ACTIVE TUBERCULOSIS CASE FINDING ON DIABETIC PATIENTS ATTENDING DIABETIC OUTPATIENT CLINIC AT JM KARIUKI COUNTY HOSPITAL, NYANDARUA COUNTY KENYA

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Declaration and Approval

Declaration Student

This thesis is my original work and has not been presented for a degree in any other University or for any other award.

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Dedication

The work herein is devoted Grace Macharia, my dear grandmother as well as my family.

Acknowledgement

Above all, I thank the Lord God for the far that I have come. I also direct appreciation to my supervisors Dr. Jackson Onyuka and Dr. Kennedy Muna for their guidance and consistent assistance in the realization of this research. Special thanks also go to Mount Kenya University and Nyandarua County Department of Health for the assistance and persistent support during my pursuit of a postgraduate degree.

Abstract

Notwithstanding the concerted efforts to attain the objectives stipulated in tuberculosis (TB) End Strategy by 2035, tuberculosis continues to be one of the principal healthcare concerns globally. Tuberculosis- Diabetes comorbidity accelerates tuberculosis disease and complicates treatment hence aggregating the possibility of poor tuberculosis outcome. The principal objective of this study is to determine missed active tuberculosis disease among diabetic patients enrolled in the outpatient diabetes management clinic at JM Kariuki County Hospital, Nyandarua County. The study investigates the prevalence of tuberculosis, estimates the positive yield of tuberculosis diagnosis by Gene Xpert, X-ray and Fluorescent microscopy (FM) diagnostic methods, and explores the socioeconomic factors of tuberculosis infection among patients with diabetes at JM Kariuki County Hospital, Nyandarua. A sample size of 139 study participants was used for the study. Data was collected through carrying out diagnostics tests which included: Fluorescent TB smear microscopy, Gene-Xpert test, Chest X-ray, blood sugar test and face to face interviews which was recorded in a structured interviewer checklist and the clinical data uploaded in various ministry of health laboratory tools. SPSS version 22 was used to analyse the data. A high prevalence rate (2.66%) of missed tuberculosis cases was recorded among diabetics. The results suggested Gene Xpert (with a positive yield of 1.60%) as the test with the highest positivity yield in the diagnosis of tuberculosis among diabetics at JM Kariuki County Hospital, Nyandarua. A notable difference was noted in the prevalence of tuberculosis among different age groups of participants ($p = 0.001$) suggesting strong statistical relationship between tuberculosis infection and age, emphasizing the established association between tuberculosis and age factor. A p-value of 0.613 suggested the existence of a weak association between the gender of diabetic patients even though a significant statistical association was noted between occupation and tuberculosis occurrence ($p = 0.003$). A significant statistical association was noted to exist between smoking and alcoholism and tuberculosis infection among diabetics ($p = 0.001$). The study proposes tuberculosis screening for all new diabetes mellitus (DM) incidences when resources allow, and prioritized screening using chest x-ray for diabetes mellitus patients and gene expert analysis for people who have suggestive symptoms and patients aged 40 above, as well as those engaging in behaviours such as habitual alcohol consumption and cigarette smoking. Additional focus is recommended for tuberculosis infections in the lower lobes of the lungs, since lower lung involvement is one of the common features of tuberculosis infection among people with diabetes mellitus. Patients suffering from both diabetes mellitus and tuberculosis face higher chances of presenting cavitation, smear-positivity during diagnosis, and they may continue being culture positive 8 weeks after the onset of the treatment plan. Additional diagnostic initiative that focuses on continuous monitoring of serum drug concentration and ensuring that the tuberculosis therapy dosage is enough is recommended to enable a sustained advancement of the patient towards tuberculosis eradication. As such, the findings of this study emphasize the need to incorporate active tuberculosis case finding in diabetes mellitus management in Nyandarua County, as a milestone towards the enhancement of the national tuberculosis strategy.

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Abbreviations and Acronyms

AFB	Acid Fast Bacilli
CDC	Centre for Disease Control
CIDP	County Integrated Development Plan
DM	Diabetes Mellitus
DOPC	Diabetic Outpatient Clinic
HIV	Human immunodeficiency virus
IDF	International Diabetes Federation
LMIC	Low and Middle-income Countries
LTBI	Latent Tuberculosis Infection
MDG	Millennium Development Goal
MDRTB	Multidrug Resilient Tuberculosis
NIDDM	Non-Insulin-Dependent Diabetes Mellitus
TB	Tuberculosis
WHO	World Health Organization

Chapter One

Introduction

1.1 Background of the Study

Despite the global efforts to eradicate tuberculosis (TB) by 2035 (being ultimate objective of End TB Strategy 2035), TB is still among the primary healthcare problems worldwide. In 2016 an international report by the World Health Organization (WHO) highlighted the increasing prevalence of TB, citing that nearly 10.3 million new TB infections in yearly rates, and that approximately 1.2 million individuals die of TB-associated health complications annually. The report also indicated that amongst the 10 million new incidences of TB reported in that year, 1.9 million cases were linked to factors including undernourishment, 0.8 million were associated with smoking, 1.0 million were linked to HIV/AIDS, and 0.8 million incidences were attributable to diabetes (World Health Organization, 2017).

WHO's worldwide TB control policy vouches for the DOTS (directly observed treatment short course strategy); an incidence identification strategy that depends on the readiness individuals who exhibit TB-suggestive symptoms to seek health care services (Sanghani & Udwadia, 2013). Although passive health care seeking behaviour of TB patients upon which the DOTS strategy is established has proven to be operative in identifying TB incidences in DM-prevalent nations such as Peru, Ethiopia and Vietnam (Shargie & Lindtjorn, 2005), uncertainties of its efficacy emerge because of the existence of other equally important risk factors for TB, such as diabetes mellitus (DM) and HIV/AIDS (Havlir, et al., 2008)

In recent years, the ability to detect TB has stagnated; an outcome that has been used to indicate weaknesses and gaps in the current TB eradication initiatives (World Health

Organization, 2017). While World Health Organization (2017) reports on the effectiveness of passive TB case findings in identification of symptomatic TB cases, passive case-finding, which typically involves when people with experiencing symptoms that are suggestive of TB voluntarily go for medical examination and treatment, has been identified to be particularly efficient in identifying and managing of TB mostly when patients reach the symptomatic stages (Harries et al., 2016). Among the major drawbacks of passive TB case-finding, which typically relies on bacteriologic examination to detect TB, are the various factors that affect the ability and decision of patients to seek diagnostic and treatment services. For example, in developing countries, individuals seeking TB care especially those who voluntarily present themselves at health facilities encounter healthcare services accessibility challenges due to distance, socioeconomic factors (inability to afford TB screening and treatment because of the related financial costs), lack of TB symptoms awareness, and lack of trained healthcare personnel to offer TB screening and treatment to the ever-increasing TB population (Harries et al., 2016). All these challenges have been found to set off delays in the delivery of health care services, which increases the duration between TB infection and treatment, and heighten the chances of adverse health outcomes and therapeutic failures (Storla, et al. 2008).

Kenya experiences a TB occurrence ratio of about 558 per 100,000 and the dominance of diabetes is evaluated to be at 4.56%. TB accounts for 750,000 deaths yearly whereas DM is estimated to cause about 20,000 mortalities annually (International Diabetes Federation, 2015). As cited in WHO (2016), the Republic of Kenya has already attained the 2015 target of the Millennium Development Goal (MDG) with regards to reducing TB mortalities among patients of different age groups (Enos et al, 2019). This state of the scenario is associated in part with the country's rigorous TB eradication strategy as articulated in the National TB Strategic Plan (2019). As articulated in the National Strategic Plan (2019-2023), among other things, the Government of Kenya offers is free TB treatment at all public hospitals. This has been reinforced by the relentlessness of the Ministry of Health (MoH) in bringing TB screening and treatment services close to the people in all counties (Suleiman et al., 2018). Regardless of the positive efforts, the rising occurrence of diabetes has proven being a major challenge to the national anti-TB initiatives (Harries et al., 2016).

Increasing rates of TB infections have been reported among people living with DM since diabetes worldwide. DM is said to affect patients' immune mechanism, hence predisposing them to tuberculosis infection (Harries, 2008). The findings of systematic analyses of studies published concerning the association between TB and DM suggest the existence of a direct correlation between the two diseases (Jeon & Murray, 2015). Even so, the dynamics of this association on TB eradication initiatives have not been confirmed in Nyandarua County. Nonetheless, while the WHO endorses the screening of TB on newly diagnosed DM cases, this recommendation has not been implemented in various parts of Kenya, including Nyandarua County, which is majorly served by JM Kariuki Memorial County Referral Hospital. The state of the circumstance presents defines the driving motive for the current study that seeks to explore missed TB cases among diabetic patients regardless of their sustained contact with local health facilities.

1.2 Statement of Problem

The TB – DM comorbidity is considered one of the leading causes of deaths and adverse health outcomes across the globe **(**Syal, Anand, & Dibyajyoti, 2015). According to International Diabetes Federation (2015) analysis, individuals suffering from DM experience an elevated risk of contracting TB in comparison to people without diabetes. Various academic efforts have been channelled towards understanding why DM patients are inequitably exposed to TB infections. Among the researchers that make notable contributions towards the understanding of this phenomena are Syal, Anand, and Dibyajyoti (2015) whose findings shed light on the impact of DM on the immunity of the host, and how DM increases exposure to other infections, TB included. According to the investigation, DM impairs immunity, which causes the patient to be increasingly vulnerable to microbial contagions such as *Mycobacterium tuberculosis*. High blood sugar levels (Hyperglycaemia) is said to provide a favourable environment for the growing of tuberculosis bacilli which causes TB **(**Syal, Anand, & Dibyajyoti, 2015).

Tuberculosis and diabetes comorbidity has also been linked to adverse health outcomes. For example, ReyPineda (2014) found out that Rifampicin, which is one of the foremost anti-tubercular medications prescribed to TB patients, disrupts the metabolic process of hypoglycaemic agents in the mouth, which affects glycaemic regulation (Jeon, Murray, & Baker, 2012). Nonetheless, DM presents challenges in treating TB patients as higher relapse and death rates have been found in patients confirmed to have both TB and diabetes than TB patients who do not suffer from diabetes. People found to have both tuberculosis and diabetes have a higher chance of being sputum positive even after commencement of TB treatment. Studies show that treating DM patients who are as well infected with TB is more challenging and may take a relatively longer duration for DM patient suffering from TB to convert to sputum-smear negative than non-DM TB patients (Dooley & Chaisson, 2009). The growing occurrence of DM, therefore turns out to be a big threat to TB control. To this end, improper DM management increase the risk of TB and is associated with higher chances of undesirable outcome in TB transmission and treatment (Sanghani & Udwadia, 2013). Diabetes – Tuberculosis comorbidity not only complicates TB treatment, but also combines challenges on DM treatment and blood-sugar management through nutrition plans (Jeon, Murray, & Baker, 2012).

The rising incidence of diabetes, more so diabetes mellitus, has justified the incorporation of active and passive TB case finding in DM treatment as part of TB eradication initiatives across the Globe (Jeon, Murray, & Baker, 2012). Regardless, the International Diabetes Federation (IDF) (2015) points out that up to two thirds of TB and almost 43% of DM cases are undiagnosed in developing economies.

1.3 Purpose of the Study

The WHO (2017) recommend active TB case finding as a corresponding strategy to curb delays of TB detection and onset of treatment, particularly in settings of high diabetes prevalence. Early TB diagnosis has been linked to several positive implications. For example, early detection of bacteriologic-positive TB decreases the chances of passing *Mycobacterium tuberculosis* to individuals that come in contact with TB patients and provides an opportunity for prompt treatment which is positively associated with higher chances of treatment success (Sekandi, Neuhauser, Smyth, & Whalen, 2009). As such, the present investigation seeks to explore missed cases in patients who are enrolled in the DM casualty clinic at JM Kariuki Nyandarua County Referral Hospital.

1.4 Study Objectives

While providing comprehensive responses to the research problem, the study seeks to address one general objective that is broken down into 3 specific objectives as summarized below:

1.4.1 General Objective

To implement active case finding of TB in diabetics subscribed to the outpatient DM clinic of JM Kariuki County Hospital, a referral facility that is in Nyandarua County in the Republic of Kenya. The study addresses the general objective by pursuing three related specific objectives as outlined below:

1.4.2 Specific Objectives

i. To estimate the point prevalence of missed TB infections in patients enrolled in the outpatient DM management clinic at JM Kariuki Nyandarua County Referral Hospital
ii. To evaluate the positivity yield of missed TB diagnosis through Gene Xpert versus X-ray and FM Microscopy diagnostic methods; and
iii. To establish the socioeconomic factors of TB infection among Diabetic Patients

1.5 Research Questions

i. What is the point prevalence of missed TB infections in patients enrolled in the outpatient DM management clinic at JM Kariuki Nyandarua County Referral Hospital?
ii. What is the positive yield of missed TB diagnosis through Gene Xpert versus X-ray and FM Microscopy diagnostic methods? and
iii. What are the socioeconomic factors of TB infection among Diabetic Patients?

1.6 Rationale of the Study

The WHO (2017) recommends the categorization of DM patients among the at-risk populations in TB eradication initiatives. This concept has been used as the basis for developing initiatives that seek to implement a bivalent diagnosis for DM and TB in health care settings (National Tuberculosis Control Program & National Leprosy and

Tuberculosis Program, 2006). The report categorically recommends the testing of people suffering from diabetes for TB at all essential health care establishments in all countries (World Health Organization, 2017). Despite these recommendations, JM Kariuki Nyandarua County Referral Hospital has not previously been engaged in interventions that involve the screening and testing of TB disease among diabetic patients. Nonetheless, TB and diabetic services are not integrated in the County, which increases the likelihood of having many undiagnosed TB cases even among DM patients who attend scheduled DOPC clinics (Kenya., & ORC Macro, 2005). Even worse, findings suggest that DM-TB patients are more contagious than TB patients who do not suffer from DM because of the prolonged duration that they remain sputum-smear and culture positive (Dooley & Chaisson, 2009). As such, by exploring the prevalence of active TB infections among people who are enrolled in the outpatient DM clinic at JM Kariuki Nyandarua County Referral Hospital, the findings of the current investigation shades light on the extent of undiagnosed TB in particular parts of Kenya, which can also be used to identify one weakness area in the delivery of health care services that may posse the danger of TB infections among DM patients in the County.

1.7 Justification of the Study

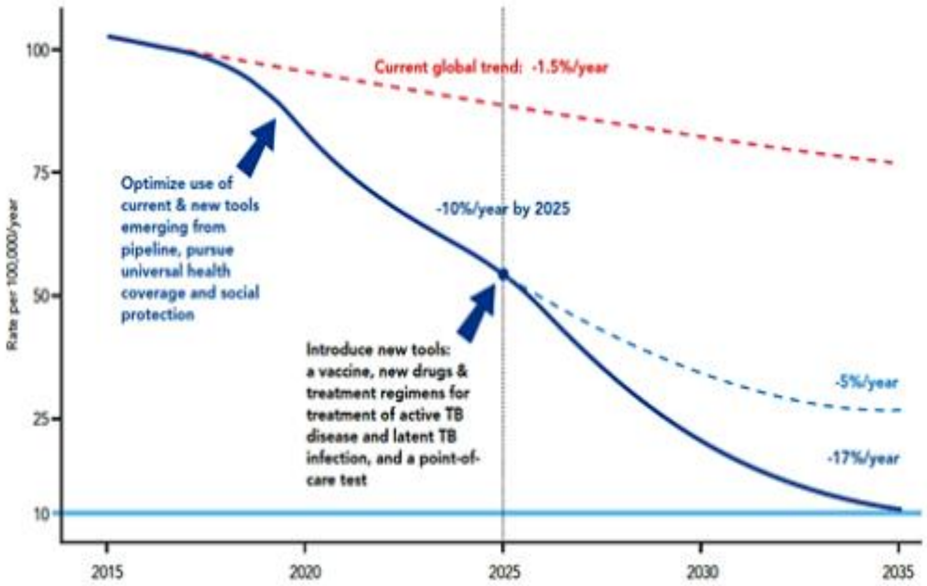
According to the WHO (2017) reports, 82,000 people were diagnosed with TB in 2015 out of the estimated 138,105 TB incidences in Kenya. This outcome reflects a gap of 40% in TB case finding, indicating a substantial percentage of TB cases that remain unnoticed and unmanaged. Out of the 82,000 identified TB incidences, 83% of patients were HIV positive (Oyando et al., 2019). Resultantly, mass efforts have been channelled towards implementing TB-eradication initiatives that target the HIV positive population, and these initiatives have borne fruits in reducing the prevalence of TB infections among this at-risk population. As such, one of the bigger challenges that remains in eradicating TB lies on HIV negative individuals. A current TB prevalence survey in Kenya projected that 138,105 get infected with TB in Kenya every year (Kenya, 2013). The lack of ability to detect TB at initial stages of infection has become the greatest contributor to the accelerated increasing prevalence of TB (factoring in that both people with confirmed TB and those who's status has not been confirmed can infect at least 10 to 15 individuals) (Havlir et al., 2008).

Among the pressing challenges in TB eradication has been the development of evidence-based approaches for at-risk populations, including people with DM. Tuberculosis is an emerging and important concern among DM patients in low-to-middle income countries where it affects 1.9% to 45% of DM patients. The wide discrepancy is associated with lack of initiatives that target this population, resulting in a scenario where at least 60% of active TB cases go undiagnosed (International Diabetes Federation, 2015). Bringing an end to TB encompasses one of Kenya's Sustainable Development Goals, particularly the Third Pillar that focuses on improving the health of the country (Harries et al., 2016). Positive advancement towards this goal requires a combination of public health, socioeconomic, and public health interventions that occur concurrently with relentless research and innovation. The End TB Strategy includes a set of initiatives that incorporate these three considerations, namely; (1) prevention and comprehensive patient-drive care that positions patients at the focal point of healthcare service delivery; (2) strong policies and supportive frameworks- that require combined effort from government agencies, private stakeholders, and communities; and (3) enhanced research and development- that stands as an mechanism to reduce the issue of TB in line with global TB strategy (Kenya, 2019).Tuberculosis associated burden and deaths hinders the success of the End TB Strategy. The ability to promote equality and human rights, provide government stewardship, establish strong partnerships between communities and civil societies, and support county-wide adoption of the strategy are the keys to success.

A focus on advocacy is required for the successful application of the End TB Plan, which necessitates collective efforts from ministries, private sector, and civil society. As per the WHO, TB is ranked one of the principal killers together with HIV. The End TB Strategy places tuberculosis as the severest health concern among the poor and at-risk populations. Being the fourth among the leading killer diseases, TB presents a significant economic stress of the nation, which is directly felt by the citizens. The End TB policy comes as a giver of hope in the vision of attaining zero TB deaths and infections and slowing TB infections by 90% by 2030. The successful implementation of the End TB Strategy will mean freedom form the exposure to catastrophic TB treatment costs for the public, which will have direct contribution towards the attainment of Universal Health Coverage (Enos, et al., 2019).

The current investigation is in positive response to WHO endorsements concerning the three founding pillars of the End TB Strategy. The current study relates directly with Pillar 1 that capitalizes on serving patients with comprehensive care that applies a preventive focus in achieving early detection and treatment (International Diabetes Federation, 2015). Approximately 8% of the estimated 1.7 billion TB-positive people have a high chance of experiencing recurrent infection in their lifespan, but the danger is even much higher among people with immuno-compromising conditions such as HIV, DM, alcohol consumption of habitual smoking, and malnutrition (Sekandi et al., 2009). Reliable progress measurements of the End TB Strategy must involve a deeper look into TB deaths, TB incidences, and TB –care costs simultaneously. This explains the pressing need to enhance surveillance in the national-wide health information and registration systems so as to understand important trends in TB (International Diabetes Federation, 2015).

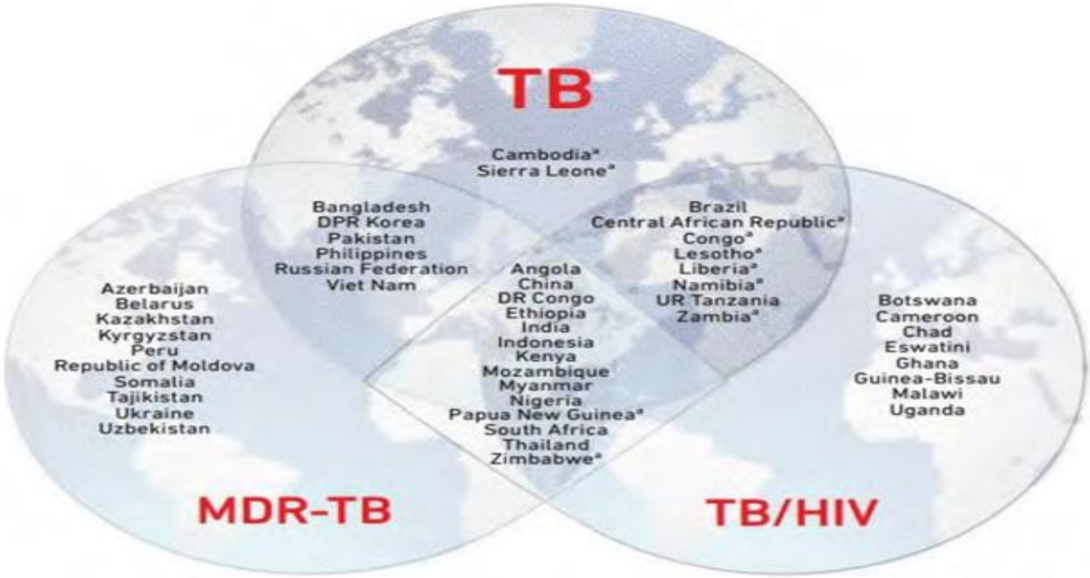
Figure 1: *Graphical Presentation of Strategies to Attain Anticipated Reduction in Universal TB Rates in line with 2035 TB Targets*



Note: (World Health Organization, 2017)

As illustrated in the figure 1 above, attaining the 2035 TB target requires the optimizing current and new initiatives and tools that align with the UHC goals (increasing access to critical healthcare by enhancing service accessibility and availability). Research and innovation are proposed as primary pillars in the discovery of new vaccines, drugs, and treatment plans for TB. Point-of-care tests are presented as the cornerstone for early diagnostics, prompt intervention, and prevention. This study is justified as Kenya is within the list of 30 countries with a devastating TB burden (refer to Figure 2 below).

Figure 2: *TB-High Burden Countries 2016-2020*



Note: (Kenya tuberculosis prevalence survey 2016, 2018)

As illustrated in Figure 2 above, Kenya is country that experience catastrophic burden caused by TB, multidrug resilient tuberculosis (MDR-TB), and TB-HIV comorbidity.

A country-wide TB prevalence study was done in Kenya in 2016, and the findings of the study indicated a pressing need for mass action to find missing/undiagnosed TB incidences in the country. With a backdrop of previous empirical evidence citing that nearly 60% of TB are yet to be diagnosed in developing countries where TB burden is at the highest, it is presumed that unreported TB is most prevalent among people with less-severe symptoms and those who have low drive to seek care. These findings emphasized the need to expand the focus on TB case finding to target people at work, residential care settings (Enos, et al., 2019). The Kenya TB prevalence survey of 2016 suggested the implementation of programs that will expand TB screening (diagnosis by Chest X-ray, Gene Xpert molecular analysis, and FM microscopy) to people exhibiting three TB-suggestive symptoms, including fever, weight loss, night sweat, and cough that lasts for more than 2 weeks as well as patients showing signs of low immunity. Screening is recommended for all people presenting respiratory symptoms at heath care facilities. All these rationalize the objectives of an academic enquiry that seeks to estimate the point prevalence of TB in diabetics; to evaluate the positivity yield of TB diagnosis by use of Gene Xpert, X-ray and FM microscopy; and to establish the socioeconomic factors predisposing the DM patients to TB infection and the viability of incorporating TB treatment and diabetic management services in Kenyan hospitals, particularly in JM Kariuki County Referral Hospital, which is the main referral centre in Nyandarua County. Being the largest hospital in Nyandarua, JM Kariuki Hospital receives the highest number of patients and can therefore supply the required number of respondents required for the study. In addition, it can also be used as a benchmark in other studies involving county referral hospital since Health services is a devolved function in Kenya.

1.8 Significance of the Study

This study seeks to contribute to the existing literature dealing with TB-DM comorbidity in Kenya. The results obtained from this study can be used to inform and guide Health policies in Nyadarua County and Kenya in matters regarding the implementation ACF for DM patients. Implementation of TB Active Case Finding for DM patients can help curtail the development of complications and reduce the burden of medical expenses on the patients.

1.9 Scope of the Investigation

The study took place at JM Kariuki County referral hospital, Nyandarua County. The research participants were patient who enrolled in the hospital's Diabetic outpatient clinic where they went for routine review and drug refills.

1.10 Study Limitations

Diabetic patients were only booked for clinic visits once in every three months (on Thursdays only) by consultants and medical practitioners hence the study took longer than expected. There was also an industrial action that involved health workers for a few weeks during the study period which also prolonged the study duration

1.11 Delimitations

Known diabetic patients who were not enrolled in the outpatient DM care clinic of JM Kariuki County Referral Hospital were excluded from the study.

1.12 Assumptions of the Study

The study is founded on an assumption that respondents gave truthful information during interviews.

1.13 Operational Definitions of Key Terms

Active TB: denotes the *mycobacterium tuberculosis* bacilli infection.

Blood-sugar level: entails the concentration of glucose in the blood of a participant measured in millimole per litre (mmol/L).

Dependent: is a youth over 18 years and below 25 years living under their guardians or parent and without any form of income.

Diagnostic methods: including clinical methods of TB detection, including FM microscopy, Gene Xpert, and chest X-ray.

DOT: entails a patient taking drugs under direct observation by a care giver.

Gene Xpert: is a nucleic acid amplification test detecting DNA sequence specific to *Mycobacterium tuberculosis* complex and rifampicin resistance.

Missed cases: cases not detected by passive case finding

Sample size: describes the minimum number of participants regarded to be adequate representation and replication of findings. The size of the sample for this investigation was confirmed by applying a method by Fisher el al. (1998) (Restrepo et al., 2014).

Socio-demographic characteristics: entail study participant foundational characteristics such as age, sex, employment status, and general affiliations that impact on individual behaviors such as cigarette smoking and alcoholism.

Socioeconomic characteristics in the context of this study entail the occupation of participants

Study areas: entail the geographical location in which the study was conducted as well as the demographic distribution of the location.

Chapter Two

Literature Review

2.1 Introduction

This part of the study provides foundational information concerning TB-DM comorbidity. The literature review section covers preliminary works on the association of TB and diabetes, clinical diagnosis of diabetes and tuberculosis, TB testing among diabetics, TB treatment among DM patients, and theoretical framework of this investigation. Also detailed herein are the research gaps in the investigation of TB-DM comorbidity in developing countries and in Kenya in particular.

2.2 Association between TB and DM

TB, caused by *Mycobacterium tuberculosis* infection, is considered worldwide concern (Subhash eta al. 2003). It is estimated that about two ninth of the 9 million people diagnosed with TB lose their lived because of disease (International Diabetes Federation, 2015). On the other hand, DM is non-infectious and a long-term disease that has spread globally because of changes in lifestyle (Harries et al., 2016). DM is related to high risk of TB infection and it also influences the results of TB management. The growing figures of DM cases is likely to complicate TB control and treatment interventions (Gold Haber-fiebert, 2011). A statistical outlook of the country reveals that Kenya currently has an occurrence ratio of 558 per 100,000, a TB o an occurrence ratio of 348 per 100,000 and one fifth of TB cases are both undiscovered and untreated (REF: Kenya tuberculosis prevalence survey 2016, 2018). The increasing prevalence of TB (especially MDR-TB), the rising DM cases, and increases diagnosis of DM-TB comorbidity have begun attracting considerable attention, particularly in understanding the relationship between the diseases that is reoccurring as a important public health challenge. As per current findings, the co-occurrence of TB and diabetes is more pronounced in emerging economies where there is a growing prevalence of DM and TB is epidemic (Havlir et al., 2008). According to WHO (2017), 180 million individuals are confirmed diabetics across the world, and the magnitude of people suffering from TB is foreseen to double in the next 20 years (Dooley & Chaisson, 2009). Countries with large populations and those enlisted among low- to middle-income countries report having the highest number of TB cases, and they are facing a rapid upsurge in the figure of DM incidences as well. Nonetheless, the notion that DM increases susceptibility to TB infection implies that DM may be having a undesirable effect on the achievement of TB management programs more so in developing /middle or low income economies (Stevenson et al., 2011).

A correlation exists between diabetes type II and TB primarily because DM weakens the host's immunity causing diabetics to be more susceptible to Mycobacterium tuberculosis infection. People with confirmed DM may lack crucial micronutrients or suffer from renal failures, pulmonary microangiopathy or malfunctioning cell-mediated, which increase the danger of opportunistic infections, including the risk of contracting TB (Perez-Guzman et al, 2000). The WHO (2017) approximated that roughly 8.8 million individuals are diagnosed with TB annually. It is projected that about a third of the people in the entire globe been infected by the bacteria that is responsible for the development of TB in their lifetime, but many do not reach the symptomatic stage because of the function of the immune response. Even so, the Mycobacterium tuberculosis may remain dominant is some people leading to active TB, and this is rampant among people with weakened immune response including the old, diabetics, people confirmed to have HIV/AIDS, and those on immunosuppressive medication (Subhash et al. 2003). The connection between TB and diabetes has also attracted research consideration because of the tendency of DM to cause TB treatment failures

(Sun et al., 2012). Additionally, DM and TB are related with shortages in micronutrients including retinol and Vitamin D (both of which have critical roles in upholding body immunity) and their lack may cause impairments the functionality of pancreas β-cell (Wang et al., 2013). The subsequent section details TB-DM epidemiology before looking at the impacts of DM on the clinical outcomes and expression of TB. Also covered hereunder are biological variables underlying TB-DM comorbidity and the significance of DM management and TB control from the perspective of public health. The following section discusses the risk factors of DM-TB coexistence.

2.3 Risk Elements and Epidemiology of DM-TB Co-occurrence

The associated risk factors of DM-TB coexistence have attracted significant research exposing DM as a re-emerging risk and problem of TB control worldwide (Syed et al., 2012). Empirical evidence indicates that type 2 diabetes makes people three times more vulnerable to TB infection, and that the prevalence of TB-DM comorbidity has surpassed that of HIV-TB comorbidity (Jeon & Murray, 2015).

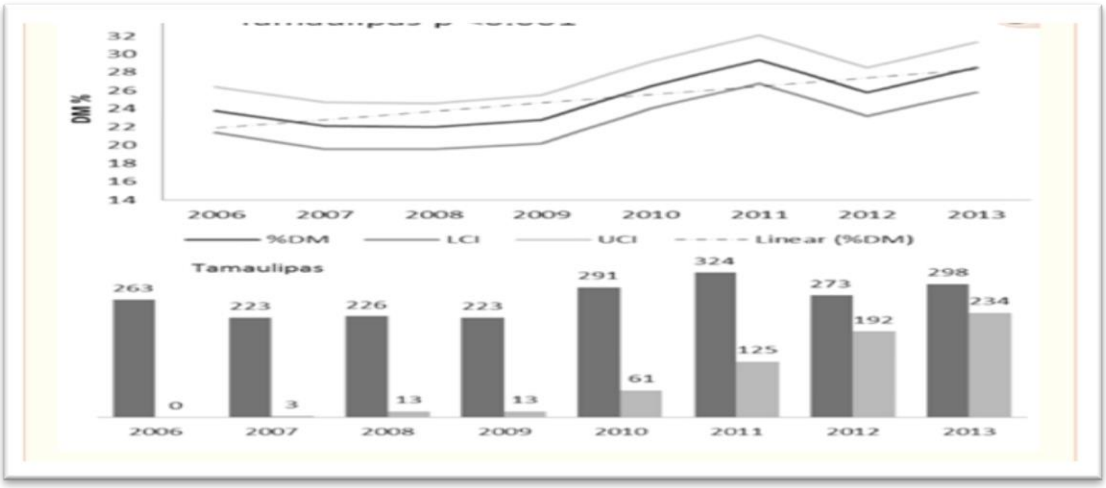
The correlation between TB and DM was first popularized in medical literature in the 19^{th} century by a Persian philosopher, but the study was limited due to its unsupported prescription of combined administration of insulin and antibiotic in TB-DM management and risk elimination (Morton, 1980). Even so, a re-emergence of TB-DM comorbidity occurred in the 1980s after TB was declared a world epidemic. The worldwide incidence of DM in adults since risen to about 20% in less than three decades, and a projected estimate of DM prevalence is set at 642 million by 2040 (International Diabetes Federation, 2015). Importantly, it is expected that the majority of TB cases (more than 80%) will continue being experienced in developing economies where TB is epidemic. As such, WHO identifies DM as an ignored, but important re-occurring risk factor to tuberculosis (International Diabetes Federation, 2015).

The prevalence of DM has increased globally, and studies link the upsurge with contemporary trends of urbanization, increasing aging population, reduction in physical activity (adoption of a dormant lifestyle), transformation in diet habits, and increasing prevalence of obesity (Webb et al., 2009). Well above three quarters (84%) of the accumulative global DM cases (it is estimated that 415 million people have DM globally) are in developing economies. The prevalence of DM is expected to experience a steady increase in areas with high TB incidence rates over the coming 30 years (Hu, 2011).

A systematic analysis of 12 observational investigations indicated that DM exonerates the risk of TB infection by a factor of 3 (associated risk 3.11; 95% confidence interval 2.27-4.426). This presents the best-described dimension of TB-DM association, but there was a wide disparity between the findings on risk ratio (spanning from 0.99 to 7.83). Generally, there have been challenges in investigating diabetes as a predictive variable for TB infection principally because of differences in healthcare accessibility, age differences, effectiveness glycaemic management, the number adverse health incidences associated with diabetes, and type of DM medication I different parts of the globe (Vallerskog, Martens, & Kornfeld, 2010). Additionally, coexistence of DM with other patient characteristics (such as smoking, macro- and microvascular complications of diabetes, and variations in social surrounding) have been reported to increase to TB exposure among DM populations (George et al., 2013). As such, there is a persistent need for further investigations that factor in diabetes and other patient elements in a multifactor evaluation in order to arrive at more consistent conclusions.

Worth noting is that the combined occurrence of tuberculosis and DM in developing countries where DM and TB are most prevalent. Out of the world's most DM affected countries, 6 low-n to middle-income countries are categorized as high-burden areas when it comes to the problem of TB (Subhash eta al. 2003). As investigations on the TB-DM epidemiology increase globally, particular regions portray especially high prevalence levels of TB among the DM population across the globe (Singhal eta la, 2014). According to WHO (2017), these countries account for more than 75% of TB cases across the world. According to Baghaei, Marjani, Tabarsi, Javanmard, and Masjedi (2013), the issue of TB-DM is under described in Africa because of lack of studies that focus on the issue. As a result, anti-TB initiatives are facing the lack of region-specific data as one of the biggest hurdles. Exacerbating the situation are projections that the DM-TB rates are likely to increase in the foreseeable future. Investigations in middle to low-income countries suggest increasing TB incidences in areas with growing DM prevalence (Baghaei et al., 2013). Similarly, TB-DM incidence increased by 2.8% in areas such as Tamaulipas (US-Mexico border) between 2006 and 2013, and this was not linked to increasing glucose testing initiated at TB care centres in Mexico (Refer to Figure 3 below) (Martinez & Kornfel, 2014).

Figure 3: *Increases in DM-TB Coexistence over 8 years (2006-2004)*



Note: (Martinez & Kornfel, 2014)

As illustrated in Figure 3 above, Tamaulipas, as an example of low-income regions with increasing DM prevalence, experienced a 2.8 upsurge in DM-TB cases from 2006 to 2013. The high rise was noted despite high estimates of undiagnosed TB in the region.

2.4 Impacts of DM on TB Control

At a population level, DM is linked to 10-20% of reported TB incidences, but this is likely to differ significantly even within a region or a country. This variation is exemplified in the UK where the risk is estimated at 10% in the general population, but the level of exposure tends to double to about 20% among Asian males (Walker & Unwin, 2010). In countries where both DM and TB are epidemic, the population-centred risk is more than 20%. Strikingly, findings indicate DM as an underlying related risk for more than 28% of TB cases among adults, and about 52% among DM patients that are between 35 and 60 years of age (Ponce-De-Leon et al., 2004). In developing economies, HIV is attributed to only 3-7% of accumulative TB incidences in adults (Stevenson et al., 2007). As such, although diabetes is linked to a considerably lower risk at a personal level (3 times) in comparison to HIV (more than 20 times), the contribution of HIV on TB can be lower than DM in communities with high DM prevalence (Getahun et al., 2010). An investigation utilizing rigorous TB infection framework to evaluate the likely impacts of diabetes on TB epidemiology in 14 states characterized with increased TB affliction found that DM prevention would prevent the occurrence of 1.1 million TB-associated deaths in developing /middle- or low-income economies in the next two decades (Pan et al., 2015). As such, there all communities across the globe need to assess the occurrence of DM as its role in TB. This information varies among regions, and is important in guiding the effective utilization of limited resources in anti-TB initiatives.

All places around the globe are experiencing a rise in non-communicable diseases (NCD), and the issue has re-emerged an important public health concern in developing economies. Accordingly, the prevalence of non-infectious illnesses in developing countries was 47% in the 1990's and is predicted to escalate to approximately 69% by the closing of year 2020. By 2030, it is presumed that the prevalence of non-communicable disease will surpass that of infectious diseases developing economies. Numerous factors have associate with this trend, including the spread of industrialization and urban lifestyle that have led to the transformation of dietary habits and reduction in physical activity. These two, in combination with other individual factors (such as race and genetic variables), have caused an upsurge in Type II diabetes and obesity among adults in developing economies where concomitant infectious diseases, including TB, are epidemic (International Diabetes Federation, 2015). Type II diabetes is believed to be the commonest health issue among the aging population in developing countries, as it accounts for nearly 90% of all diabetes cases in this population (Satyanarayana et al., 2013).

The double liability of non-communicable and infectious diseases in Africa's Sub-Saharan parts further worsen the control of both diseases. The negative impacts of the comorbidity between communicable and non-communicable epidemics have been documented. For example, some studies describe DM-TB comorbidity as one of the most rampant occurrences in low-income countries. The correlation is partly explained by the high prevalence of both diseases, i.e., low to middle-income countries that harbour 95% of worldwide TB occurrences and 70% of DM cases (Jeon, Murray, &

Baker, 2012). Regardless of the existence of studies indicating low healthcare access as an issue in TB case finding and debates as is a significant TB predicting element, tuberculosis-diabetes comorbidity is an underexplored topic in developing countries (International Diabetes Federation, 2015). Consequently, there is a call for further investigations that shall focus on demystifying the physiological connection between TB and DM. Generally, type 2 diabetes is believed to decrease a host's immune response, thereby elevating the chances of contracting active TB after mycobacterium tuberculosis infection. Similarly, TB has been reported to cause temporal glucose tolerance impairments that increase the risk of developing DM (Golub, Mohan, Comstock, & Chaisson, 2005). Additionally, serious contagions such as tuberculosis are linked to idiopathic hyperglycaemia that arises because of high generation of counter-regulatory stress hormones (such as growth hormone, cortisol, glucagon, and epinephrine) that function synergistically (Jeon, Murray, & Baker, 2012).

Findings relating to DM prevalence in TB patients differ significantly in the South Saharan parts of Africa, depending on study settings and background characteristics of study participants (Syal, Anand, & Dibyajyoti, 2015). For example, studies report a 1.9% prevalence of DM in TB patients Benin whereas the rate is as high as 38% in Nigeria. A systematic review of DM-TB comorbidity studies in South Saharan Africa suggests a high prevalence of this association despite highlight measurable discrepancies, calling for the implementation of cost-effective healthcare initiatives that shall bring TB and DM care together, thereby reducing the prevalence of this association (Baghaei et al., 2013).

2.5 Profile of DM-TB Patients

There is a general agreement among researchers that specific population-based data should be used to guide DM-TB initiatives in respective regions, countries, and areas (Martinez & Kornfel, 2014). This argument is founded on strong evidence reflecting the characteristics of people diagnosed with both TB and DM. Even so, the profile characteristics of DM-TB patients, in comparison to non-DM TB patients, vary substantially. When compared with general TB patients, DM-TB patients are typically found to be older, and most of them have additional characteristics such as HIV-AIDS, consumption of illicit substances, incarceration, a high body weight index (obesity), and alcohol abuse (Martinez & Kornfel, 2014). As such, there is a need to consider the evolving nature of TB contagion and apply non-traditional approaches that incorporate the socio-demographic characteristics of patients when examining individuals exhibiting signs of pulmonary diseases to enable accelerated TB detection (Havlir et al., 2008). There are also higher chances for DM-TB patients (in comparison with those diagnosed with TB only) to have higher levels of unemployment and lower educational attainments; both of which indirectly complicates DM and TB management because of the association between these socio-demographic characteristics with poor glucose control and lower access to healthcare (Sun et al., 2012).

From a biological perspective, diabetes heightens the exposure to developing active TB after opportunistic mycobacterium tuberculosis infection. This is principally because hyperglycaemia provides a high sugar environment that favours the growth of bacilli (Vallerskog eta al., 2010). DM further impacts on the immune system of the host - it leads to increases in the production of cytokines and interleukin 10 and reduces the generation of T-cell lymphocytes- thus reducing the ability to kill mycobacterium tuberculosis bacilli. In comparison to the general population, people with type 2 diabetes are more susceptible to latent TB infections, and they are less likely to develop extra pulmonary TB than pulmonary TB. In addition to being likely to exhibit more active lesions than non-DM patients, DM-TB patients have been found to experience TB infections in the lower lung lobes. What is more, people with poorly controlled blood sugar levels are likely to present more advanced TB infections with a 4 time higher chances of TB relapse, TB treatment failures, and TB-associated deaths (Singhal eta la, 2014).

2.6 Directional Association of DM-TB

The majority of DM-TB investigations are observational with small sample sizes (the majority of which are retrospective findings on medical records), so it is not yet possible to make an accurate description of directionality in the relationship. The majority of cohort studies up to date show that TB infection develops after diabetes, and those with additional profiling of DM patients imply that not just DM, but poorly managed diabetes increases the exposure of patients to TB infection (Kuo et al., 2013). Cross-sectional investigations similarly support the chronology of tuberculosis coming after diabetes, with TB infection being comparatively common among patients with an extended history of DM (chronic DM with a median duration of 8 years) and those presenting additional DM complications (Martinez & Kornfel, 2014). This illuminates the missed opportunity to implement TB prevention initiatives among confirmed diabetics who have supposedly had interacted for an extended period with healthcare providers. Even so, patients diagnosed with both tuberculosis and diabetes should be differentiated from tuberculosis-infected persons with increased hyperglycemia that occurs after inflammation caused during TB (Boillat-Blanco et al., 2016).

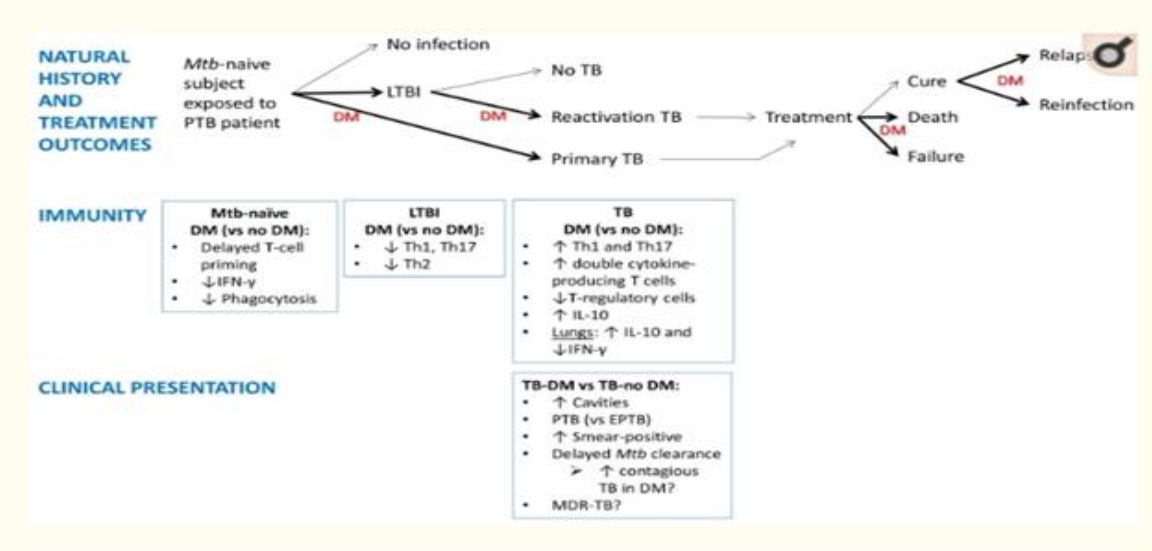
2.7 Integration of DM and TB on Early Diagnosis and Control of TB-DM comorbidity

Factoring in that nearly 50% of diabetics in developing countries are not informed of their DM condition, TB care delivery centres and clinics are gradually becoming hubs for diagnosing new DM across the globe (Subhash eta al. 2003). Some investigations show that newly diagnosed diabetes patients who have tuberculosis comorbidity (compared to patients with a longer history of DM) have variant profile characteristics, with higher chances of them being younger male patients with lower HbA1cs (Sun et al., 2012). The state of the scenario indicates the significance of TB care centres in reaching male patients who are likely to experience reduced access to the healthcare system in comparison to females and in identifying patients at an early stage of diabetes before the onset of further and typically permanent macro- and micro vascular complications. As such, an increasing public health problem for developing economies where both DM and TB are likely to coexist, is to integrate the long-term care needed for DM patients with the instant short-term care needed for TB treatment.

2.8 Clinical Manifestation of TB in DM-TB Patients and Implications on Public Health

The majority of investigations suggest that DM is linked to the clinical manifestation of TB (Sun et al., 2012). Specifically, there are higher chances DM-TB patients (in comparison to TB patients without DM) exhibit cavitary (in comparison to non-cavitary), pulmonary (in comparison to extrapulmonary), and sputum-smear affirmative tuberculosis at the point of testing. Patients with both tuberculosis and diabetes take a prolonged duration (in comparison to non-DM TB patients) to move from sputum smear-positive to sputum-smear negative (Gomez et al., 2013). Other investigations also indicate that patients with confirmed diabetes are inequitably more prone to exhibit multi-drug resilient and drug-resilient tuberculosis infection, even though this association is not explicit in all investigations (refer to Figure 4)

Figure 4: *Effect of DM on TB History: Connection to Disrupted Immunity and Clinical Features*



Note: (Gomez et al., 2013)

As illustrated in Figure 4, exposure of MTB-naïve patients to patients with pulmonary TB generally led to primary TB or LTB1 (30%) or no infection (70%). Among patients who contracted TB, the long-term exposure to recurrent TB is 10%. Exposure to TB rises by 3-fold when the patient has DM (most likely poorly-controlled and chronic), even though the contribution of DM to primary TB, reactivation TB, or LTBI has not been specified. TB relapsed can take place among assumedly cured TB patients. A background of tuberculosis does not guarantee or cause protection against re-infection with other strains of TB, and subsequent exposure increases the risk of recurrence. The bold arrows in Figure 4 and DM represent stages of DM at the point where DM seems to have an effect. The immunity response of DM patients evolves in a different way than that of non-DM patients as TB evolves. Patients with both tuberculosis and diabetes face higher chances of presenting symptomatic characteristics connected with increased tuberculosis transmission, even though the significance of TB spread has not been explored in depth. The disrupted immune response of DM patients to TB agents is bound to affect the advancement, observable manifestation, and consequences of tuberculosis, but the involved processes are shallowly understood (Gomez et al., 2013).

2.9 Extra-Pulmonary Versus Pulmonary TB

Pulmonary TB is linked to the largest proportion (75% - 80%) of TB incidences, and it is universally agreed that immune dysfunction facilitates hematogenous distribution of *Mycobacterium tuberculosis* inclining to extra-pulmonary TB. The case is typical to people taking TNF blockers or HIV-AIDS patients (Syed et al., 2012). This is associated with DM-TB patients who have a low likelihood of exhibiting extra-pulmonary TB (Yamashiro et al., 2014). The association is likely to be caused by hyper reactive cell mediated reaction to TB agents in people with diabetes, which may be insufficient for controlling *Mycobacterium tuberculosis* development within the lungs, but sufficient to suppress its spread and recurrence in other parts (Singhal eta la, 2014).

2.10 Smear –Positive and Cavitary TB

Mycobacterium tuberculosis triggers a vigorous cell-mediated immune response causing the development of pulmonary tubercles (granulomas) that are believed to have both benefits and negative effects on the host (Guirado et al., 2013). At the initial point, granules exhibit *Mycobacterium tuberculosis* development, but these structures go through central caseation with spilling and rupturing of bacilli in the respiratory tract of patients in whom TB agents keep on developing. The cavitary TB is liked with sputum smear-positive (Vallerskog eta la., 2010). Patients with DM-TB coexistence are more prone to carvoitary TB that is characterized by a significant bacillary load in sputum in comparison to TB-only patients. In combination, a higher PTB versus smear-positive tuberculosis, cavitary tuberculosis, and extrapulmonary TB at the point of testing and extended treatment duration suggest that DM-Tb patients are comparatively more contagious than TB-only patients (Vallerskog, Martens, & Kornfeld, 2010). Nonetheless, few investigations have been conducted in this regard, but if affirmed, this will introduce other public health effect for tuberculosis-diabetes comorbidity (Restrepo, 2007).

2.11 Multi-Drug and Drug-Resistant TB

The link between multidrug –and drug-resilient tuberculosis in diabetes patients is not fully understood, with contradictory outcomes on the association between multidrug-resilient TB and higher drug tuberculosis in DM-TB patients in comparison to TB patients without diagnosed TB (Perez-Navarro et al., 2015). In a systematic analysis of published research u to 2101, the prevalence of multidrug resistant or drug-resistant TB incidences was not more common in DM-Tb patients (1.25, CI 95% 0.72, 2.16) (Baker et al., 2011). Even so, these outcomes were found in few studies (n=4). This implies a need for more investigations that look into the association between multidrug-resistant TB or drug resistant TB and DM comorbidity, with proper testing for multidrug-resistant TB comorbidity at the instance of TB testing. (not limited to patients with therapeutic failures), multivariable evaluation to specify the independent roles of DM in comparison to other significant but hidden variables, and the features of the population under study and framework for local TB control initiatives so as to appreciate the conditions under which DM and multidrug resistant TB may be synergized.

2.12 TB Therapy Results in DM-TB Patients

There is an emergent body of proof that suggests a strong association between adverse TB therapy outcomes and DM-TB comorbidity versus TB treatment outcomes in non-DM TB patients (Pan et al., 2015). Preliminary investigations indicate that DM-TB patients experience higher chances of delayed mycobacterium clearance, re-infection, TB relapse, treatment failures, and death (Baker et al., 2012).

DM-TB in comparison to no-DM TB patients face higher chances to exhibit sputum smear-affirmative results after passing the rigorous stage of treatment, and this result has been found to be an early indicator of therapeutic failures (culture of sputum-smear positive after five months of clinical intervention), an outcome that is equally more likely in DM-TB patients than in TB patients who are not diabetic (Delgado-Sanchez et al, 2015). Meanwhile, death was an assurance in patients suffering from both TB and diabetes in the 1950's with investigations indicating that patients with DM-TB comorbidity faced a high chance of succumbing to TB or diabetic coma (Silwer & Oscarsson, 1958). In a meta-analysis and systematic evaluation of current investigations, Baker et al. found out that the chances of dying of causes including TB in more than 20 adjusted investigations was almost two-fold (RR 1.89; C1 95%52-2.37), and this raided to about 4.96 (CI 95%) in 4 investigations that adjusted to likely confounders and age (Baker et al., 2011).

2.13 TB-DM Patients Vs Non-DM TB Patients

Empirical findings suggest that DM patients are equitably exposed to TB infection and that DM-TB comorbidity is more linked to adverse treatment outcomes than non-DM TB patients (Syed et al., 2012). These findings imply a need for prospective cohort investigation that aim at ascertaining these observations and pinpointing causal variables that lead to therapeutic failures among DM-TB patients. Two elements turn up as suspected variables in these implied associations, including poor blood glucose control and low plasma concentration of anti-mycobacterial antibiotics in TB-DM patients versus those suffering from TB alone (ReyPineda, 2014). The first possible factor, poorly managed blood glucose levels, is linked to reduced immunity to TB agents in DM patients (refer to Figure 4), which tends to reduce the effectiveness of antimycobacterial therapy. Hyperglycemia is also likely to compromise mycobacterium tuberculosis eradication by disrupting the microvasculature and lowering the flow of blood in lung tissue. Reducing lung tissue perfusion decreases the flow of antibodies in to target tissues thereby decreasing immune surveillance. Even so, the need for investigation to analyze the impact of blood sugar management on tuberculosis therapy results is uncertain International Diabetes Federation (2015), and the World Health Organization conceptualizes the existing information enough to support glucose optimization as an aspect of DM-TB management and improving the outcomes of TB therapy outcomes in DM patients (ReyPineda, 2014).

Meanwhile, studies concerning the impact of low antimycobacterial antibiotics concentration in DM patients have conflicting outcomes and further analyses are required to assess the association between this fact and the failure of TB treatment in DM patients (Jeon, Murray, & Baker, 2012). An important area of concern is the possible development of multidrug resistant TB in DM patients. Currently, a standard framework for managing drug susceptible TB in DM patients has been proposed. At the start point, depending on the epidemiology and resources of the community, DM diagnosis/screening is required for all individuals existing within the range of 45 years and above, those with a body mass index of more than 25, people with first degree family members with diabetes, and those belonging to ethnic groups that are inevitably exposed to DM including Pacific Islanders/ Hawaiian Natives, Alaska Natives/American Indian, African Americans, Hispanics, and Asians (Jeon, & Murray, 2008).

The second consideration is the issuing of INH and Vitamin B6 to DM patients because of their high exposure to neuropathy. Thirdly, considering that DM patients have a high chance of exhibiting cavitations, smear-positivity at screening or sustain culture-positivity after 8 weeks of therapy, the sustained stage of seven months is required, for a 9-month treatment. Another suggestion is to factor in the concentration of the drug in the serum of the patient which helps in analysing the adequacy of drug dosage and making necessary adjustments. Treatment drug concentration monitoring is especially recommended to inform drug dosage adjustment at the time of dialysis and for evaluating drug interaction for patients with end-stage renal disease (International Diabetes Federation, 2015).

Figure 5: *Association between Hyperglycaemia and Dysfunctional Immunity in DM-TB Patients*

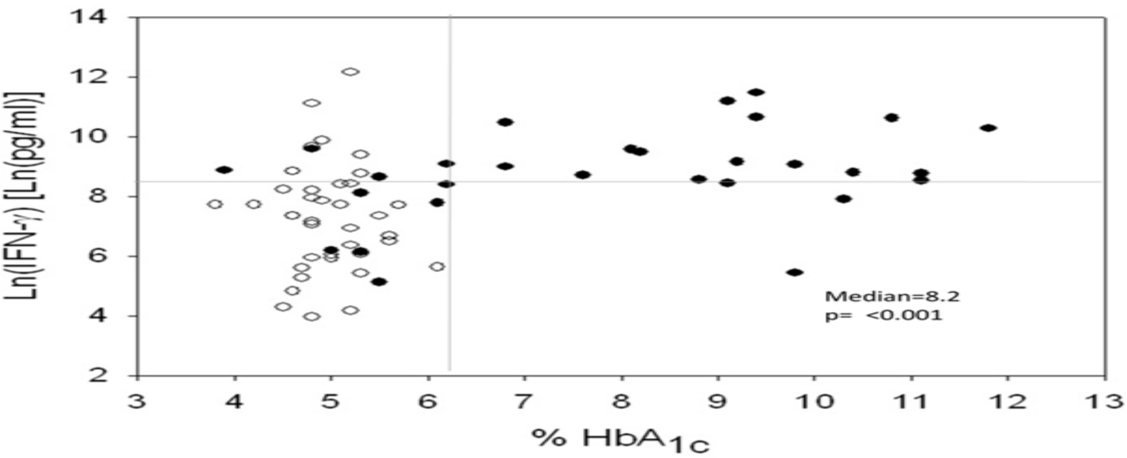


Figure 5 illustrates a lower IFN-γ production in response to purified protein extract (PDD) in patients exhibiting a higher HbA1c in contrast to TB patients with normal HbA1c. Blood drawn from non-DM TB patients was incubated with Mtb PPD for 18-24 hours after which IFN-γ production was measured using ELISA in culture supernatants. The scatter plot illustrates the outcomes in which a circle stands for one TB patient, the black dots indicate DM patients, and the white dots represent non-DM TB patients. The vertical line situated at HbA1c of 62% haemoglobin represents the upper extent of elevated (right) and normal (left) HbA1c level whereas the horizontal line represents the media IFN-γ concentration. The natural (Ln) scale was used to provide IFN-γ level (International Diabetes Federation, 2015).

2.14 Clinical Diagnosis of DM and TB

Significant research efforts have been channeled towards understanding the definitive features that separate non-DM TB patients form TB patients who are not diabetic. Accordingly, the typical indications of diabetes and TB include night sweat, exhaustion, and weight loss, but research has shown that diabetics who have TB exhibit an upper body weight than non-DM TB patients (Viswanathan et al., 2014). While some studies suggest the existence of comparatively similar clinical characteristics among patients recorded to suffer from both diabetes and TB and TB patients who are not diabetic, Kumar et al (2013) curried out an investigation aimed at exploring the impacts of diabetes in TB and found out that non-DM TB patients are more likely to exhibit extra-pulmonary infects than TB-DM patients. Nonetheless, empirical findings suggest that how patient respond to treatment can also be used to differentiate DM-TB patients from non-DM tuberculosis patients. Specifically, it has been suggested that DM-TB a notable proportion of patients with both TB and diabetes fail to respond satisfactorily to anti-TB antibiotics and that diabetes is a main clinical variable for the presence of a higher concentration of AFB (acid-fast basilica) in patients 's sputum smear. These associations have been reported in numerous studies, and it is currently conclusive that TB-DM comorbidity can be identified through the presence of pulmonary TB in patients who equally exhibit indications such as general tiredness, fever, and drastic loss of body mass (Yamashiro et al., 2014).

2.15 Testing of TB in DM Patients

Early testing of TB is recommended as a way of supporting prompt detection and treatment, which can help in preventing the spread of TB infections. Even so, the methods for testing DM patients for TB is yet to be established except for the use of chest x-ray among newly diagnosed DM (Harries et al., 2016). Satyanarayana et al. (2013) recommend one of the comprehensive strategies for testing TB among DM patients, which includes considering DM patients that exhibit TB-suggestive symptoms (including resistant cough that exceeds 21 days, loss of body weight, abnormal chest x-ray, and fever) for further diagnosis and TB testing once TB has been confirmed. Worth noting is that most of preliminary studies discourage TB testing among at the point of DM diagnosis and favored TB tests at later stages of DM treatment among DM patients who showed TB-associated symptoms as articulated above. The strategy was justifiable considering that DM may cause blood glucose levels to increase, which may trigger the activation of cytokine that may cause false positive results when TB testing is conducted too early among DM patients (International Diabetes Federation, 2015). Nonetheless, postponed TB testing also cause DM patients to miss out on the chance of benefiting from tailored treatment. What is more, the access to regular subsequent laboratory testing is a challenge in many high-TB burden areas, especially in Africa were the delivery of health care services is decentralized (Yamashiro et al., 2014).

The most convenient methods for screening ought to be explored pee, irregular blood glucose and glycatedhaemoglobinA1c (HbA1c)]. Cases diagnosed by the two screening methodologies mentioned before should be conveyed imminent studies analysing the effect of non-DM and DM hyperglycaemia on TB treatment results, utilizing institutionalized TB regimens and results, whereby other frustrating elements (age, weight, HIV and alcohol and whether smoking or not) are considered. The level of hyperglycaemia as well as type of DM control, estimated, for example, instance through HbA1c, are vital variables to take into account. Primary treatment results ought to incorporate; pharmacokinetic levels of rifampicin and oral DM medications, the functioning of the liver, TB treatment results, repeat of TB, one year after completing TB treatment as controlled by medication sensitivity testing and sputum culture at the initial TB treatment stage and at the time of TB recurrence to evaluate the relationship and linkages with drug resilient TB (Pablo-Villamor et al., 2014). Death rates are high in diabetic patients who are receiving TB treatment, a study is therefore necessary to answer some queries such as; when does death occur in connection to beginning of anti-TB treatment, and if it's more helpful to use DM control measures or modified TB medication regimens, the time taken for the anti- TB treatment and TB sedate doses decrease the possibility of death (Ottmani et al., 2010).

2.16 TB active case finding

While Kenya has a high burden of TB, only 46% of the cases were diagnosed in 2016(D. Okelloh et al.,2021). It is recommended that each TB programme has to figure out which combination of Active Case Finding activities would be most appropriate in the locality (Yuen et al. ,2015). D Okelloh et al.,2021 found that lattendance of TB screening in rural Western Kenya was maximized when implemented as a single event and the CHV paid a daily wage. Onyango etal.,2o18, found that most childhood TB cases in Kenya are detected through passive case finding. The authors recommended that active case finding be intensified among HIV infected children

2.17 Diagnosis and Treatment

The most broadly utilized diagnostic technique for TB associated with diabetes mellitus is examination of stained smears of sputum. Chest radiographs are regularly used to aid diagnosis. Analysis of LTBI is done using the tuberculin skin test (Payam et al., 2016). By and large, active TB is adequately treated with a blend of four medications taken for no less than half a year (Payam et al., 2016). The treatment of TB patients who are HIV positive is more muddled, as the best treatment regimen must take into account the progression of HIV/Aids in the cases and the interaction of medications, more so when protease inhibitors are involved. Treatment of MDR TB involves complex processes which require the utilization of costlier and more toxic second-line tranquilize regimens (Payam et al., 2016). MDR TB will probably be deadly in developing nations due to lack of effective treatments. It is possible to treat LTBI with several medication regimens. In numerous industrialized countries, treatment is generally suggested for people with LTBI at high danger of developing active TB. For example, HIV positive patients and people who TB patients come into contact with (World Health Organization, 2017).

2.18 Theoretical Framework

In general, models of health are three, namely; the biomedical framework of health, the wellness framework of health, and the biopsychosocial model health. Current health framework differs in merit and emphasis. This study relates to the biomedical framework that emphases on the physical and metabolic aspects of a disease and suggests the utilization of medical framework of care in clinical interventions. The theory guides the activities of the current study (especially active TB case finding) the process of the current investigation as it centers on clinical tests, therapeutic interventions, and the application of objective and empirical strategies in disease diagnosis and treatment. In line with the theory's emphasis on objective scientific methods of disease diagnosis, the current study involves the application of Gene Xpert, X-ray, and FM microscopy tests to diagnose TB among confirmed diabetics. This theory is considered important in the health discipline because it supports the application of evidence-based practice and encourages research and development that founds innovation in treatment and diagnostic strategies (Syed et al., 2012). The basic argument of the medical model of health is that disease is identified and detected through an organized course of observation, explanation, and isolation in line with acceptable protocol standards such as tests, description of a set of symptoms, or medical examination. A major strength of the medical model is its foundation in scientific research that paves the way for objective results. Nonetheless, opponents argue that biomedical theory has a narrow focus because it fails to look into the cause of disease as well as the psychological dimension of illness/well-being.

The principal difference between the biomedical theory of health and the biopsychosocial theory focuses on the need to address the biological, social, and psychological aspects of health instead of disease and injury (Vallerskog, Martens, & Kornfeld, 2010). The design of the current study is linked to this theory of health as both look at factors that influence the health of an individual. In essence, the biopsychosocial model encourages health research that factors in population understanding of a disease and supports the active involvement of community members in improving community health and way of living. In line with this theory, the current study looks at socioeconomic and behavioural elements (including type of job, excessive intake of alcohol as well as smoking habits) and their relation to TB infection among diabetes patients.

The biomedical theory and the biopsychosocial model are applicable in this study because TB can be diagnosed using biomedical methods, and its risk of occurrence can be minimized by reducing exposure to risk factors (such as contact with infected persons, exposure to respiratory irritants, and behavioural elements such as excessive intake of alcohol as well as smoking habits) (Vallerskog eta la., 2010). The strength of this theory is that is that it relies on self-reported information that is readily available. Additionally, the theory is founded on interpretive analysis of data that helps in the identification of interventions that best address population-based health concerns (Zumla et al, 2015). As a way of addressing the short falls of the biopsychosocial and biomedical theories, the current investigation is guided by the wellness model of health since the findings are intended for use in improving the general health and life experiences of diabetics.

The wellness model conceptualizes health care as the constant process of optimizing the functionality of an individual by maintaining a state of balance among the various dimensions of life, i.e., the occupational, physical, intellectual, social, emotional, and spiritual aspects of life. The wellness model of health is theoretically conceptualized as a foundation for multidisciplinary approach to health, which allows collaboration among health professionals in improving health outcomes (Syed et al., 2012). The model presents a theoretical basis for an integrated examination of an individual's health rather than majoring solely on the focal points of traditional health care interventions. This holistic outlook at health and health care is liked to various admirable outcomes, including the potential to support the realization of integrated care that is attainable through a consistent and sustained collaboration of health professionals from diverse specialties in the delivery of evidence-based practice, which is linked to better patient outcomes (Dooley & Chaisson, 2009). TB and diabetes have historically been conceptualized as independent diseases that require different preventive, diagnostic, and management/treatment approaches. However, by looking at comorbidity and relationships of the two, the current study purports the development of an inclusive care environment where TB and diabetes can be addressed in inclusion, thus improving the health of diabetics.

2.19 Conceptual Framework

The dependent variable of this investigation is TB-DM coexistence whereas the independent variables include demographic variables (age and sex), social behavioural elements (alcohol abuse and smoking), and socioeconomic activities (occupation). The conceptual framework of this investigation is founded on the biomedical model, biopsychological model, and the wellness model. In line with the biomedical model, it is generally presumed that the application of objectivist methods of diagnostic testing will result in the general improvement in the health of DM patients in Kenya and an overall decline in the prevalence of active TB in the country. Objective clinical (FM microscopy, chest x-ray, and Gene Xpert) methods have been used to test dualism of TB-DM coexistence and independent variables. A decline in active TB cases shall only be attainable through evidence-based practice that is informed by population-based information as per the risk factors of TB infection and correlated elements among people with diabetes (International Diabetes Federation, 2015). The study is also linked to current evidence indicating active case finding as an instrument of early diagnosis, which is statistically tied to better treatment outcomes among TB-DM patients (World Health Organization, 2017).

Chapter Three

Research Methodology

3.1 Introduction

The current section articulates the methodologies adopted in this investigation. Discussed herein are the study design, study area, sample selection strategies, data collection strategies, data analysis methods, and ethical considerations.

3.2 Study Design

The goal of the current investigation is to determine active TB among diabetic mellitus patients attending diabetic outpatient clinics at JM Kariuki Memorial County Referral Hospital. The principal difference between interpretive and empirical analytical research approaches is that the first focuses on disclosing the interpretive practices of human subjects, the latter category capitalizes on objective knowledge and deploys deductive reasoning that applies existing theories in formulating testable hypotheses (Anon, 2015). Considering the quantitative nature of the research problem in question, the current investigation assumes the objectivist approach that uses scientific methods to answer research questions. The approach uses objective diagnostic techniques in active TB identification, and applies quantitative analytical approach to investigating TB-diabetes comorbidity and the role of underlying factors such as age, occupation, and behavioural elements. Individual susceptibility to *Mycobacterium tuberculosis* bacilli infection was analysed based on patients' demographic characteristics (including age and sex), behavioural and lifestyle characteristics (such as alcohol consumption and smoking history) and socioeconomic variables, i.e., occupation.

3.3 Study Area

The study area was carried out in JM Kariuki County Hospital in Nyandarua County (one of the 47 counties in the Republic of Kenya). Nyandarua County has an area of 3,245.25 Km^2 (Refer to Appendix III). The County is on the lee-ward side of the Aberdare ranges and has high altitude which influences temperature, rainfall, and humidity. It is generally wet throughout the year and this enables the residents to practice crop farming and animal husbandry both on large and small scale. Its neighbouring counties include; Nyeri to the east, Murang'a to the east, Laikipia to the north, Nakuru to the west and Kiambu to the south. According to the 2019 census, the population of Nyandarua Country was 638,289 (KNBS, 2019). The projected population for the year 2020 is 652,117 (KNBS, 2019). The County's population is growing at an increasing rate, and this is leading to increased demand for medical facilities. There is also an increasing need for health workers to augment the economic prosperity, growing population, and health and wellbeing of the county's populace. There are five constituencies which form the Sub-Counties, namely; Kinangop, Kipipiri, Ol'Kalou, Oljoroorok and Ndaragwa (Nyandarua CIDP, 2019).

3.4 Study population

The study capitalized in diabetic patients enrolled in the Diabetic outpatient clinic at the JM Kariuki County Hospital as the study population. All consented patients who met the criteria underwent TB screening and done Gene Xpert, FM microscopy, and X-ray tests as part of their constitution in the study.

3.4.1 Sample Size Determination

The formula by Fisher *et al* (1998) was used to determine the sample size since the catchment population of JM Kariuki County referral hospital is greater than 10,000 (Restrepo et al., 2014). The formula is summarized below:

$$n = \frac{Z^2 \times pq}{d^2}$$

Below is a list of representations in the above formula:

n = Minimum sample size,

Z = Normal standard deviation set at 2.58 which is equivalent to 99% confidence interval,

p = Prevalence of diabetes in Kenya is 4.56% (International Diabetes Federation, 2015) and 0.05 was used

q = 1-p

d = accuracy degree which was set at 0.05

Hence;

$$n = \frac{2.58^2 \times 0.05 \times 0.95}{0.05^2}$$

n = 126

An additional 10% of participants was added in the study to cater for the errors arising from non-conforming responses. As such, a sample size of 139 was considered the minimum number of diabetic patients to be included in the study.

3.5 Data Collection and Sampling

3.5.1 Sampling Techniques

J.M. Kariuki County Hospital was selected as a study area since it is the only facility in the county that has Gene-Xpert testing, fluorescent microscopy testing, and radiology diagnostic facilities. In selecting the diabetic patients, the study employed the simple random sampling technique.

3.6 Inclusion and Exclusion Criteria

3.6.1 Inclusion

Only patients who met specific criteria were included in the investigation. More specifically, one had to be diabetic patients living in Nyandarua County for not less than six (6) months to engage in the investigation. Only patients who were not undergoing anti- TB chemotherapy and not showing symptoms that were suggestive of TB were considered for participation, and they had to agree to take part in the research by signing a consent form.

3.6.2 Exclusion Criteria

The study excluded diabetic patients who were showing symptoms suggestive of Tuberculosis to minimize bias selection. Nonetheless, all patients not willing to take part in the study were excluded from study participation. Also, participants aged below 18 years were excluded when consent was not provided by the guardian/parent.

3.7 Data Collection Procedures

Data on patients' sociodemographic information, socioeconomic status, and personal behavioural habits relevant to TB infection was collected through face-to-face interviews and recorded in a structured interviewer schedule. On the other hand, data on patients' microscopy test, Gene Xpert and radiological examination was clinically done, and results decoded through observation. The outcomes of the tests were recorded in a structured observational checklist.

3.7.1 Laboratory Procedures

3.7.1.1 Collection of sputum specimen

Sputum specimens were collected from all diabetic patients (Lab diagnosis of TB by Sputum microscopy 2013 edition). Participants were encouraged to flush their mouth two rounds prior to producing the specimen. This practice was adopted to expel any contaminating microbes and remains of food in the mouth. Study participants were also told to breath twice, cough energetically, and spit the cough into the clean 100ml blue cap screw-capped bottle. This procedure enabled sputum to be expectorated from deep down the lungs. Patients were encouraged to hold the sputum container near the lips and expectorate in it carefully after a cough. At the fridge lab, standard Acid-fast bacilli (AFB) direct smear microscopy utilizing fluorescent staining was done on each of the sampled sputum (Richard, 2013). Gene Xpert Molecular Technique (World Health Organization, 2017) was also done on the samples and patients were also subjected to Chest X ray to confirm TB in patients suspected to have the disease.

3.7.1.2 TB smear microscopy using fluorescent microscope

Procedure for auramine staining of slides was done as described below:

First, the frosted slides were positioned in sequential arrangement on a staining bridge, with the smear side up, while taking care that they did not meet one another. Filtered 0.1% auramine stain was applied on the slides after which the auramine stain was left on the slides for 20 minutes, rinsed with water and excess water drained off. Acid alcohol was then applied as the decolorizing solution for 1-3 minutes, after which they were wash with water and excess drained off. Subsequently, 20% methylene blue was applied on the slides as the counterstain for 1 minute, cleaned with water and extra poured out. The stained slides were air dried on slide rack after which dried stained smeared slides were examined by a fluorescent microscope at power 10 then power 40 for presence of the *Mycobacterium tuberculosis* bacilli: (Lab diagnosis of TB by sputum microscopy handbook by Richard et al., 2013)

FM microscopy results interpretation was:

i. 0 for No TB bacilli seen in the smear

ii. 1+ for 10-100 AFBs per 100 fields TB bacilli seen.

iii. 2+ for 1-10 AFBs per field (50 fields) TB bacilli seen.

iv. 3+ for >10 AFBs per field (20 fields) TB bacilli seen.

v. Less than 10 AFBs per 100 fields, the specific number of AFBs was indicated.

Table 1 below indicates a summary of Microscopy results and interpretation

Table 1: *FM Microscopy Results Interpretation*

IUATLD/WHO scale	ZN 1000 x magnification, 100 HPF per length of the smear	FM Power200-250 magnification, 30 fields= 300 HPF per length of the smear	FM Power400x magnification, 40 fields= 200 HPF per length of the smear
Negative	Zero AFB/1 length	Zero AFB/1 length	Zero AFB/1 length
Scanty	1-9 AFB/1 length	1-29 AFB/1 length	1-19 AFB/1 length
1+	10-99 AFB/1 length	30-299 AFB/1 length	20-199 AFB/1 length
2+	1-10 AFB/1 HPF on average	10-100 AFB/1 field on average	5-50 AFB/1 field on average
3+	>10 AFB/1 HPF on average	>100 AFB/1 field on average	>50 AFB/1 field on average

3.7.2 Identification of *Mycobacterium tuberculosis* using Gene-Xpert molecular Technique

Molecular examination using Real-time PCR was utilised to detect *mycobacterium tuberculosis* complex and rifampicin drug resistance. The Gene-Xpert sample reagent was added into the falcon tube containing a sputum sample, vigorously mixed and incubated for 15 minutes at room temperature. Secondly, 2mls of the liquefied sample was aspirated using a pipette into the cartridge. The cartridge was then loaded into the Gene-Xpert machine after which it was incubated for 2hours before reading the results by Global laboratory initiative, 2020.

The following criteria were adapted in results interpretation:

i. MTB not detected- Negative results
ii. MTB detected Rifampicin sensitive- 1st line Drug sensitive TB
iii. MTB detected Rifampicin resistance- 2nd line Drug sensitive MDR TB

3.7.2.1 Radiological Evaluation

The sampled TB-positive DM patients were subjected to Chest X-Ray. X-rays were taken for the anterior-posterior view and the results were analyzed by the radiologist. The X-Ray was categorized as one-sided/bilateral penetration with/without holes, invasion with hilar lymph node enlargement and unilateral/bilateral pleural effusion.

A four-point scoring scheme was utilized for results interpretation as described below:

i. No pathology,
ii. Pathology not consistent for TB,
iii. Pathology consistent for TB, and
iv. Pathology highly consistent for TB) was introduced to report on the TB resulting Chest X-Ray.

A participant was denoted as TB positive when X-ray score ranged between iii and / or iv, which indicated pathology that was consistent and/or highly consistent for TB. Features such as mediastinal shadows, pleural effusion, small nodular shadows or solitary hilar were considered as consistent for TB whereas nodular or patchy shadows, cavitation and calcified shadows were regarded to be highly consistent with TB (WORLD HEALTH ORGANIZATION, 2014)

3.7.2.2 Random blood sugars levels

Fasting and random blood glucose level was measured using a glucometer which estimates blood glucose levels quantitatively. The capillary whole blood samples were drawn from the fingertips. A test was thereafter conducted by putting 1ul of blood drawn from the fingertip of the patient on a test trip and inserting the strip in the glucometer. Finally, the blood glucose index (mmol/l) of the patient was read after 60 seconds.

The interpretation of blood sugar index was done based on the guidelines WHO (2006) on the diagnosis and definition of diabetes and intermediate hyperglycaemia. As such, 3mmol/l to 7mmol/l was used to indicate normal blood glucose levels whereas levels above 8mmol/l indicated diabetes (World Health Organization, 2014).

3.8 Data Analysis Techniques

After coding the data, the SPSS version 22 was used to analyse the data. Descriptive statistics such percentages and frequencies were used to summarize data on socio demographic information, socio economic status and personal habits relevant for TB infection. Chi square test of independence and Fishers' test were used to draw generalization and inference on association between diabetes and TB. Univariate odds ratio (OR) and 95% confidence interval (CI) was used to assess accuracy of estimated relationships between TB and DM. A p value of ≤ 0.05 was considered statistically significant in estimating the strength of an association.

3.9 Ethical Consideration

Ethical clearance was obtained from Mount Kenya University Ethical Committee. Permit to carry out the study was sought from the National Commission for Science, Technology and Innovation. Permission to conduct the research was sorted from Nyandarua County Health Office and JM Kariuki County Hospital before commencing the study. Informed consent was obtained by filling the consent form by patients before collecting the specimen and interviewing them. All patient data obtained was handled with confidentiality. Laboratory coding was used to identify patients from whom samples were collected. Furthermore, APA ethical guidelines were used to prevent the infringement of copyright provisions. As such, due recognition has been given to all borrowed concepts, ideas, and findings.

Chapter Four

Research Findings and Discussion

4.1 Point Prevalence of TB among Diabetic Patients

Although both point prevalence and prevalence measure the percentage of population suffering for the disease under study, point prevalence differs from prevalence because it involves estimating the spread of a disease in a particular point in time. The following formula was used to estimate the point prevalence of TB among diabetics

Formula 1: $$\boldsymbol{Prevalence} = \frac{\boldsymbol{Number\ of\ Cases}}{\boldsymbol{Population\ Size}} \times \mathbf{100}\%$$

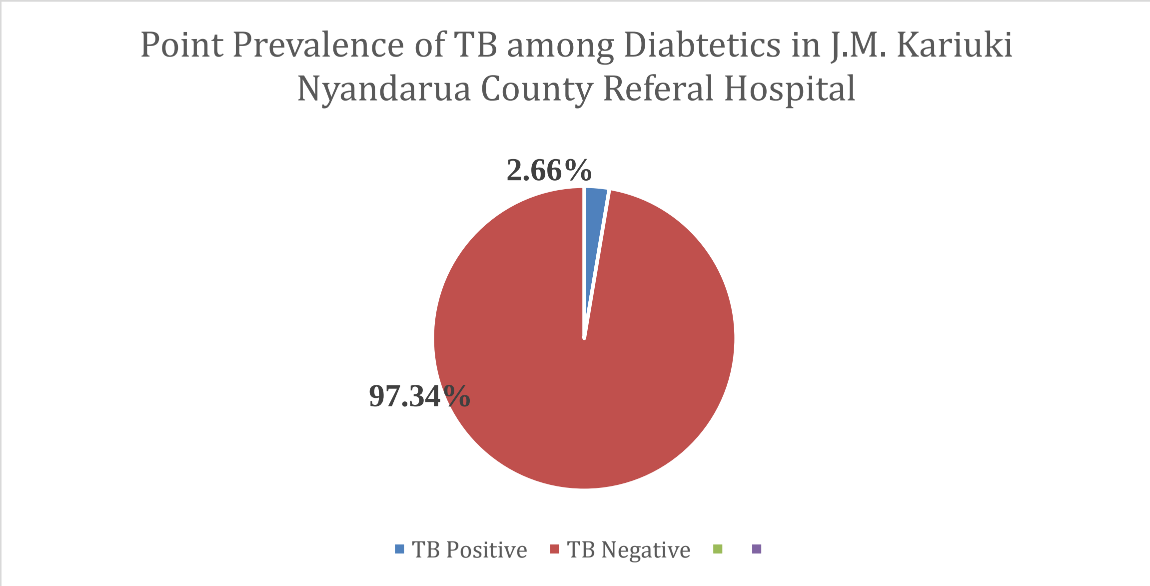
This formula was adopted from the U. S. Centres for Disease Control (CDC) report on Obesity in the US (Payam et al., 2016). Table 2 summarizes the frequency of positive TB cases as well as the prevalence of TB among the study participants:

Table 2: *TB Point Prevalence among Diabetics*

Value Label	*Frequency*	*Percent*
Positive	5	2.66
Negative	183	97.34
Total	188	100.0

The point prevalence of TB among the selected diabetics was 2.66%. The implication in this instance is that, out of the 188 diabetic patients, 5 (2.66%) were suffering from reported or unreported TB infection. Figure 6 below gives a graphical representation of Point Prevalence of Diabetes among DM Patients.

Figure 6 : *Point Prevalence of TB among DM Patients*



4.2 Positive Yield of TB diagnosis by Gene-Xpert versus X-ray and FM Microscopy diagnostic methods?

Three testing criteria- Gene Xpert, FM-Microscopy, and Chest X-ray- were used to identify active TB cases among diabetic patients seeking out-patient medical attention at JM Kariuki County Hospital. The table 3 below describes the positive yield of TB based on the results of each diagnostic methods.

Table 3: *The Positive Yield of Gene Xpert, Chest X-ray, and FM Microscopy*

Type of Test	Positive TB yields	Sample size	Prevalence
Gene Xpert	3	188	1.60%
Chest X-ray	1	188	0.53%
FM Microscopy	1	188	0.53%

The positive yield of Gene-Xpert was 3 (prevalence rate of 1.60%) while that of Chest X-ray and FM Microscopy were both 1 (prevalence =0.53%). The frequency of positive cases and the sample size were used to calculate confidence intervals using the equation described in Formula 2:

A default 5% value was used to estimate measurement accuracy and data variability. E error bar in Figure 7 estimate the estimated disparities between the actual value and reported values in as far as test-specific positive yield is concerned.

Figure 7: *Error Graph: Positive Yield of TB Diagnosis by Gene-Xpert Versus X-ray and FM Microscopy Diagnostic Methods*

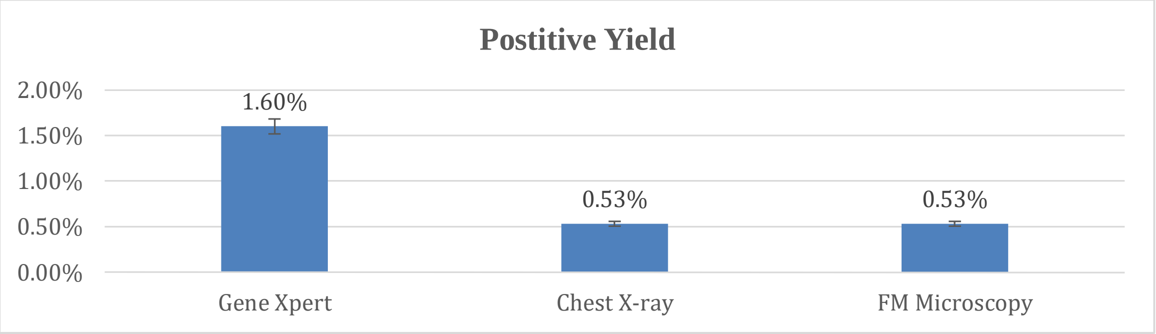


Figure 7 above illustrates the positive yield of TB diagnosis by FM microscopy, and chest Xray. As illustrated above, the highest positive yield (p= 1.60%, 95%) was noted for Gene Xpert in comparison to Chest Xray and FM microscopy (p= 0.053%, 95%). No statistically significant difference was noted in the effectiveness of the diagnostic methodologies in testing for active TB in DM patients.

4.3 Association between Socioeconomic Factors and TB infection among Diabetic Patients

The study factors in socio-economic elements, including age, occupation, gender, and health behaviour (i.e., alcohol consumption, smoking, and blood sugar management outcomes) as socioeconomic elements in the investigation of the occurrence of TB infection among diabetics. The section focuses on age and gender before going to occupation, alcohol consumption and smoking where establishment of association between specific socioeconomic factors and TB-Diabetes co-occurrences was done.

4.3.1 Age of TB-Infected Diabetic Patients

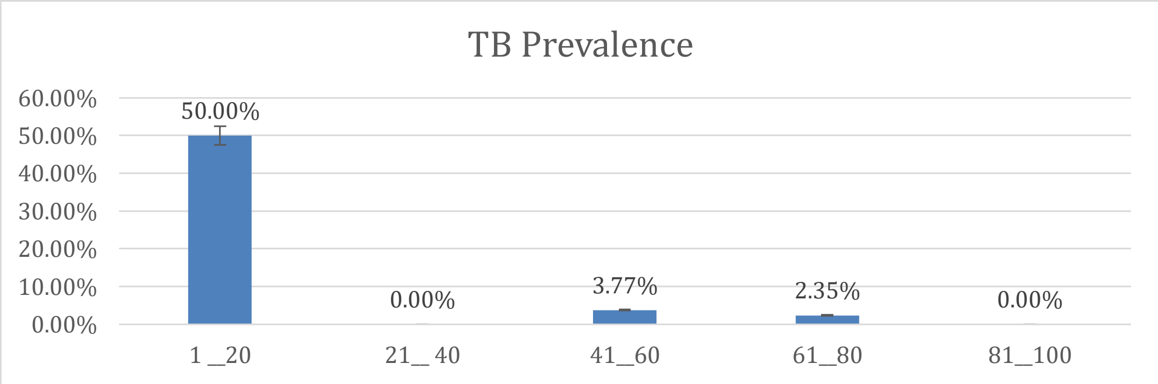
This sub-section identifies the most affected age-groups when it comes to TB infection among diabetic patients. Table 4 illustrates the number of TB cases as per the age-group of patients taking diabetes treatment at the outpatient clinic in question.

Table 4: *Age-Group Comparison of TB Occurrence among Diabetics at JM Kariuki County Referral Hospital*

Age	Positive TB yields	Sample size	Prevalence
1-20	1	2	50.00%
21-40	0	28	0.00%
41—60	2	53	3.77%
61-80	2	85	2.35%
81-100	0	20	0.00%

As indicated in Table 4 above, the prevalence of TB was 50% among patients aged 1-20, and 3.77% and 2.35% among patients aged 41 to 60 and 61 and 80 years respectively. The prevalence of TB in different age-groups was used to develop error graphs in Figure 7 below

Figure 8 : *Comparison on TB Occurrence among Different Age-Groups of Diabetics*



As illustrated above, the prevalence of TB infection was 3.77% among the 41-60 age group and 2.35% among the 61-80 age-group. Although 50% of patients aged 1-20 years had active TB infections, this outcome is not statistically meaningful because of the reduced sample size proportion of patients in this age category (n=2).

The confidence interval (refer to Formula 2 in Section 2.0) of age group 1-20 was null considering that the difference between the sample size and the frequency (n-x) must be greater or equal to 5 for estimations to occur. Pearson's Chi-square test was further used to test the existence of a statistical association between the age of diabetics and TB infection. The results are as summarized below:

Table 5 : *Chi-Square Test: Relationship between Age-group and TB-Diabetes Co-occurrence*

Statistic	*Value*	*df*	*Asymp. Sig. (2-tailed)*
Pearson Chi-Square	18.80	4	0.001

A P-value of 0.001 (≤0.05) was found, suggesting the existence of a strong statistical relationship between TB infection and the age of diabetic patients. What these results suggest is that diabetes patients get more susceptible to TB infection as they age

4.3.2 Gender of TB-Infected Diabetic Patients

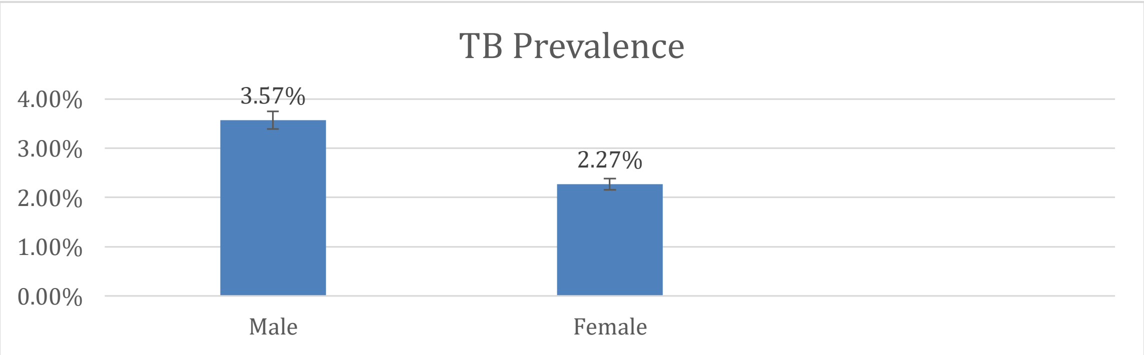
This sub-section identifies the most affected gender when it comes to TB infection among diabetic patients. Table 6 illustrates the number of TB cases per gender of patients taking diabetes treatment at the outpatient clinic in question.

Table 6: *Gender Comparison of TB Occurrence among Diabetics at JM Kariuki Hospital*

Gender	Positive TB yields	Sample size	Prevalence
Male	2	56	3.57%
Female	3	132	2.27%

As described in Table 6 above, 2 out of 56 diabetic males tested TB positive whereas 3 of 132 female diabetics tested positive of TB. Figure 8 illustrates these findings in terms of error bars.

Figure 9: *Comparison of TB Occurrence by Gender among the diabetic patients in the study findings.*



The prevalence of TB among male diabetics was 3.57% which was comparatively higher than the prevalence of TB among female diabetics (2.27%) and in the general cohort (2.66%).

Pearson's Chi-square test was applied to evaluate the existence of a relationship between the gender study participants and TB infection. The results are as summarized below:

Table 7: *Chi-Square Test: Relationship between Gender and TB-Diabetes Comorbidity*

Statistic	*Value*	*df*	*Asymp. Sig. (2-tailed)*
Pearson Chi-Square	0.26	1	0.613

A p-value of 0.613 (≥0.05) suggests the lack of existence of an association between the gender of diabetic patient and TB infection. These findings suggest that gender does not influence the risk of TB infection among diabetic patients.

4.3.3 Occupation of TB-Infected Diabetic Patients

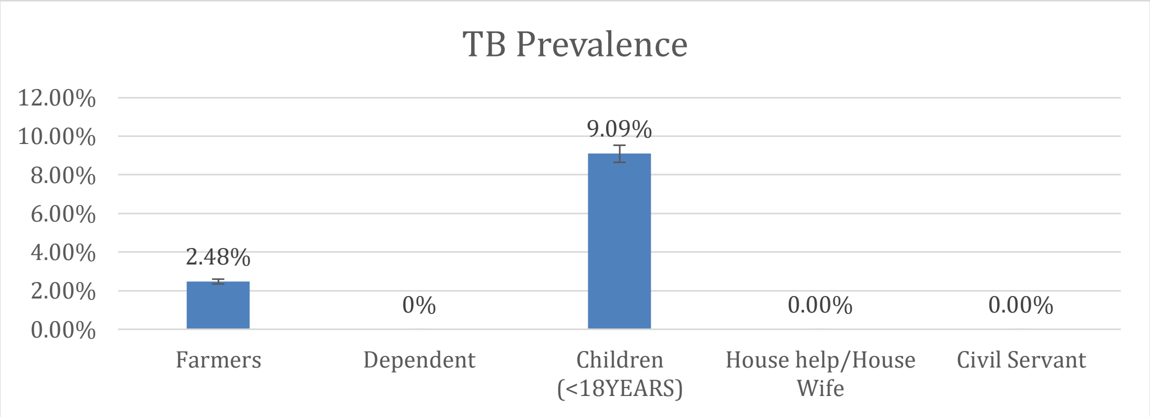
The current sub-section describes the occupation of TB infected diabetic patients. Table 8 illustrates the number of TB cases as per occupations of diabetic patients.

Table 8 : *Occupation of TB-Infected Diabetic Patients*

Occupation	Positive	Negative	Sample Size	Prevalence
Farmer	4		161	2.5%
Dependents	0		3	0
Children	1		11	9%
House help	0		4	0
Civil Servants	0		4	0
Others	0		5	0

4 of 161farmers and 1 of 11 children had TB. Zero TB cases were noted in dependents (above 18yrs but not working) (N=3), House-helps/House-wives (N-4), civil servants (N=4) and others (N=5).

Figure 10: *Comparison on TB Occurrence among Different Occupations of Diabetics Patients*



As indicated in Figure 9 above, TB infection was noted in two specific occupation groups, including children with a prevalence rate of 9.09% (CI 95%) and Farmers, with a prevalence rate of 2.48% (CI 95%).

Table 9: *Chi-Square Test: Relationship between Occupation and TB-Diabetes Co-occurrence*

Statistic	**Value**	**df**	**Asvmo. Sio. (2-tailed)**
Pearson Chi-Square	17.92	5	0.003

The p-value is 0.003(≤0.05), suggesting the existence of association between TB and Occupation. These findings suggest that TB is most prevalent in Farmers and Children, implying that daily socioeconomic activities influence the exposure of DM patients to TB infection.

4.4 Health Behaviour of TB-Infected Diabetic Patients

Two categories of health behaviours were considered in as far as TB-Diabetics co-occurrence is concerned, namely; alcohol consumption and cigarette smoking. The researcher dealt with each of these two components independently as shown below:

4.4.1 Smoking Behaviour in TB-Infected Diabetics

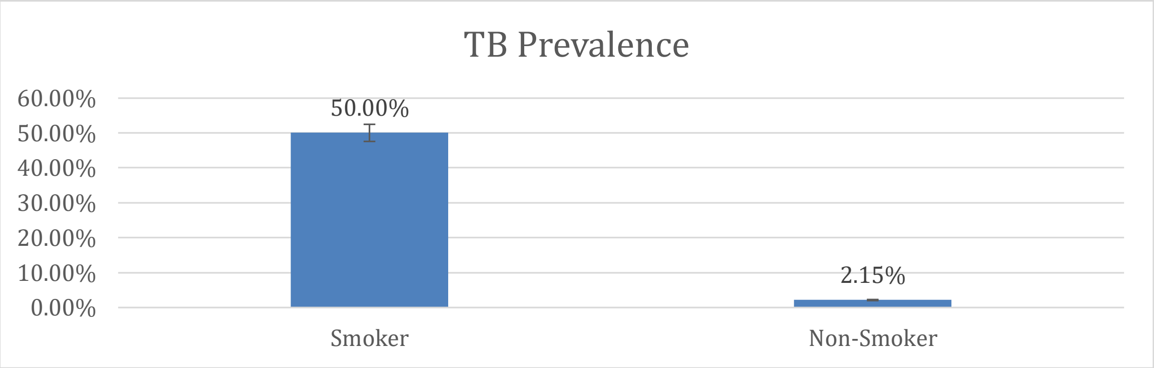
Considering cigarette smoking as a TB risk factor, participants were asked to indicate whether or not they smoked tobacco. The results were as shown in Table 10 below:

Table 10: *Smoking Habits and TB Infection among Diabetics*

Sub-group	Positive	Sample Size	Prevalence
Smoker	1	2	50.00%
Non-Smoker	4	186	2.15%
Total	5	188	

As indicated in Table 10, 1 of the 2 participants with smoking habits tested positive for TB. The 1 of the 5 positive TB cases were smokers, implying that 20% of positive TB cases and 0.53% of the entire study population were smokers.

Figure 11: *Comparison on TB Occurrence amongst Diabetics Patients with Smoking Habits and Diabetes Patients without Smoking Habits*



A chi-square analysis was done to determine the existence of an association between tobacco smoking and TB infection among diabetic patients. Results were as shown in Table 11 below:

Table 11: *Chi-square Tests: Relationship between Tobacco Smoking and TB-Diabetes Co-occurrence*

Statistic	**Value**	**Df**	**Asvmo. Sio. (2-tailed)**

Pearson Chi-Square	17.50	**1**	0.000
Likelihood Ratio	4.73	**1**	0.030

As indicated, chi-square analysis resulted in a value of 0.000 (<0.05), suggesting the existence of statistical association between smoking and TB infection among diabetics. These findings imply that tobacco smoking increases the exposure of diabetes patients to TB infection.

4.4.2 Alcohol Consumption in TB-Infected Diabetics

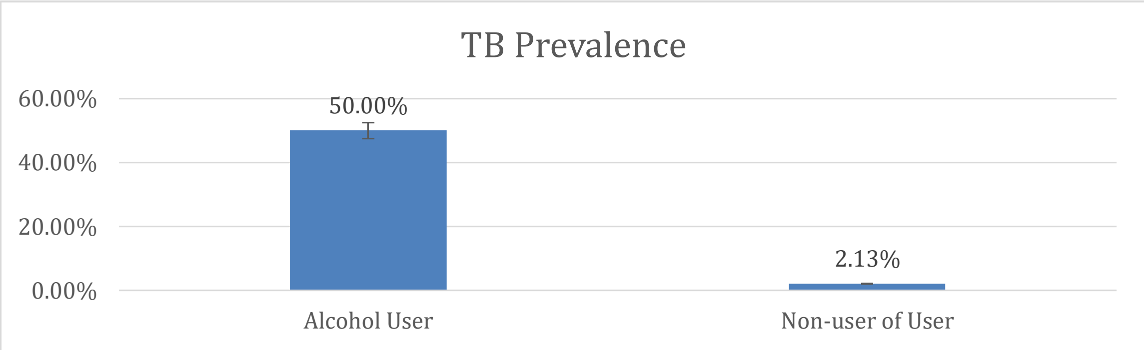
Alcoholism was considered one of the risk factors for TB among diabetics. As such, an item was included to query whether study participants had alcohol consumption habits.

Table 12: *Alcohol consumption and TB infection among Diabetic*

Alcohol Consumption	Positive	Negative	Sample Size	Prevalence
Alcohol User	**1**	**1**	**2**	**50.00%**
Non-user of User	**4**	**182**	**186**	**2.13%**

The results where as shown in error bars in Figure 12 below:

Figure 12: *A comparison of TB Infection among Diabetics with Alcohol Consumption Habits and Diabetic Patients who are Non-users of Alcohol*



As indicated in Table 12 above, 1 study participant has alcohol consumption habits, who turned out to be one of the positive TB cases among the sampled diabetic patients.

A chi-square test was subsequently conducted to estimate the association between alcoholism and TB infection among DM patients.

Table 13: *Chi-square tests: Relationship between Alcoholism and TB-Diabetes occurrence*

Statistic	**Value**	**Df**	**Asvmo. Sio. (2-tailed)**
Pearson Chi-Square	17.50	**1**	0.000

Consequently, a value of 0.000 (≤0.05) was obtained suggesting a statistical correlation between alcohol consumption and TB infection among diabetics. These findings mean that alcohol consumption increases the chances for TB infection among diabetes patients.

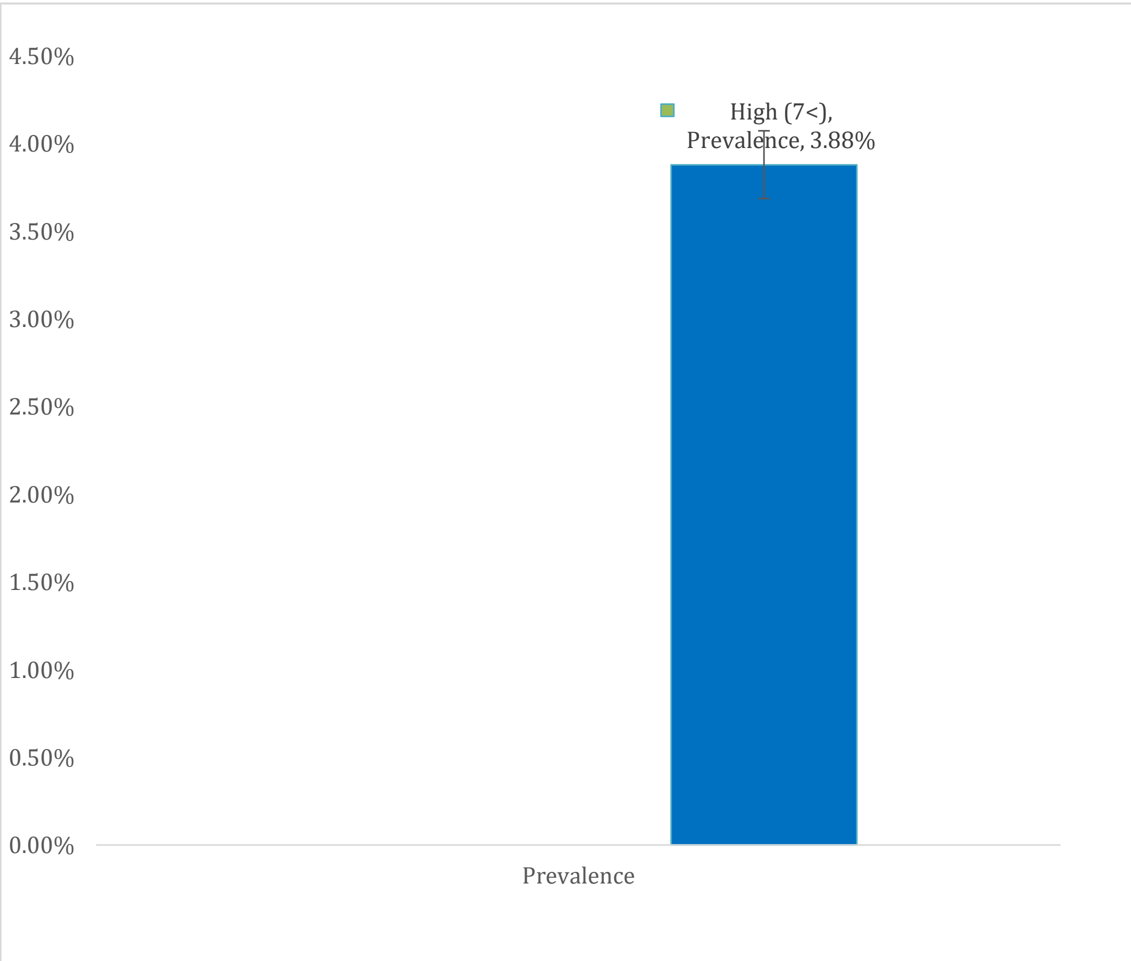
Table 14: *A comparison of TB Occurrence amongst Diabetics with Low, Moderate, and High Blood Sugar Levels*

Sugar level	TB Positive cases	Sample Size	Prevalence

Low (<3)	0.00	6	0.00%
Normal (3.5-7)	0.00	52	0.00%
High (7<)	5.00	129	3.88%

All Positive TB cases had high sugar levels. The prevalence rate of TB cases in people with diabetes was 3.88%. The outcomes are as illustrated in the error graph below:

Figure 13: *Prevalence of TB in Diabetics*



4.5 Discussions

The connection between TB and diabetes is a significant challenge for global TB control. Empirical findings suggest that exposure to TB is almost three times higher among diabetics than the general population (Dooley & Chaisson, 2009). Even so, programs for managing this are greatly lacking in developing /middle or low-income economies where DM is seen as a minor problem and not treated as the TB epidemic (Ruslami et al., 2010). This view is, however, changing with increasing prevalence of diabetes in developing economies and slowing down of decreases in global TB cases. Numerous studies have reported the issue of TB management when it occurs with DM. Diabetics have pulmonary microangiopathy, micronutrient deficiency, renal insufficiency, and impaired cell-mediated immunity, all of which predispose diabetics to pulmonary TB (Wang et al., 2013). Research indicates a higher bacillary load in the sputum of people with TB-diabetes, whereas sputum conversion is almost twice slower in TB-diabetes patients than general TB patients. Furthermore, TB-diabetes patients have more cavitary lesions, which makes them more infectious in transmitting TB, and their altered immune response makes them more susceptible to MDR (multidrug-resistant) TB strains (Wang et al., 2013).

The findings of the current study support the hypotheses as well as findings from previous DM-TB correlation studies. Various TB testing methods presented different TB-positive results in this investigation in which case the highest positive yield was noted with Gene Xpert (1.60%). This could indicate that Gene-Xpert can be prioritized in resource limited areas as a means to detect TB among diabetic patients. Nonetheless, many of cross-sectional TB-diabetes comorbidity studies in the past use a combination of primary data (including fasting blood glucose test, structured questionnaire, and anthropometric measurements) and secondary data (such as TB treatment category and patient smear status) (Tenaye et al., 2019). Other data collection strategies, including interviews and pre-tested questionnaires present valuable tools for gathering clinical and sociodemographic characteristics, which are crucial in understanding the issue of TB-diabetes comorbidity in a particular population (Tenaye et al., 2019).

Meanwhile, findings on the point prevalence of TB indicate a gradual increase in the spread of TB infection among DM patients (***2.66%)***, which is also indicated in WHO (2017). In its global report (2016), the World Health Organization (WHO) highlighted the occurrence of 10.3 million new diagnosable infections of TB with 1.2 million people dying of TB. Among the 1.4 million cases of TB reported in the year, 1.9 million cases were as a result of undernourishment, 0.8 million due to smoking, 1.0 million resulted from HIV infection, and 0.8 million cases were attributed to diabetes (World Health Organization, 2017). The reported point prevalence rate is comparatively lower than the prevalence of TB among DM patients in Asia 4.72% (95% CI 3.62–5.83) and Africa 5.13% (95% CI 4.34–5.92) in general (Tenaye et al., 2019). Even so, the findings of this study exclude already diagnosed and suspected TB cases, thus representing the missed TB cases among patients attending regular clinics in Nyandarua County health facilities. With the International Diabetes Federation (2015) report highlighting a TB prevalence rate of 4.56% among diabetics in Kenya, the additional 2.66% prevalence rate in Nyandarua County could represent the graveness of the problem associated with undiagnosed TB among diabetes patients in the country. Undiagnosed TB in developing economies was also estimated to be 3.3% in 2015, a figure reported to be a regional projection and an underestimation as more than two-thirds of people diagnosed with diabetes in the country typically present to health facilities with apparently unrelated complaints (Galgallo, 2019). According to the Kenya National Diabetes Strategy 2010-

2015, nearly 60% of people with diabetes are unaware of their condition, and this is reflected in the findings of this investigation (Enos, et al., 2019).

In resource-limited regions, TB continues causing high mortality rates. While the most prevalent causes of deaths in middle-income and low-income countries are cerebrovascular disease and ischemic heart disease, TB and HIV exist among the five leading causes of death (World Health Organization, 2017). Similar to the WHO (2017) report, the finding of this study exposes a strong connection between socioeconomic and behavioral characteristics and TB-diabetes comorbidity. For example, a high prevalence rate was noted among farmers and children (dependents who are less than 18 years of age), outlining these two as the most at-risk groups among diabetic patients in Nyandarua county. In general, poor access to health services, and poverty have been stated as important risk factors when it comes to TB care provision, but few investigations focus on how these issues affect hard-to-reach groups such as diabetes patients (Mburu et al., 2018). The WHO reported 10.5 million new TB cases and about 1.8 million TB-associated deaths in 2017. The WHO reported 10.5 million new TB cases and about 1.8 million TB-associated deaths in 2017. The report outlines 416 million cases of DM and 4.9 million DM-associated deaths in the past five years. Similarly, 75% of DM case and 96% of TB cases existed in developing /middle or low-income economies (such as South East Asia and Africa) (World Health Organization, 2017).

Similarly, the findings of the current investigation indicate that TB is most common among people aged 40 and above, among cigarette smokers, and alcoholics. Chi-square -value of less 0.05 indicates alcoholism and cigarette smoking as risk factors for TB-diabetes comorbidity. The WHO and international collaboration against TB and Lung

Disease (IUATLD) developed a TB and diabetes control framework that is premised on implementing a bi-directional screening for DM and TB that priorities DM patients who are above the age of 40 for TB testing. WHO recommends screening for TB among older diabetic patients in all primary health-care setting for all countries across the world (World Health Organization, 2017). The framework emphasized the application of active TB case finding in inpatient and outpatient DM management centres as a way to allow early TB detection, which increases the chances for successful TB treatment (Havlir et al., 2008; Wu et al., 2016). Nonetheless, targeted screening presents a preferable initiative in resource-limited contexts. Targeted screening (encompassing making screening decisions based on local epidemiology data) has also been proposed by Huang et al. (2017) who presents DM-patient sub-groups including those above 40 years of age, those who are overweight (body mass index of more than 25), those with alcohol consumption, and cigarette smoking habits as most-at-risk populations.

Comorbidities such as that of TB and DM present more challenges when it comes to tuberculosis treatment. A number of investigations indicate that co-affiliation with diabetes and TB is common in low-income countries (Tenaye et al., 2019). DM and TB comorbidity is an emerging public health in developing countries, just like the findings of this study reflects on Kenya, particularly Nyandarua County. TB has been found to be in the third position among the most common causes of deaths among patients with non-communicable diseases such as DM. For instance, the magnitude of patients with DM-TB co-morbidity is comparatively higher than people with HIV-TB comorbidity worldwide (World Health Organization, 2017). The increasing prevalence of TB is an important challenge to DM control as well. This state of the scenario is said to be caused by exposure to uncontrolled hyperglycaemia for diabetic and TB patients with significant compromised immune systems. In essence, diabetics are three times predisposed to TB, and roughly 16% of TB cases are associated with diabetes globally. What is more, people with TB-DM coexistence have been found to more likely to experience worsening TB treatment results and death during TB regimen (World Health Organization, 2017). Such complications are more likely to occur with increased exposure to common risk elements for TB including cigarette smoking, alcoholism, malnutrition, and HIV (World Health Organization, 2014).

Putting in mind the scarcity of health resource in developing countries such as Kenya, it is important to note that the yield of testing for TB in DM patient is influenced by both the method for diagnosing for TB and the underlying TB prevalence (ReyPineda, 2014). What this means is that more people will be screened to identify one extra TB case in places of low prevalence (such as less than 100 cases in 100, 000 people), which is cost-intensive. On the other hand, screening for TB in high prevalence settings may be cost-effective with a higher positive identification rate per a given population (Havlir et al., 2008). Interestingly, while it is advisable to consider DM patient for TB screening only in areas of high prevalence, there seem to be a strong link between TB and socioeconomic variable in which case poverty is directly assisted with TB incidence rates. For example, Baghaei et al. (2013) found out that countries with middle to low-income economies are the homes of more than 78% of all diagnosed TB, and that this statistic only represents 30% of actual TB active TB cases. With these in mind, Obermeyer, Abbot, and Murray (2008) suggest that people with newly diagnosed TB should be considered for TB diagnosis in resource limited countries.

A pressing matter is, therefore, how to manage the additional cost of TB diagnosis in the overall plan address the problem of TB-DM comorbidity in resource-limited areas. Jeon and Murray (2015) present three proposals with this regard, including (1) using direct observation and enquiries to identify DM patients that exhibit symptoms that are suggestive of TB, (2) referring patients with TB-suggestive symptoms for further TB investigation, and (3) educating DM patients about their increased exposure to recurrent and new TB, the signs and symptoms of TB, factors that further increase the risk of TB infection (such as smoking and alcohol dependency), and the need to present to health providers when they think they may be having TB (International Diabetes Federation, 2015).

Nevertheless, the question of how TB screen should be done on people with DM has attracted significant research attention in the past. For example, Baghaei et al. (2013) suggest a combination of DM detection strategies that incorporate identification of TB symptoms and specialized clinical examinations. According to (ReyPineda, 2014), TB screening is recommended for all new DM cases in high TB prevalence setting. Newly diagnosed DM cases in areas of high prevalence should be asked whether they are in TB treatment or if they are experiencing TB-suggestive symptoms before being referred for further investigation. Among the symptoms that health practitioners should watch out for while considering DM patients for DM screening include cough for more than 14 days, drastic weight loss, night sweat, and fever. Other symptoms of TB in DM patient include cervical lymphadenopathy or swelling of glands in the neck, which may be indicative of extra pulmonary TB (ReyPineda, 2014). Nonetheless, chest radiography may be recommended for newly diagnosed DM patients regardless of availability of observable symptoms (Sekandi et al., 2009). Radiographic diagnosis is recommendable because of higher sensitivity in comparison to symptom-based screening in TB detection (International Diabetes Federation, 2015).

The use of chest radiography in testing for TB is supported by various investigations that highlight the structural markers for TB infection in DM-TB patients. Investigating in DM patients, findings by Obermeyer, Abbot, and Murray (2008) suggest a lower lung involvement as a common radiographic feature among the majority of DM patients. This is somewhat different from Obermeyer, Abbot, and Murray (2008) findings which indicates upper-lobe infiltration as a common feature among non-DM TB patients. Other studies support these findings. For example, Dooley and Chaisson (2009) emphasize that pulmonary TB in DM patients presents typical radiographic distribution and pattern, more so exhibiting lower lung involvement. This typical radiographic pattern and distribution of TB infection in DM patients is clinically important since it is possible to misdiagnose lower-lung TB as cancer or community-acquired pneumonia (Harries et al., 2016). Nonetheless, people with pulmonary TB that lacks upper-lung involvement have high chances of presenting negative sputum smear and culture (Havlir et al., 2008).

While findings indicate that well above one fifth of patients with DM exhibit lower lobe involvement, findings on lower-lobe involvement in DM-TB comorbidity is greatly lacking, and there is an urgent need for further investigations looking at the factors behind the radiographic patters of TB in DM patients and whether there are clear differences in TB presentation between DM patients and non-TB patients. Interestingly, there are investigations indicating the age-biasness of radiographic distribution of TB infection in DM patients. For example, Obermeyer, Abbot, and Murray (2008) noted that lower-lobe involvement is more typical in older DM patients. It has also been suggested that preferential transformation in the lower-lobe alveolar oxygen stress to DM or old age favours lower-lobe infections in these groups (Viswanathan et al, 2005). Moreover, multi-lobular infection or the existence of multiple cavities is less rampant in controls than in DM patients of most series, except, may be people aged over 40 years in which case Syal, Anand, and Dibyajyoti (2015) suggest there might be uniform trends between this age-group on non-DM patients and general DM patients because, possibly, of compromised host immunity.

International Diabetes Federation (2015) suggest the used additional confirmatory diagnosis methods on patients exhibiting suggestive signs or symptoms of TB, preferably those indicating lung parenchymal transformations. It is advisable to classify patients indicating suggestive signs as presumptive TB and considering them for further laboratory investigations, preferably using Xpert MTB/RIF (International Diabetes Federation, 2015). The WHO suggests Xpert MTB/RIF is as the first line recommendation for sputum samples in TB clinics even though sputum smear microscopy can be used as the second priority were the essay is unavailable (World Health Organization, 2017).

Even so, findings of enquiries investigating sputum-culture transformation indicate mixed findings based on the choice of outcome variables including 2-month sputum conversion, proportion exhibiting positive microscopic analysis of sputum after 60 days of therapy, and transformation to negative after competing intensive-path tuberculosis therapy (ReyPineda, 2014). Investigations that evaluate sputum-culture transformation after 60 day of TB treatment (an important surrogate marker applied in predicting the relapse of TB) show transformations that are somewhat similar between controls and diabetic patients. For instance, in an investigation in Indonesia, DM was not a exposure variable for sputum-culture or sputum-smear positivity at 60 day after adjustment for sex, body-mass index, sex, standard sputum mycobacterial load, chest radiographic outcomes, and study site (Pablo-Villamor, Benedicto, Benedicto, & Perez, 2014).

On the other hand, DM patients appeared to take a longer duration to exhibit culture negativity in investigations that evaluate the duration of sputum conversion (Harries et al., 2016). This was evident where Pablo-Villamor et al. (2014) found out that DM-TB patients who were undergoing TB treatment took longer to experience sputum conversion than non-DM TB patients (68 vs 56 days, p=0.02) (Pablo-Villamor, Benedicto, Benedicto, & Perez, 2014). In Similarly, in investigation that utilized survey analysis to estimate the culture conversion duration, the median duration to achieve culture negativity was measurably shorter among non- DM TB patients than DM-TB patients (39 vs 49 days, p=0.09). Accumulatively, these findings may be used to suggest that a higher bacillary concentration among DM patients leads to a longer duration for sputum transformation, but non-DM-TB patients and TB-DM patients experience similar rates of sputum-culture transformation within 60 to 90 days of TB therapy (Pablo-Villamor et al., 2014).

Chapter Five

Summary, Conclusions and Recommendations

5.1 Summary

The prevalence of Tuberculosis in asymptomatic Diabetic patients observed in our study is notable and may indicate an emerging threat of Tuberculosis Diabetes comorbidity in Nyandarua County. Health education about the importance of getting tested for Tuberculosis should be given to all Diabetic patients in the study area.

5.2 Conclusion

Despite the concerted efforts to achieve Tuberculosis (TB) end strategy by 2035, TB remains one of the leading healthcare concerns worldwide. Diabetes comorbidity for TB accelerates TB disease, complicates treatment, hence increasing the risk of poor TB outcome. In Kenya, the prevalence of TB is an estimated 558 per 100,000 Population and the prevalence of diabetes is gauged to be 4.56%, accounting for 750,000 persons and yearly deaths amounting to 20,000 (International Diabetes Federation, 2015). The World Health organization recommends screening of TB on diabetics' patients. However, the recommendation has not been implemented in Nyandarua County JM Kariuki Memorial County Referral Hospital. The findings of this investigation indicate a high prevalence rate of TB (2.66%) among diabetics in Nyandarua County. Considering that the World Health Organization (2017) reported that 60% of TB cases in diabetes patients are yet to be diagnosed in developing /middle or low-income economies, these findings indicate a need to implement active TB case finding programs in diabetes management initiatives in Kenya.

In the light of worrying diabetes-TB comorbidity outcomes in Kenya, the principal objective of the study is to determine the feasibility of incorporating active TB case finding in diabetic mellitus management program at JM Kariuki County Hospital, Nyandarua County. The study investigates the commonness of tuberculosis among patients suffering from diabetes through active tuberculosis case finding among diabetic patients attending diabetic outpatient clinic at JM Kariuki County Hospital. The particular objectives of the underway study are (i) to determine the Point prevalence of TB among diabetic patients; (ii) to estimate the positive yield of TB diagnosis by Gene-Xpert versus X-ray and FM Microscopy diagnostic methods; and (iii) to explore the socioeconomic factors of TB infection among Diabetic Patients.

TB has been associated with poor clinical outcomes among DM patients in various studies (Pablo-Villamor et al., 2014). Interestingly, many researchers associate such outcomes with factors including compromised immunity, poor blood glucose control, low concentration on TB treatment drugs in the serum, low plasma anti-mycobacterium antibiotics levels in the serum of DM patients, and most importantly, treatment failures due to inaccuracies associated with application of standard TB testing guidelines in testing for active TB in DM patients. International Diabetes Federation (2015) contends that screening of TB among DM patients should be conducted by first looking at the epidemiology of the community in question, which should inform the application of TB screening for newly diagnosed TB cases more so for people exhibiting TB-risk factors such body mass index of 25 and above, age of 45 and above. On the same note, ReyPineda (2014) argues that DM-TB patients face higher chances of presenting cavitations, smear-positivity during diagnosis, and that they may continue being culture positive 8 weeks after the onset of TB treatment plan. While this argument presents a supportive background for a prolonged treatment of 9 months, Pablo-Villamor et al. (2014) recommends an initiation of an additional diagnostic initiative which focuses on continuous monitoring of serum drug concentration and ensuring that the TB therapy dosage is enough to enable a sustained advancement of the patient towards TB eradication.

International Diabetes Federation (2015) suggest regular TB testing for adult DM patients in most settings and countries across the globe considering global findings that describe DM patients as 3-4 times at risk of TB infection than non-DM patients. In support of this contention, International Diabetes Federation (2015) proposes the application of a standardized screening approach whose onset is at the point of DM diagnosis in TB epidemic settings such as the developing countries that are documented to harbour close to 80% of all TB cases in the world. Screening for TB in high prevalence areas is considered cost effective considering the higher number of positive cases per a given number of screens. Empirical evidence suggests that DM patients are more exposed to TB infection in the initial months after DM detection than later in the course of DM management (International Diabetes Federation, 2015). Screening DM patients for TB is proposed to include active observation and enquiring about TB symptoms in DM patients and referring DM patients with suggestive symptoms to TB clinic for further medical examination. In the light of the connection between drug-resistant-TB and DM, Pablo-Villamor et al. (2014) recommend the use of Xpert MTB/RIF in diagnosing TB in DM patients. Further ReyPineda (2014) recommends the implementation of TB education initiative to sensitize DM patients of the symptoms, risk factors, and information on where they access screening and treatment services in case of TB infection.

5.3 Recommendations

End the Global TB Epidemic, a worldwide TB-eradication strategy, was published by the WHO with the aim of lowering the universal TB incidence to 100 per million from

1000 per million by year 2035. Being a partisan of the strategy, Kenya aims at attaining the objective stipulated in the End the Global TB Epidemic, but resource availability continues being a major challenge in the implementation of early TB diagnosis, more so in at-risk groups such as diabetics (Zumla et al., 2015). Being a developing economy, TB-DM presents a significant burden to the country even as the need for active case finding increases. With these considerations in mind, it is recommendable for Kenya to adopt 8 criteria as outlined in WHO's recommendations for low-income countries, namely:

1. To exhibit political commitment, stewardship, and financial support for TB management planning and services;
2. To address the most hard-to-reach and mots –at-risk groups,
3. To address the issue of TB by including migrants and supporting TB management initiatives internationally,
4. To plan for and support the implementation of active LTBI and TB case finding and proper treatment for high-risk populations,
5. To strengthen the prevention and treatment of MDRTB,
6. To foster resilience in surveillance and promote the analysis of case-based information management,
7. To invest in new tools and research, and
8. To support worldwide TB prevention, control, and treatment

Considering the problem of diabetes TB comorbidity issue in Kenya, the findings of the current study suggests that;

i. TB diagnosis and treatment should be incorporated in diabetes management programs and vice-versa in JM Kariuki County Hospital;

ii. Further studies should be done on the financial implications of active TB case finding as a TB eradication strategy among diabetics in JM Kariuki County Hospital;

iii. JM Kariuki County Hospital should prioritize TB screening among a range of DM-patient subgroups, including those above 40 years of age, those who are overweight (body mass index of more than 25), those with alcohol consumption and cigarette smoking habits; and

iv. Researchers and scholars to explore and conduct more studies on related topics such as the financial viability of incorporating TB treatment and screening in DM management in JM Kariuki County Hospital

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Appendices

Appendix I: Informed Consent Form

Part One: Information Sheet

Introduction: My name is Everlyne Macharia, I am carrying out a research study to fulfill my academic credentials and be awarded a Master's Degree in Medical Laboratory Sciences at Mt. Kenya University.

Purpose of the study: I am going to provide you with information and welcome you to take part in this research. You don't need to decide today if or not you will take part in the research. Before you choose, you can converse with anybody you feel comfortable with about the examination. There might be a few words that you don't capture very well. It would be ideal if you request that I stop as we go through the information and I will set aside some time to clarify. On the off chance that you have questions you can ask them.

What will the study involve? The study will involve asking some clinical questions related to TB disease and collecting sputum samples where TB infection has been clinically and diagnostically confirmed by a clinician.

Participation selection: You have been asked to take part in the study because they are specific signs of TB infection that has been observed by the clinician and we would like to make an early intervention before it becomes complex and start infecting others.

Voluntary participation: Participation is intentional and on consenting to participate in the research you will be asked to sign this participants' waiver form. In case you choose to quit the examination it will be considered and in the event that you so wish your information will be decimated.

Participation in the research will be kept as a secret: Yes. I will guarantee that no pieces of information to your personality show up in the thesis. Any concentrates from what you say that are cited in the proposal will be totally anonymous.

The information which you will provide: The information will be kept secret for the span of the investigation. On consummation of the proposition, they will be held for a further a half year and afterward obliterated.

The results: The results will be presented in the proposal. They will be seen by my supervisor, a second marker and the outside examiner. The postulation might be perused by future learners on the course. The investigation might be published in a research journal.

This research has been reviewed by: Approval has been given by the County Health Department Ethics Committee and JM Kariuki County Hospital before studies like this can happen.

Any further questions? On the off chance that you require any additional data, you can get in touch with me: Everlyne Macharia, versatile number-0721-390211, email address-evamash@gmail.com.

On the off chance that you consent to participate in the investigation, if it's not too much trouble sign the assent frame overleaf:

Part two: Informed consent form

I… … …………………………..consent to take part in this research.

The reason and nature of the investigation has been disclosed to me in writing.

I am taking part intentionally.

I comprehend that I can pull back from the investigation, without repercussions, whenever, regardless of whether before it begins or while I am participating.

I comprehend that I can pull back authorization to utilize the information inside two weeks of the interview, in which case the material will be erased.

I comprehend that anonymity will be guaranteed in the review by masking my personality.

I comprehend that hidden concentrates from my meeting might be cited in the postulation and any resulting productions in the event that I give authorization underneath:

(Please tick one box :)

I consent to citation/distribution of extracts from my interview

I don't consent to citation/distribution of concentrates from my interview

Signed …………………….   Date……………………..

Appendix II: Questionnaire

Part I. Introduction:

Hello. My name is Everlyne Macharia and am interviewing you because there has been an increase of suspected TB cases in the country and in our community and we are working to intensify its early detection in our Diabetic patients for early treatment and to avoid complications in case one is infected.

Concern: I understand that the clinician has suspected you could be having the signs and symptoms suggestive of TB.

This will take about 10 minutes. Can we go ahead?

Part II. Clinical information

Tb Intensified Case Finding Tool

Name of client.. Age.......................................

Sex................................ Physical Address...

Mobile Phone................................... Occupation..

Treatment Supporter Name... Mobile phone............................

Medical Outpatient Patient Hospital Number..

Date..................................

PART A: Random Blood Sugar Levels

1. Blood sugar measurement results……………………………………

2. Tuberculosis screening

Signs/Symptom	**Indicate Yes or No**	
	Yes	**No**
Cough for ≥2 weeks with or without production of sputum		
History of close contact with confirmed TB or chronic cough		
Hotness of the body or sweating at night even when it's cold		
Noticeable weight loss		
Chest pain		
Night sweats ≥ 2 weeks		
Smoker/ Alcohol consumer		
Patient is on oral DM medication.		
Patient on injectable DM treatment		

If YES to any of the above TB castellation of symptoms request the patient for the following tests:

3. FM Microscopy test results: …………………………………………………

4. Gene Xpert molecular test: …………………………………………………

5. Radiological Chest X-ray: ………………………………………………….

Appendix III: Reagents and Equipment used

Equipment and reagents and for fluorescence smear microscopy

1. Fluorescent microscope
2. Balance, with a sensitivity of 0.1 g
3. Brushes to clean bottles before reuse
4. Containers for the newly prepared stains (dark amber glass bottles or plastic bottles)
5. Distilled or purified water
6. Flasks (conical or flat-bottomed), capacity at least 1 litre
7. Filter papers, large (appropriate size for funnels)
8. Funnels, large, for filling bottles
9. Labels for bottles
10. Stirring plate, heated, and magnetic stirrers
11. Chemicals, outlined below:

Stain solution

Auramine	1.0 g	certified grade
Alcohol (denatured ethanol or methanol)	100.0 ml	technical grade
Phenol crystals	30.0 g	analytical grade
Distilled or purified water	870.0 ml	

Decolorizing solution

Hydrochloric acid	5 ml	technical grade
70% ethanol	1000 ml	

Counterstaining solution: permanganate

Potassium permanganate	5.0 g	certified grade
Distilled water	1000.0 ml	

Auramine method	**Quantity of reagent**	**Volume prepared**	**Date**	**Signature**
Auramine Ethanol Phenol Distilled water **Auramine 0.1%**	1.0 g 100 ml 30.0 g 1000 ml	1 litre		
Hydrochloric acid Ethanol	5 ml 1000 ml	1 litre		

Potassium permanganate Distilled water **Counterstaining**	5 g 1000 ml	 1 litre		

<u>Gene Xpert equipment and reagents</u>

1. Gene Xpert Cartridge:
   - Single-use disposable Xpert MTB/RIF cartridges
   - Sample extraction, amplification and detection are all carried out within this self-contained cartridge.
2. Class II biological safety cabinet (BSC)
3. Sample reagent (provided in Xpert MTB/RIF kit), 8ml volume pack per each cartridge.
4. Permanent marker pens.
5. Sterile transfer pipettes– with single mark for minimum volume of sample transfer to cartridge (provided in Xpert MTB/RIF kit).
6. Sterile screw-capped specimen collection containers/cups.
7. Discard containers for pipettes and sputum containers.

<u>Blood sugar testing reagent</u>

1. Glucometer
2. Blood sugar strips
3. Blood lancet

Appendix IV: Structured Observation Checklist

					TB/ DM SCREENING									LAB INVESTIGATIONS				
Unique Identifier	IP NO	SEX	AGE(Yrs)	OCCUPATION	Cough for over 2 wks with or without sputum production (YES/NO)	History of contact with TB or chronic Cougher(Yes/No)	Body Hotness/ Night sweats(Yes/No)	Weight Loss(Yes /No)	Chest pains(Yes/No)	Smoker(Yes/No)	Alcohol(Yes/No)	Patient on Oral DM medication(Yes/ No)	Patient on Injectables DM medication(Yes/ No)	FM microscopy(Pos/Neg)	Gene Xpert (Pos/Neg)	Chest Xray(Pos /Neg)	Blood Sugar(mmoles/L	Confirmed TB Patient

Appendix V: Ethical Clearance Letter

Mount Kenya University

AUGUST 23, 2018

Ref. No. MKU/ERC/0954

CERTIFICATE OF ETHICAL CLEARANCE

This is to certify that the proposal titled **"ACTIVE TUBERCULOSIS CASE FINDING ON DIABETIC PATIENTS ATTENDING JM KARIUKI COUNTY HOSPITAL, NYANDARUA COUNTY"** Whose Principal Investigator is Ms Everlyne Macharia (MMLS/000202/113/23605) has been reviewed by Mount Kenya University Ethics Review Committee (ERC), and found to adequately address all ethical concerns.

Dr. Francis W. Makokha
Secretary, Mount Kenya University ERC

Sign: ________ **Date:** 23·08·2018

Prof. Francis W. Muregi
Chairman, Mount Kenya University ERC

Sign: ________ **Date:** 23·8·18

The Chairman
Mount Kenya University
Ethics Review Committee
P. O. Box 342 - 0100, Thika

Main Campus, General Kago Road, P.O. Box 342-01000 Thika. Tel: +254 67 2820 000,
Cell: +254 720 790 796, 0709 153 000
Email:info@mku.ac.ke, Web: www.mku.ac.ke
Chartered and ISO 9001 : 2008 Certified Institution.
Unlocking Infinite Possibilities

Appendix VI: Introduction Letter from School of Postgraduate Studies

Mount Kenya University

MKU — Unlocking Infinite Possibilities

SCHOOL OF POSTGRADUATE STUDIES

MMLS/000202/113/23605

13th September, 2018

The Director, Research Coordination Division
National Commission for Science, Technology & Innovation
Utalii House, 8th & 9th Floor
P.O Box 30623- 00100
NAIROBI

Dear Sir/ Madam,

RE: EVERLYNE MACHARIA- REGISTRATION NO. MMLS/000202/113/23605

The purpose of this letter is to introduce the above named student who is pursuing **Master of Science in Medical Laboratory Sciences (Microbiology)** in the Department of **Medical Laboratory Sciences** in the **Medical School.**

The title of her research is *"Active Tuberculosis Case Finding on Diabetic Patients Attending JM Kariuki County Hospital, Nyandarua County."*

She has been cleared by the University's Ethics Review Committee (Certificate attached) and now has to proceed to the field to collect data for her research between **September and November, 2018.**

Any assistance accorded to her will be highly appreciated.

Thank you.

Registrar
School of Prograduate Studies
Mount Kenya University
P. O. Box 342 - 01000, Thika

Daniel Gatungu
Registrar, School of Postgraduate Studies
Enc.

Main Campus, General Kago Road, P.O. Box 342-01000 Thika. Tel: +254 67 2820 000,
Cell: +254 720 790 796, 0709 153 000
Email:info@mku.ac.ke, Web: www.mku.ac.ke
Chartered and ISO 9001 : 2008 Certified Institution.

Appendix VII: Research Permit from NACOSTI

THIS IS TO CERTIFY THAT:
MS. EVERLYNE NYAWIRA MACHARIA
of MOUNT KENYA UNIVERSITY,
69589-254 NAIROBI,has been permitted
to conduct research in *Nyandarua*
County

on the topic: *ACTIVE TUBERCULOSIS CASE FINDING ON DIABETIC PATIENTS ATTENDING JM KARIUKI COUNTY HOSPITAL, NYANDARUA COUNTY*

for the period ending:
27th February,2020

Permit No : NACOSTI/P/19/80258/27947
Date Of Issue : 27th February,2019
Fee Recieved :Ksh 1000

Applicant's Signature

Director General
National Commission for Science, Technology & Innovation

AppendixVIII: Similarity Index

Turnitin Originality Report

Processed on: 18-Dec-2020 00:52 EAT
ID: 1478078538
Word Count: 20108
Submitted: 1

Similarity Index	Similarity by Source	
18%	Internet Sources:	7%
	Publications:	6%
	Student Papers:	11%

ACTIVE TUBERCULOSIS CASE FINDING ON DIABETIC PATIENTS ATTENDING DIABETEC OUTPATIENT CLINIC AT JM KARIUKI COUNTY HOSPITAL, NYANDARUA COUNTY KENYA By Everlyne Macharia

9% match (student papers from 09-Jul-2018)
Submitted to Mount Kenya University on 2018-07-09

1% match (Internet from 10-Apr-2012)
http://www.tbcare1.org/publications/toolbox/tools/eqa/afb_microscopy/AFB_Microscopy_Participant_Text.doc

1% match (Internet from 16-Jul-2020)
https://www.ghanahealthservice.org/downloads/SOP_for_TB_Microscopy.pdf

1% match (publications)
Blanca I. Restrepo. "Diabetes and Tuberculosis", American Society for Microbiology, 2017

< 1% match (student papers from 20-Nov-2020)
Submitted to Higher Education Commission Pakistan on 2020-11-20

< 1% match (Internet from 07-Mar-2019)
https://businessperspectives.org/images/pdf/applications/publishing/templates/article/assets/7628/imfi_en_2016_03_Holtzhausen.pdf

< 1% match (Internet from 19-Mar-2020)
https://bmcresnotes.biomedcentral.com/articles/10.1186/s13104-018-3390-x

< 1% match (Internet from 22-Jul-2020)
http://erepository.uonbi.ac.ke/bitstream/handle/11295/63050/Musau_Effects%20of%20quality%20management%20systems%20on%20Treatment%20of%20tuberculosis%20patients?isAllowed=y&sequence=3

< 1% match (Internet from 19-Sep-2017)
https://preview-bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-5-111

< 1% match (Internet from 31-Aug-2012)

Appendix IX: Map showing Nyandarua Health Facilities