepewa nafasi ya kuuliza maswali. Na hakikisha kuwa amepewa uhiari wa kuamua kushiriki au kutoshiriki.

Jina la shahidi : _____ Alama za kidole gumba mkono wa kulia

Sahihi ya shahidi: _____

Tarehe: _____

siku/mwezi/mwaka

Imepokelewa na: _____

Tarehe: _____

siku/mwezi/mwaka

Jina la mtafiti: _____Sahihi ya mtafiti: _____