ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

THE MAGNITUDE AND ASSOCIATED FACTORS OF TUBERCULOSIS AMONG DIABETIC PATIENTS AT TIKUR ANBESSA SPECIALIZED TEACHING HOSPITAL IN ADDIS ABABA, ETHIOPIA.

BY

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List of Acronyms and Abbreviations

AA	Addis Ababa
ADA	American Diabetic Association
AOR	Adjusted Odds Ratio
AIDS	Acquired Immune Deficiency Syndrome
BMI	Body Mass Index
COR	Crude Odd Ratio
CIs	Confidence Intervals
DM	Diabetes Mellitus
DMTB	Diabetic Mellitus among Tuberculosis
HbA1c	Glycosylated haemoglobin
HIV	Human Immune Virus
IDF	International Diabetic Federation
OR	Odds Ratio
OAA	Out of Addis Ababa
PTB	Pulmonary Tuberculosis
RR	Relative Risk
SPSS	Statistical Package for Social Sciences
SD	Standard Deviation
TB	Tuberculosis
TBDM	Tuberculosis among Diabetic Mellitus
TASTH	Tikur Anbessa Specialized Teaching Hospital
USA	United States of America
WHO	World Health Organization

Abstract

Background: - Tuberculosis is a chronic infectious disease caused by the bacillus *Mycobacterium tuberculosis*, and it is a major cause of morbidity and mortality throughout the world. The link between tuberculosis and chronic diseases particularly diabetes mellitus have long recognized but underappreciated connection between the two revealing that diabetes makes substantial contribution to the burden of both incidence and prevalence of tuberculosis at the world wide level. People with diabetes have more than three times higher risk of developing active tuberculosis than people without diabetes. However, still there are a few studies on the burden of tuberculosis among diabetic patients in Ethiopia, particularly at Tikur Anbessa Specialized Teaching Hospital. Therefore, this study aimed to assess the magnitude and associated factors of tuberculosis among diabetic patients at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia.

Objective: - To assess the magnitude and factors associated with tuberculosis among diabetic patients in Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia.

Methods: - Retrospective study was conducted at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia, from January 2010-January 2014. A total of six hundred eight one known diabetic patients aged ≥ 18 years were included in the study. Data was collected using checklist. Data were analyzed using SPSS for window version 20. Descriptive statistics such as frequency, proportions, means, medians and standard deviations were calculated. A binary logistic regression model was used to identify associated factors of tuberculosis among diabetic groups. The results were expressed by using adjusted odds ratio with 95% confidence interval a significant threshold was considered at $p < 0.05$.

Results: - The magnitude of tuberculosis among diabetic populations was 3.8%, 95%CI (2.5%-5.3%). Age from 51-65 years (AOR=21.4; 95%CI; 1.2-385) , type-I diabetes mellitus (AOR=7;95%CI: 1.1-41.6) and age over 66 years (AOR=51; 95%CI: 3-877), body mass index less than 18 kg/m^2 (AOR=27.6; 95%CI: 1.7-442), and prolonged duration of DM (AOR=5.1; 95%CI: 1-24) were significantly associated factors of tuberculosis among diabetic patients.

Conclusion and recommendations: - In this study higher magnitude of tuberculosis was reported compared to other studies in developing countries. Age, low body mass index, type of diabetes mellitus and duration of diabetes were the significantly associated factors leading to occurrence of tuberculosis among diabetic patients. All diabetic patients should be screened for tuberculosis at their diagnosis time and they have regular follow up, and it is better to conduct further large scale epidemiological studies with large sample size and advanced tuberculosis diagnostic technologies.

1. INTRODUCTION

1.1. Background

Tuberculosis (TB), is an infectious airborne disease caused by the bacillus *Mycobacterium tuberculosis*, and ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV). In 2013, an estimated 9.0 million people developed TB and 1.5 million deaths (1.1 million among HIV-negative people and 0.4 million among HIV-positive people). Of the estimated 9 million people who developed TB in 2013, more than half (56%) were in the South-East Asia and Western Pacific Regions. A further one quarter was in the African Region, which also had the highest rates of cases and deaths relative to population (1).

The African Region had approximately one quarter of the world"s cases, and the highest rates of cases and deaths relative to population (280 incident cases per 100 000 on average, more than double the global average of 126) (1). Ethiopia ranks eighth among the world"s 22 high burden TB countries. According to the World Health Organization"s Global TB Report 2013, Ethiopia had an estimated incidence rate of 210 per 100,000 population and 16 deaths per 1000 population with an estimated prevalence rate of 200 per 100,000 population(2).

Diabetes mellitus is a complex metabolic disorder that is characterized by high level of blood sugar either because the body does not produce enough insulin or cells don"t respond to insulin (3). It has a genetic component and some people are simply more susceptible to developing diabetes than others (4). In 2013, there were an estimated 382 million people living globally with DM, of these 175 million people (48%) with diabetes are undiagnosed, with numbers expected to rise to 592 million by 2030. Diabetes caused 5.1 million deaths in 2013, and 80% of people with diabetes live in low- and middle-income countries. The greatest numbers of people with diabetes are between 40 to 59 years of age, the number of people with type 2 diabetes is increasing in every country (5).

According to International Diabetes Federation (IDF) estimate the national prevalence of diabetes among adults in Ethiopia was 4.36%, and diabetes related death among 20-79 years of age was 34,262 in 2013(6). Diabetes also exacerbates major infectious diseases such as TB, HIV/AIDS and malaria. People with diabetes are three times more likely to develop TB when infected and approximately 15% of TB globally is thought to be associated to diabetes (3).

The association between tuberculosis (TB) and diabetes mellitus (DM) and their synergetic role in causing human disease and suffering has been recognized for centuries. However, recent evidence has shown that

there is a more significant link between diabetes and TB than previously thought: People with diabetes have a 2-3 times higher risk of developing TB disease compared to people without diabetes (6). People with TB and coexisting diabetes have 4 times higher risk of death during TB treatment and higher risk of TB relapse after treatment(5).

DM impairs cell-mediated immunity by impairing the function and activation of macrophages, monocytes and lymphocytes, with additional potential roles played by pulmonary micro-angiopathy, renal dysfunction and vitamin deficiencies (7). In addition, patients with uncontrolled hyperglycemia appear to be at higher risk for TB than those with controlled blood glucose levels, suggesting that uncontrolled hyperglycemia is an important determinant in this interaction (7).

Despite modern treatment options for DM, its association with TB has remained strong. With the current prediction that the prevalence of DM will increase to close to 592 million by the year 2030, it is most likely that the rise in the number of people with DM may complicate TB care and control and vice versa – especially in many areas where the two diseases coexist. This suggests further study to identify how much the relation is existing in our contextual situation and identifying socio-demographic correlates which leading to TB among DM patients.

1.2. Statement of the Problem

International Diabetes Federation estimated about 15% of TB disease cases globally are linked to diabetes mellitus (3). TB infected individuals with diabetes may have a weak immune system because of chronic diseases, particularly type-1 and at a higher risk (2-6 fold) of progressing to active TB disease which is late, under or misdiagnosed (8,9). The link between TB and DM still exists nowadays, and the risk of death is five times greater among diabetic patients (9, 10). The merging epidemics of diabetes mellitus and tuberculosis have raised concerns by many experts but no large scale screening and intervention have been launched yet, especially in low-income countries like Ethiopia.

People with TB and coexisting diabetes have 4 times higher risk of death during TB treatment and higher risk of TB relapse after treatment (5). Also systematic review of treatment outcomes reveal that a relative risk of death of 1.89 among TB patients with diabetes when compared to non-diabetic patients and after controlling for potential confounders, the pooled risk of death among TB patients with diabetes was five times greater than those without diabetes (9). One prospective study examined sputum culture at the completion of 6 months of TB treatment, finding positive culture in 22.2% of patients with diabetes and 6.9% in those without diabetes (11).

One national study showed that the magnitude of smear positive pulmonary tuberculosis among suspected diabetic patients was 6.2%, and also it identified that place of residence, religion, past history of TB, presence of TB patients in the family and duration of diabetes was significantly associated with the occurrence of pulmonary tuberculosis among diabetics (10). Different studies shows the patterns of the occurrence of TB in people with diabetes and without diabetes is different, One study in Ethiopia showed that, out of 71 diabetic-tuberculosis patients 56 (78.9%) had pulmonary TB , 8 (11.2%) had extra pulmonary TB and 7(9.8%) had disseminated tuberculosis, although this study outlined that not only the patterns of TB occurrence but also it explored that its occurrence differs as the types of DM differ, Out of the above study total cohorts 76.05% was insulin dependent diabetes mellitus(IDDM) and 23.9% were non-insulin dependent diabetes mellitus (NIDDM) , and the relative risk of developing active tuberculosis differs between the types of diabetes, another facility based study in Ethiopia showed that the relative risk of developing active TB among IDDM was 26 fold and that of NIDDM was 7 fold compared with the general populations (12).

Studies suggested that the tremendous increase in tuberculosis among diabetics is attributed to age greater than 35 years, BMI greater than 25kg/m^2 ,alcoholism, malnutrition, smoking, family history of TB, contact with TB patient, intravenous drug users and HIV/AIDS as compared to non-diabetics (9,13).

As a result, our country is facing this burden of tuberculosis among diabetics, and still there are inadequate studies in identifying the magnitude and factors associated and their patterns. The aim of this study was to assess the magnitude and associated factors of tuberculosis among diabetic patients.

1.3. Rationale of the Study

Tuberculosis and diabetes mellitus are problems of the country leading to morbidity and mortality. Even though few studies are done in the country some years back and showed the relation between the two diseases, still a problem, of DM and TB are growing challenges of the country and the co-existence of the problem is common in most of the hospitals and caring such kinds of patients.

In addition, there is no national guideline that indicates how and when to screen for TB in a diabetic patients. Therefore, to achieve the Stop TB goal and limit the complications of the problem and premature death among the diabetic patients, identifying the magnitude of the problem and factors related to the problem helps for designing interventions. So, this study aimed in showing the relation between diabetes and tuberculosis and associated factors using hospital based data. This will help for the policy makers and program implementers to consider the prevention and treatment on co-manifestation of the disease at facility and community based interventions.

2. LITERATURE REVIEW

2.1. Impact of Diabetes on Tuberculosis

The WHO has identified DM as a global epidemic, mostly affecting low and middle income countries where 80% of all deaths due to DM occurs and about 15% of global TB cases of death are linked to diabetes (5). Simultaneously, TB continues to be a major cause of death worldwide despite the fact that the epidemic appears to be on the average of declining (1). The global burden of disease due to DM and TB is immense. In 2013, the World Diabetes Federation (WDF) estimated that about 385 million people worldwide had DM, a number which is expected to grow to at least 592million by the year 2030, with approximately 5.1million deaths. Eighty percent (80%) of these people live in low and middle income countries where tuberculosis is highly prevalent (5). In 2013, there were an estimated 9 million people with TB, 1.5million deaths (WHO 2014) (1).

Diabetes mellitus impairs cell-mediated immunity by impairing the function and activation of macrophages, monocytes and lymphocytes, with additional potential roles played by pulmonary microangiopathy, renal dysfunction and vitamin deficiencies. In addition, patients with uncontrolled hyperglycemia appear to be at higher risk for TB than those with controlled blood glucose levels, suggesting that uncontrolled hyperglycemia is an important determinant in this interaction (13).

2.2. Diabetes-Tuberculosis Association

It is well known that tuberculosis is associated with HIV, smoking, malnutrition and underlying lung disease, though presently the association between tuberculosis and diabetes mellitus is less familiar. In recent history, clinicians were familiar through to this connection: „during the latter half of the 19th century, a diabetic patient appeared doomed to die of pulmonary tuberculosis if he/she succeeded in escaping coma". And before the introduction of insulin and indeed for many years, thereafter, tuberculosis was a major cause of mortality in the diabetic population (14).

Epidemiological studies have elucidated an association between DM and the development of TB (16). The association between tuberculosis (TB) and diabetes mellitus (DM) and their synergetic role in causing human disease and suffering has been recognized for centuries (16).

However, recent evidence has shown that there is a more significant link between diabetes and TB than previously thought. People with diabetes have a 2-3 times higher risk of developing TB disease compared to people without diabetes (5) Diabetes is a risk factor for developing active TB.

There is strong evidence for this association, with studies examining the incidence of TB showing it to be two to five times higher in diabetic patients than in non-diabetic patients (15-16).

Cohort and case control studies have shown an association between DM and TB (18-19),with the rising prevalence of DM in countries where TB is endemic, there has been renewed interest in the question of whether DM increases the risk of active TB and thus could significantly add the world burden of disease. An English study published in 2010 found that a twofold to threefold increased risk of TB among patients admitted to hospital because of diabetes (19).

A meta-analysis of cohort studies conducted in 2008 showed that DM was associated with an increased risk of TB (RR=3.11, 95%CI 2.27 to 4.26) and, people with DM had approximately a three times higher risk of developing TB than people without diabetes, and this has been evidenced by biological support of the causal relationship between diabetes and host immunity to TB (20).

A general population based cohort study, conducted among South Korean civil servants, identified an increased risk of TB among people with DM (21). Another large population based study in Australia revealed that people with DM have a 1.5-fold increased risk of developing TB (23). Several studies have looked at the association between diabetes and tuberculosis in developed countries and found that people with diabetes are around 2.5 times more likely to develop tuberculosis (11, 23).

In 1995, a population based prospective study of pulmonary TB in Southern Mexico showed that almost one-third of TB patients have been previously diagnosed with DM (24).

The increasing co-occurrence of TB and DM is a clear case in point, especially in countries with rapidly emerging economies such as India and China , and that has resulted in the confluence of two pandemics one communicable and another non-communicable (25). The convergence of these two epidemics may lead to an increased incidence of TB, especially in low and middle-income countries with increasing number of people with DM and associated TB. DM almost triples the risk of developing TB (26).

Another systematic review, in Mexico, on the impact of DM on TB treatment outcome has revealed that DM increases the risk of the combined outcome of treatment failure, death and relapse. The risk of death has been reported to be 6.5-6.7 times higher in TB patients with DM (27).

Studies from different parts of the world have shown that 5-30% of patients with TB have concomitant DM, (24, 28, 29) and available evidence indicates that DM is a risk factor for the development of TB. Data from the 1930s reported that patients with DM had a three to four-fold increased risk of developing TB (30, 31).

TB is the third cause of death among subjects with non-communicable disease (NCD), and among the NCD, DM is one of the most important (32, 33).

A systematic review of bi-directional screening for DM and TB in 2009 identified 12 studies on screening people with DM for TB and 18 studies on screening TB patients for DM (37). In persons with DM, screening for TB showed high rates of TB, ranging from 1.7% to 36%, with the screening yield being highly dependent on the underlying TB prevalence and on the severity of DM (33).

In china screening of 11,331 diabetic cases showed that over three quarters cases of TB, but the notification rate of TB in general population was 77/100,000 (15). Also in India screening of 13068 diabetic cases for TB revealed that over three quarters of the cases were TB (15).

The prevalence of active TB in people with DM ranged from 1.7% in Sweden in 1954 to 36% in Korea in1962, this study also showed that the annual incidence of TB ranged from 280/100,000 in people with DM in Korea to 488/100,000 in people with DM in Ethiopia (34).

HIV is by far the strongest risk factor for TB at an individual level, but DM may be the most important at the population level. For example in India, a recent study estimated that DM accounts for 14.8% of pulmonary TB cases, while HIV infection accounts for 3.4% of cases (26).

A prospective cohort study showed that patients with DM and TB have more severe clinical manifestations, delayed sputum conversion and a higher probability of treatment failure, recurrence and relapse, and also the study revealed that about 30% of TB cases also are attributed to diabetes (34).

Studies suggest that the occurrence of TB among diabetics is more complicated and it shows different clinical manifestation and patterns. For example one facility based study in Shanghai (Chain) revealed that; out of 2,141 TB patients, 203(9.5%) were complicated by DM (type 1=7; type2=196) and 36 (17.7%) TB patients with DM had multiple drugs- resistance (MDR) TB, the proportion being significantly higher than of non-diabetics with TB (9.3%) ($P<0.001$) (36).

In South Africa, a study on 66 persons with type-1 diabetes (by medical records) and with no comparison group found that the incidence of TB per 100,000 was 10,606. However, the short coming of this study was that TB prevalence was determined by X-ray diagnosis and thus its prevalence may be overestimated (23). In India, a community based studies in 1984 in 219 persons with diabetes and TB diagnosis made by positive sputum smear on three consecutive days reported an incidence of 4,110 TB cases per 100,000,while another study in 2002 reported an incidence of 6,000 TB cases per 100,000 where the diagnosis was made by chest X-ray and sputum smear(34).

A facility based cross-sectional study in Ethiopia showed that the prevalence of TB among DM were 5.8% and 6.2% respectively (10, 12). Data from case control and cohort studies have shown that DM is a risk factor for active TB regardless of study design, incidence o f TB in the community, or the place of study (16).

2.3. Factors associated with TB among Diabetics

A facility based screening for Tuberculosis in Diabetic patients", in South India, showed that there was a significantly higher proportion of TB-among DM (DM-TB) patients among male, older and those with lower education level and socio-economic status than the DM-only patients. More patients in the TB-DM group consumed alcohol compared to the DM-only group. The percentage of subjects defined as current cigarette smokers was also higher in the TB-DM group than that in the DM-only group, but the difference was not statistically significant, and also there were significant differences between the TB-DM and DM-only groups: there was a stronger family history of DM in the DM-only group; the mean BMI was lower in the TB-DM group; and the TB-DM group had a higher proportion of patients with a duration of DM >10 years, and who were on combined oral medication and insulin (33). This study revealed that DM patients with TB tended to be male, older, have low BMI and were more likely to consume tobacco and alcohol than patients without TB.

A national, general population based, historical study at Australia revealed that the RR of TB was 1.78 (95 %CI 1.17 to 2.73) in all people with DM and 2.16 (95% CI 1.19 to 3.39) in those who were using insulin, and the same study showed that the prevalence of TB among diabetic people using insulin was 9.1/100,000/year 95% CI 7.6 to 10.9 (23). In Mexico, 20% of cases of TB are associated with DM; however, the behavior of the factors related to this co-morbidity is unknown but a facility based case-control study here showed that the risk factors for TB in diabetics were age greater ≥ 35 with an OR of 2.5 (95%CI; 1.4 -4.3) and BMI ≥25kg/m^2 with an OR of 8.5 (95% CI; 3.1-23.3) (36).

One of the hospital based study in Malaysia in 2005 showed that, out of 241TB-DM patients 0.5% had history of alcohol consumption, 3.6% were intravenous drug users, 44.1% had BCG vaccination, 32.2% were positive for tuberculin skin tests, 6.8% had past history of TB as well as 18.5% had contact with TB patients and it revealed that pulmonary tuberculosis (91.4%) was the commonest form TB that was found in diabetics (13).

More recent studies also showed that the type of DM itself should be considered as a risk factor for the development of tuberculosis, since their (type-1 DM and type-2) contribution is not the same for the development of tuberculosis. For example, TB is more common in insulin dependent diabetics and the risk of TB disease and death increases as complications of diabetes increase (22). Even though type-2 DM is more prevalent, type-1 carries a strong risk of contracting TB (38) other risk factors for developing TB in people with type-1 DM includes a low body weight, young age and poor glycemic control. Before the discovery of insulin, diabetes occurrence represented a death sentence with a mean survival time of less than five years and the usual cause of death was TB (22).

A study conducted in Ethiopia outlined that, out of 71 TB-DM patients 76.05% were had type-1 and 23.9% were had type-2 diabetics (12). But a systematic review of 13 observational studies, in USA, showed that DM increases the risk of TB, regardless of different study designs, background TB incidence, types of DM or, geographic region of the study (38). A prospective cohort study in Hong Kong showed that diabetic subjects with hemoglobin A1C $\geq$7% were at increased risk for TB with adjusted hazard ratio of 3.11(95%CI:1.63-5.92)(39).

A facility based cross sectional study in Ethiopia showed that; urban residence, past history of TB, contact with TB patients and long duration of DM were significantly associated with development of TB among diabetics (10).

In general, the conceptual frame work (Fig 1) summarizes DM and non-DM potential factors that can affect the occurrence of TB.

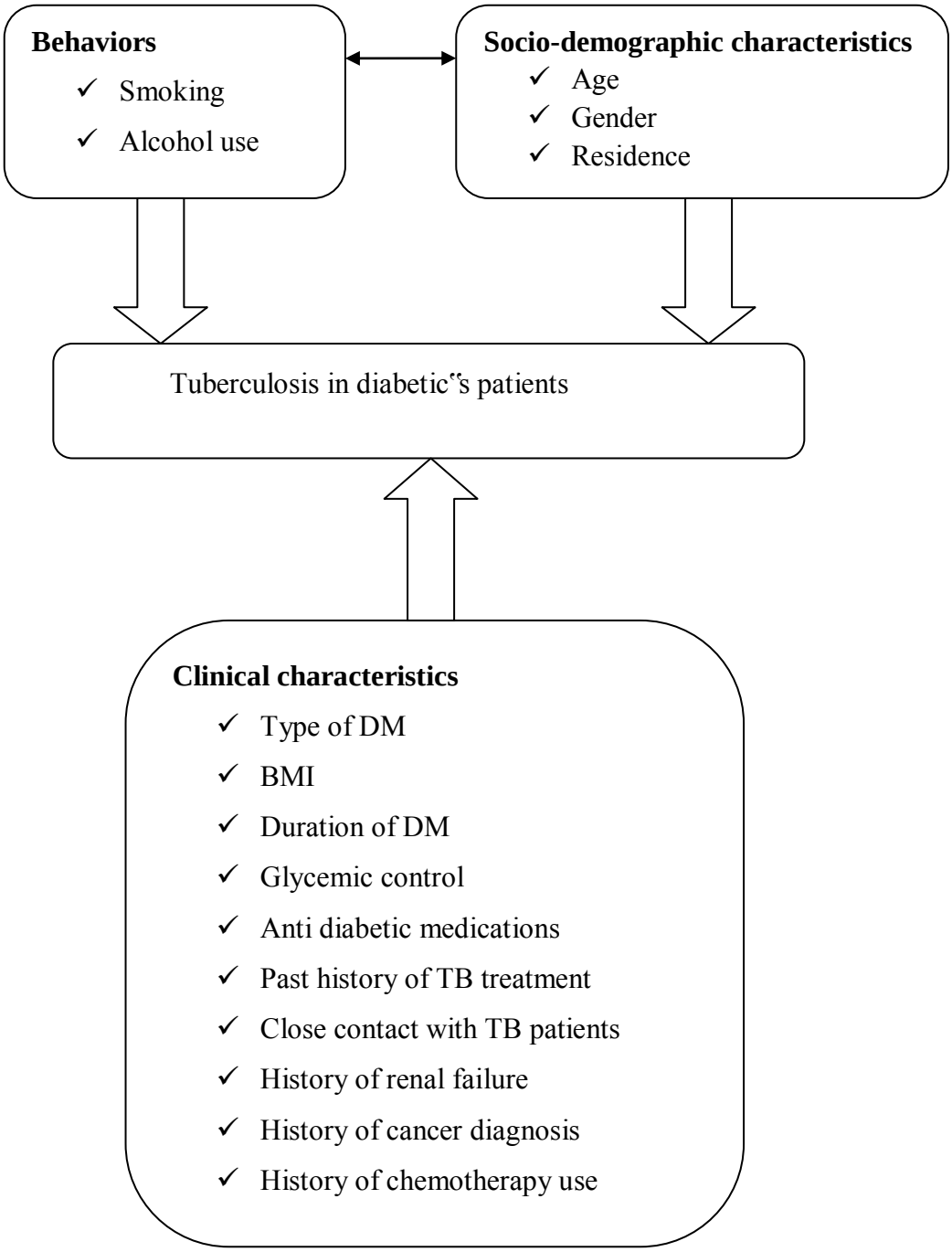


Figure 1: Conceptual framework for factors associated with tuberculosis among diabetic patients

3. OBJECTIVE

3.1. General Objective

To assess the magnitude and associated factors of tuberculosis among diabetic patients at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia, 2015.

3.2. Specific Objectives

3.2.1. To determine the magnitude of tuberculosis among diabetic patients at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia, 2015.

3.2.2. To identify factors affecting tuberculosis among diabetic patients at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia, 2015.

4. METHODS

4.1. Study Area and Period

This study was conducted in Tikur Anbessa Specialized Teaching Hospital (TASTH), Addis Ababa, Ethiopia. Addis Ababa is located at the heartland of the country at an area of about 540 square kilometers. The city is divided into 10 administrative sub-cities and there are 116 districts, hosting population of more than 3.2 million. Tikur Anbessa Specialized Teaching Hospital is found in Addis Ababa City, Lideta Sub City. The hospital has been inaugurated by the title "Prince Mokonnen" Memorial Hospital on 3/11/1973. On 24/5/1975 it was named Tikur Anbessa Hospital.

Tikur Anbessa, the largest referral hospital in the country, with 700 beds and is the main teaching hospital for both clinical and preclinical training of most disciplines. It is also an institution where specialized clinical services that are not available in other public or private institutions are rendered to the whole nation. TASTH has 200 doctors, 379 nurses and 115 other health professionals dedicated to providing health care services. The various departments, faculties and residents under specialty training in the School of Medicine provide patient care in the hospital. This study was conducted at Endocrinology and Metabolism unit of the Department of Internal Medicine, Faculty of Medicine at Tikur Anbessa hospital, Addis Ababa University, from Feb 2015 to May 2015. Which is one of the specialty units of the hospital, provides services for more than 100,000 clinical visit per year as follow up and new cases for both Type I and Type II diabetes patients in 2014.

4.2. Study Population

4.2.1. Source population

The source population of the study were the list all diabetic patients‟ registers under treatment in the hospital.

4.2.2. Sampling frame

The sampling frame was list of diabetic patients‟ medical records that have been used for routine care of DM from January 2010 to January of 2014.

4.2.3. Study population

The study population was all diabetic patients‟ who fulfilled the inclusion criteria based on the medical records that have been used for routine care of DM from January, 2010 to January, 2014.

Inclusion criteria

- All diabetic patients who have been treated in the diabetic center from 2010-2014

Exclusion criteria

- Patients who were under 18 years of age
- Gestational diabetic patients
- Incomplete and unavailable medical records

4.2.4. Sample size determination

Since it was a medical record review on the cohort of DM patients all the available patients‟ medical records during the study period was subjected to the study.

In this study a total of 1,635 medical records were reviewed, out of the records 681 medical records fulfilled the inclusion criteria of the study and of 551(80.9%) were type-II diabetic patients, 121(17.76%) were type-I diabetic patients and 9(1.3%) of them had no classification of DM (see figure2).

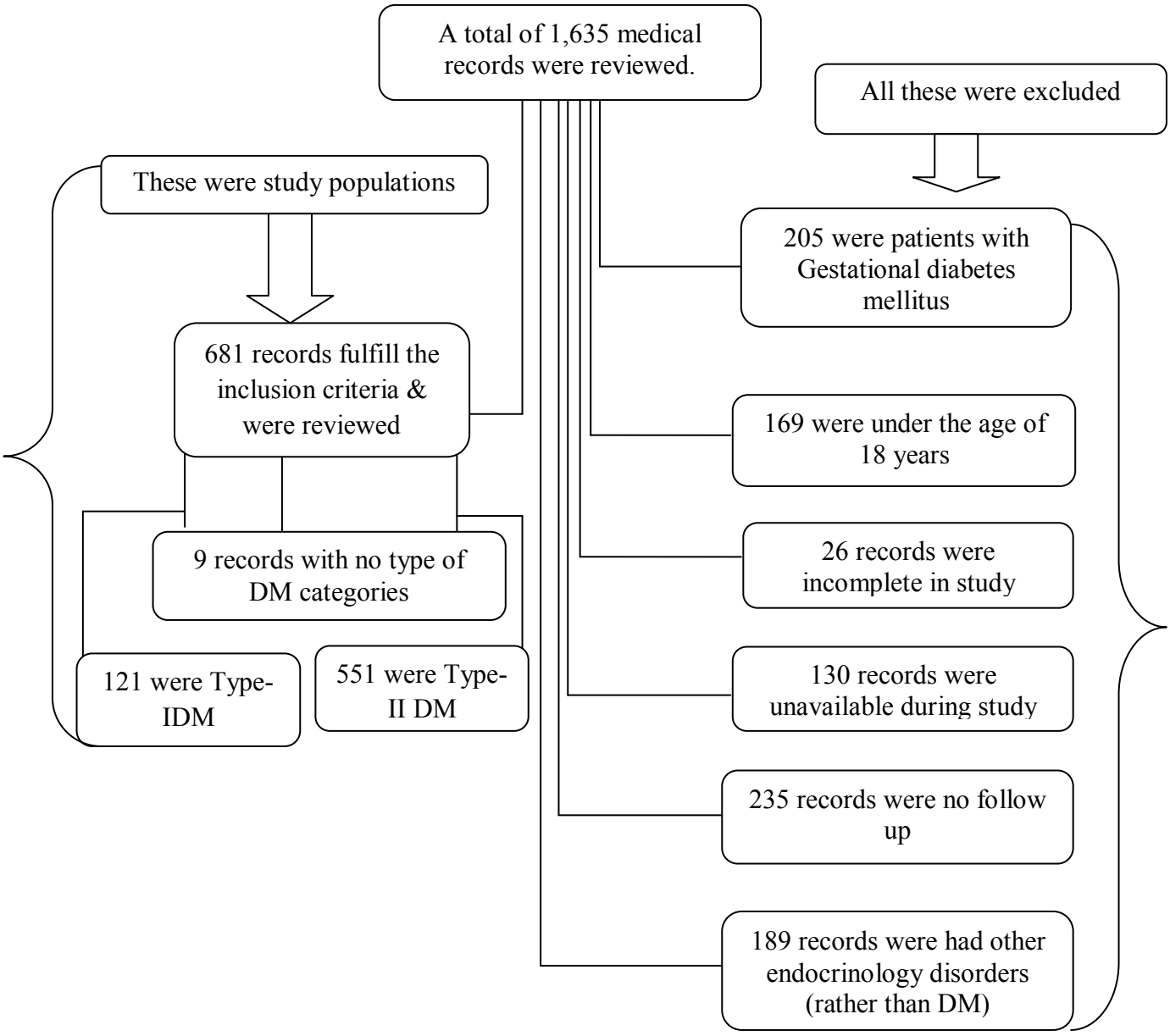


Figure 2: Diagram shows the diabetic patients at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia from January 2010 to January 2014.

4.3. Study design

A retrospective study was conducted to assess the magnitude and associated factors of tuberculosis among adults, 18 and above years old, diabetic patients.

4.4. Study Variables and Operational Definitions

4.4.1. Dependent Variable

- Cases of tuberculosis

4.4.2. Independent Variables

- Socio-demographic variables such as age, sex, and place of residence.
- Past history of tuberculosis, and close contact with tuberculosis patients
- Family history of diabetes mellitus
- Duration of diabetes mellitus
- Body mass index (BMI)
- History of smoking and alcohol consumption
- Types of anti diabetic medication used by the patient
- Glycemic control

4.4.3. Operational definitions

- Cases of tuberculosis: - a diabetic patient in whom his/her disease was declared by clinician as TB which was diagnosed either clinically or bacteriologically.

4.5. Data collection tools and procedures

Data collection tools were developed by reviewing the existing medical records and other previous studies questionnaires and check lists. The data collection format consisting of closed and open ended questions were prepared in English version only, since it is secondary type of data based on medical record review. Data collectors were eight Bsc nurses working outside of the diabetic center, and additional two health officers were recruited for supervision. One day training was given for data collectors and supervisors on methods of extracting the pertinent data through reviewing the patient‟s medical records. How to fill the information on a check list, the ethical aspect in keeping the confidentiality of their information were

another focus of the training. The supervisors had monitored the data collection process of the reviewers and taken corrective measures with consultation of principal investigator.

4.6. Data Quality control

To assure the quality of the data, the check list were prepared using simple and easily understandable language by including the study variables , and one day training was given for data collectors prior to data collection. The check list was pre-tested for appropriateness to the local context. It was done in other health facility, on 5% of the medical registry of the diabetic patients and modified accordingly. During data collection, the supervisors monitored the data collection process by checking completeness of the data and took the correction on the spot of data collection site when any problem happened and the principal investigator rechecked the completeness of data. Data were checked again for its completeness during data entry and the cleaning process was done by running simple frequency after data entry for its consistency. When inconsistency happens to the data, it was checked again by referring the hard copy checklist. Finally, data analysis was begun after completion of the cleaning process.

4.7. Data processing and analysis

Data was extracted from the medical records and entry and analysis were done using SPSS, version 20. Ten percent double entry was done to validate the data entry. Descriptive statistics such as frequencies, proportions, means, medians and standard deviation (SD) were calculated. Continuous variables such as age, BMI, duration of DM and FBS were converted to categorical variables.

To estimate the magnitude of the association between associated factors and tuberculosis among diabetic patients, odds ratio (OR) with 95%confidence intervals (CIs) were used.

A logistic regression model was used for both bivariate and multivariate analysis in order to identify associated factors of tuberculosis among diabetics groups of independent variables. Variables significantly associated ($p < 0.05$) with tuberculosis among diabetics in the binary logistic regression analysis were entered in to the multivariate logistic regression analysis model. The finding was expressed in OR with 95%CIs and a significant threshold was declared at $p < 0.05$.

4.8. Ethical Consideration

This study was done after getting ethical clearance from Research and ethical committee of the school of public health, Addis Ababa University. Written permission was also secured from Black Lion hospital particularly from, the Unit of Endocrinology and Metabolism Department of Internal Medicine, diabetic center. The information collected from the medical record was used only for the research purpose and was kept confidential. Patients who were available during the study period was informed and requested for their permission and verbal consent was obtained for the participation.

4.9. Plan for Dissemination and Utilization of results

The final report of this study was submitted to the Addis Ababa University College of health sciences, department of public health. The result of this study was presented during thesis defense, as a partial fulfillment of master of public health. Moreover, the findings of the study will be disseminated through publication in local and international journals.

5. RESULT

5.1. Description of the Study Subjects

5.1.1. Socio-demographic characteristics of the diabetic patients

Of the 681 known diabetic patients 345 (50.7%) were male populations. The mean age of the study population was 51.6± 14.2 (SD) years (ranging from 18-88 years). Regarding to age distribution of diabetic patients, 100 (14.7%) of them were under the age of 35 years, 191 (28.1%) of them were at the age interval of 36-50 years, 270 (39.8%) were within the age range between 51-65 years and 118 (17.4%) of them were above 66 years old. Five hundred thirty five (80.1%) of the participants were from Addis Ababa and the remaining 133 (19.9%) were also from dwellers out of Addis Ababa (see table 1).

Table 1: The socio-demographic characteristics of DM patients with and without TB at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia 2014.

Characteristics	Frequency	Percentage
Sex		
Male	345	50.7
Female	335	49.3
Age		
≤35	100	14.7
36-50	191	28.1
51-65	270	39.8
≥66	118	17.4
Mean(SD)	51.6±14.2	
Place of residence		
Addis Ababa	535	80.1
Out of Addis Ababa	133	19.9

DM = diabetes mellitus; TB =tuberculosis; SD= standard deviation; ≤ = less than or equal to; ≥ = greater than or equal to

5.1.2. Behavioral characteristics of the diabetic patients.

Out of 681 reviewed medical records 225 had assessed personal characteristics of DM patients towards smoking, and of 225 study subjects 32 (14.2%) had history of smoking, 22 (9.7%) had history of alcohol use and 19 (8.4%) had both history of smoking and alcohol use (see table 2).

Table 2: Behavioral characteristics of the diabetic patients with and without TB at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia 2014.

Behavioral characteristics	Frequency	Percent
History of smoking		
Yes	32	14.2
No	193	85.8
History of alcohol use		
Yes	22	9.7
No	204	90.3
History of both smoking and alcohol use		
Yes	19	8.4
No	206	91.6

5.1.3. Clinical characteristics of diabetic patients

Thirty four (23.3%) diabetic patients have a family history of DM where as 112 (76.7%) had no family history of DM. The majority 551 (82.0%) of the study participants had Non - insulin dependent diabetes mellitus and insulin dependent DM accounts for 121 (18.0%).

The duration of DM in all patients varied from 1 year to 59 years, with a median duration of 5.0 years. Three hundred sixty two (53.2%) had DM for less than five years durations, 190(27.9%) had for 6-10 years duration and 129(18.9%) had for more than ten years durations. Out of the total diabetic patients whose medical records reviewed 551(82%) of them had type-II (Non-Insulin dependent Diabetes mellitus) DM and the remaining 121(18.0%) had type-I (Insulin Dependent Diabetes Mellitus). The body mass index of the participants showed that 266 (39.1%) of them had normal, 40 (5.95) of them were under weight and the majority 375 (55.1%) of them were overweight. Regarding to their current treatment 449 (67.7%) were on Oral hypoglycemic agents only, 158 (23.8%) were on insulin only and the reaming 56 (8.4%) of them were taken both oral hypoglycemic agents and insulin. The glycemic control revealed that 189 (28.2%) diabetic patients were normal whereas the rest 482 (71.8%) were poorly controlled with mean FBS below 70 and above 130mg/dl inclusive (see table 3).

Table 3: Frequency distribution of clinical characteristics of DM patients with and without TB at Tikur Anbessa Teaching Hospital in Addis Ababa, Ethiopia 2014.

Characteristics	Frequency	Percent
Family history of DM		
Yes	34	23.3
No	112	76.7
Type of DM		
Type-I	121	18.0
Type-II	551	82.0
DM medications		
OHA only	449	67.7
Insulin only	158	23.8
Both OHA and insulin	56	8.4
Glycemic control(mg/dl)		
70-130	185	27.2
≤69.99	6	0.9
≥130	490	72.0
Body mass index(kg/m^2)		
18.5-24.99	266	39.1
<18	40	5.9
≥25	375	55.1
Duration of DM (years)		
≤5	362	53.2
6-10	190	27.9
≥10	129	18.9
Renal failure		
Yes	61	18.3
No	272	81.7
Cancer		
Yes	12	5.6
No	204	94.4
Chemotherapy use		
Yes	8	4.2
No	183	95.8
Sero-status for HIV		
Positive	27	27.0
Negative	73	73.0
Past history of TB treatment		
Yes	19	5.8
No	311	94.2
Close contact with TB patient		
Yes	16	4.4
No	345	95.6

DM=diabetes mellitus, TB=tuberculosis, OHA= oral hypoglycemic agent, HIV=human immunodeficiency virus

5.2. Burden of TB among Diabetic Patients

5.2.1. Magnitude of Tuberculosis among diabetic patients

Out of 681 known diabetic patients, the magnitude of tuberculosis was reviewed in 26 of the patients" medical records (17 males and 9 females); all the identified cases were declared by a clinician as tuberculosis diagnosis. Out of the record reviewed overall magnitude of TB was 3.8% in the study population, of these pulmonary TB accounts for 24 (92.3%) and 2 (7.7%) were extra-pulmonary tuberculosis, and 9 (34.6%) of these were had past history of TB treatment and the remaining 17(65.4%) were new TB cases. In addition, 4 (15.5%) TB-diabetic patients were also infected with HIV. Relatively higher proportion of TB was identified among the age group of 51 years and over 20(76.9%), male diabetics 17(65.4%), in Addis Ababa dwellers 17(65.4%). Most of the TB-diabetes patients had type-II diabetes 16(61.5 %) and type-I accounted for 10(38.5 %) (see table 4).

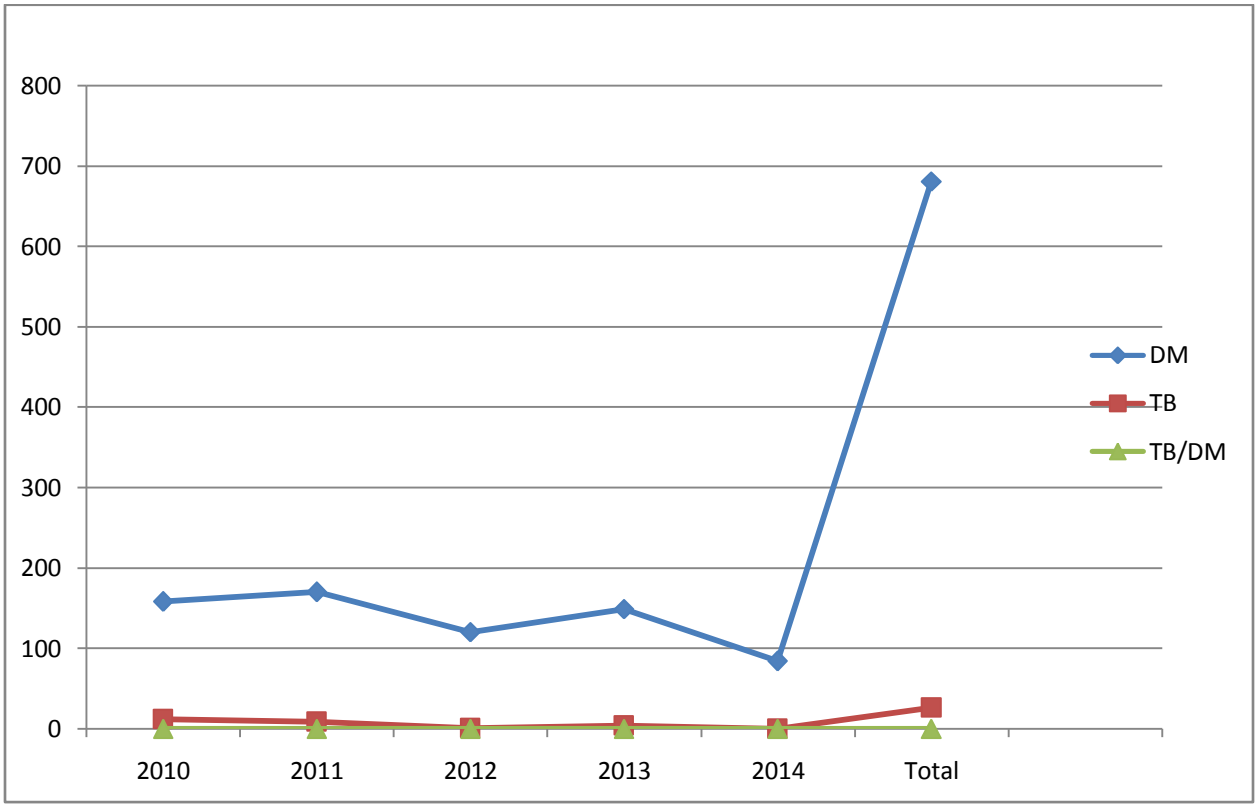
Table 4. Types and categories of TB in DM patients at Tikur Anbessa Specialized teaching hospital in Addis Ababa, Ethiopia 2014.

Category and type of TB	Frequency
New	17
Pulmonary TB	15
Extra-pulmonary TB	2
Retreatment	9
Relapse PTB	9
Failure of PTB	0
Return after default PTB	0
Total	26

TB=tuberculosis; DM= diabetes mellitus; PTB=pulmonary tuberculosis

5.2.2. Trend of TB among diabetic patients

Magnitude of TB among DM patients at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia, from Jan 2010 to Jan 2014, with their respective years of diabetes diagnosis made.



DM=diabetes mellitus; TB=tuberculosis; TB/DM=tuberculosis among diabetics, vertical axis =shows the number of diabetic patients (frequency), horizontal axis= shows the year of diagnosis made for diabetes mellitus.

Figure 3.Trend of TB among diabetic patients at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia, 2014.

5.3. Factors associated with TB among diabetic patients

5.3.1. Socio-demographic and behavioral characteristics associated with TB outcomes

On bivariate analysis, there were no significant associations concerning socio-demographic characteristics for sex and residence except for age. But history of smoking, alcohol use and both history of smoking and alcohol use were significantly associated with TB among diabetics.

Diabetic patients who were over 66 years old were 9 times (COR=9.2; 95%CI=1.2-72) odds to develop TB than from those who were less than 35 years, and diabetic patients who had history of smoking were 26 times (COR=26.2; 95%CI=9.7-70.6) odds to develop TB than who did not have history of smoking (see table 5).

Table 5. The socio-demographic and behavioral characteristics associated with TB outcomes among DM patients at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia 2014.

Characteristics	DM patients with TB	DM patients without TB	COR,95%CI	P-value
	N (%)	N (%)		
Sex				
Male	17(4.9)	328(95.1)	1.8(0.8-4.3)	0.133
Female	9(2.7)	326(97.3)	1.0	
Age				
≤35	1(1.0)	99(99.0)	1.0	
36-50	5(2.6)	186(97.3)	2.6(0.3-23.1)	0.375
51-65	10(3.7)	260(96.3)	3.8(0.5-30)	0.205
≥66	10(8.5)	108(91.5)	9.2(1.2-72.1)	**0.036**
Place of residence				
Addis Ababa	17(3.2)	518(96.8)	1.0	
Out of Addis Ababa	9(6.8)	124(93.2)	0.4(0.2-1)	**0.061**
History of smoking				
Yes	17(53.1)	15(46.9)	26.2(9.7-70.6)	**<0.001**
No	8(4.1)	185(95.9)	1.0	
History of alcohol use				
Yes	7(31.8)	15(68.2)	5.9(2.1-16.6)	**0.001**
No	15(7.4)	189(92.6)	1.0	
Smoking and alcohol use				
Yes	7(36.8)	12(63.2)	7.4(2.5-21.7)	**<0.001**
No	15(7.3)	191(94.1)	1.0	

AA= Addis Ababa; BMI= body mass index; CI= confidence interval; DM= diabetes mellitus; COR= crude odd ratio, TB= tuberculosis; OAA= out of Addis Ababa; HIV= human immunodeficiency virus.

5.3.2. Clinical Characteristics associated with TB outcomes

No significant differences were noted between TB-DM group and only DM group with respect to current treatments (types of DM medication) and glycemic control for an outcome variable. HIV sero-status, renal failure, organ transplantation, history of cancer and chemotherapy use also are not associated with the TB outcome among DM patients, but family history of DM, type of DM, BMI and duration of DM were significantly associated.

Diabetic patients who had family history of DM were 4 times (COR=4.3, 95%CI=1.6-11.6) more likely to develop TB than those who did not have family history of DM. Study subjects with Type-I DM were 3 times (COR= 3; 95%CI=1.3-6.8) more likely to have TB than participants with type-II. Participants who had body mass index less than 18 kg/m^2 were 18 times (COR=18.6; 95%CI=4.6-75) odds to develop TB than those who had body mass index of 18.5-25kg/m^2 and also those diabetic patients who had body mass index of over 25kg/m^2 were about 4 times (COR=3.9,95%CI=1.1-13.5) more likely to develop TB than from those who had body mass index of 18.5-25 kg/m^2. Diabetic patients who had duration of more than 10 years were 8 times (COR=8, 95%CI; 2.1-30.3) more likely to develop TB than who had less than five years duration of DM and diabetic patients who had past history of TB were 25 times (COR=25.5, 95%CI=8.8-73.4) odds to develop TB than those who did not have past history of TB (see table 6).

Table 6. Clinical features associated with TB outcomes among DM patients at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa, Ethiopia 2014.

Characteristics	DM patients with TB n (%)	DM patients without TB n (%)	COR,95%CI	P-value
Family history of DM				
Yes	11(25.6)	32(74.4)	4.3(1.6-11.6)	**0.004**
No	8(7.4)	100(92.6)	1.0	
Type of DM				
Type-I	10(8.3)	111(91.7)	3(1.3-6.8)	**0.008**
Type-II	16(2.9)	535(97.1)	1.0	
Type of DM medications				
OHA only	16(3.6)	433(96.4)	1.0	
Insulin only	10(4.3)	148(93.7)	1.8(0.8-4)	0.145
Glycemic control(mg/dl)				
70-130	4(2.2)	181(97.8)	1.0	
≤69.9	0(0.0)	6(100)	0.9(0.0-0.0)	0.9
≥130	22(4.5)	468(95.5)	2.1(0.7-6.3)	0.2
BMI(kg/m2)				
18.5-24.99	3(1.1)	263(98.9)	1.0	
<18.49	7(17.5)	33(82.5)	18.6(4.6-75)	**<0.001**
≥25	16(4.3)	359(95.7)	3.9(1.1-13.5)	**0.032**
Duration of DM(in years)				
≤5	3(0.8)	359(99.2)	1.0	
6-10	15(7.9)	175(92.1)	10.3(2.9-35.9)	**<0.001**
≥10	8(6.2)	121(93.8)	8(2.1-30.3)	**0.003**
History of cancer				
Yes	2(16.7)	10(83.3)	3.2(0.6-16.3)	0.161
No	12(5.9)	192(94.1)	1.0	
Chemotherapy use				
Yes	2(25)	6(75.0)	4.7(0.8-26.10	0.0734
No	12(6.6)	171(93.4)	1.0	
Sero-status for HIV				
Positive	4(14.8)	23(85.2)	1.2(0.3-4.4)	0.734
Negative	9(12.3)	64(87.7)	1.0	
Past history of TB				
Yes	10(52.6)	9(47.4)	25.5(8.8-73.4)	**<0.001**
No	13(4.2)	298(95.8)	1.0	
Close contact with TB patients				
Yes	8(50.0)	8(50.0)	19.3(6.5-57.6)	**<0.001**
No	17(4.9)	328(95.1)	1.0	

BMI= body mass index; CI= confidence interval; DM= diabetes mellitus; COR= crude odd ratio, TB= tuberculosis; OHA= oral hypoglycemic agents; mg/dl = milligram per deciliter; Kg/m2= kilogram per meter square.

5.3.4. Over all factors associated with TB among DM patients

In the multiple logistic model, after adjusting for possible confounding variables, diabetic patients above age 51 years, patients with body mass index less than 18 kg/m^2, type-I DM and duration of DM from 6-10 years were significantly associated with TB among diabetics, but diabetic patients with BMI ≥25kg/m^2, duration of DM greater than 10 years and family history of DM were not significantly associated with TB.

Variables such as, history of close contact with TB patients, smoking, alcohol use, both smoking and alcohol use and past TB treatments were dropped from multiple logistic regression analysis because they contained very small cell values, which imprecise the result of analysis.

Diabetic patients who were at the age interval of 51-65 were 21 times (AOR=21.4; 95%CI=1.2-385) more likely to develop TB than from those who were less than 35 years, also diabetic patients over the age of 66 years were 51 times (AOR=51; 95%CI=3-877) more likely to develop TB than those were under the age of 35 years. Participants with body mass index less than 18kg/m^2 were 27 times (AOR=27.6; 95%CI=1.7-442) times more likely to have TB than diabetic patients with body mass index of 18.5-25kg/m^2 . The odds of TB among type-I DM patients was 7 times (AOR=7; 95%CI=1.1-41.6) higher than those of type-II DM patients.

Regarding duration of patients with DM, diabetic patients who had a duration for 6-10 years were 5 times (AOR=5.1; 95% CI=1-24) more likely to develop TB than those of diabetic patients who have less than five years (see table 7).

Table 7. Multivariate analysis of factors associated with TB among DM patients at Tikur Anbessa Specialized Teaching Hospital Addis Ababa, Ethiopia 2014.

Characteristics	DM patients with TB n (%)	DM patients without TB n (%)	COR,95%CI	AOR,95%CI	P-value
Age					
≤35	1(1.0)	99(99.0)	1.0	1.0	
36-50	5(2.6)	186(97.3)	2.6(0.3-23.1)	4.6(0.3-70.5)	0.267
51-65	10(3.7)	260(96.3)	3.8(0.5-30)	21.4(1.2-385)	**0.038**
≥66	10(8.5)	108(91.5)	9.2(1.2-72.1)	51(3-877)	**0.007**
BMI(Kg/m2)					
18.5-25	4(1.4)	278(98.6)	1.0	1.0	
<18.5	3(11.5)	23(88.5)	9(1.9-43)	27.6(1.7-442)	**0.019**
≥25	14(5.8)	226(94.2)	4.3(1.4-13.2)	9(0.9-90)	0.059
Family history of DM					
Yes	11(25.6)	32(74.4)	4.3(1.6-11.6)	0.3(0.05-2.1)	0.240
No	8(7.4)	100(92.6)	1.0	1.0	
Type of DM					
Type-I	10(8.3)	111(91.7)	3(1.32-6.8)	7(1.1-41.6)	**0.032**
Type-II	16(2.9)	535(97.1)	1.0	1.0	
Duration of DM(years)					
≤5	3(0.8)	359(99.2)	1.0		
6-10	15(7.9)	175(92.1)	10.3(2.9-35.9)	5.1(1-24)	**0.042**
≥10	8(6.2)	121(93.8)	8(2.1-30.3)	2.6(0.3-23.6)	0.400

BMI= Body mass index; CI= Confidence interval; DM= Diabetes mellitus; COR= Crude odd ratio, TB= Tuberculosis; mg/dl = milligram per deciliter; Kg/m2= Kilogram per meter square; AOR=Adjusted odd ratio.

6. DISCUSSION

Previous studies have identified an association between diabetes and tuberculosis, in that DM is one of the risk factors for the development of active tuberculosis (3, 5, 6, 11, 15, 16-20, 23). However, in Ethiopia, particularly in Tikur Anbessa Specialized Teaching Hospital, little is known about the magnitude and associated factors of TB in the population those with DM. Hence, the present study tries to provide insights into the magnitude of tuberculosis among diabetic patients, as well as to identify common risk factors.

In this study, the magnitude of TB among known diabetic patients was 3.8%, 95%CI; 2.5%-5.3%. It is higher than the 2013 WHO estimated prevalence of TB in the general population of 0.2 % (1). This finding is in line with reports from China (3.7%) and India (2.6%) (15). However, the finding of the current magnitude of TB among diabetics was much lower than the magnitude reported from South Africa (10.6%), Northeast Ethiopia (Dessie) (6.2%) (10,23). This variation could be due to the use TB diagnosis methods, in South Africa it was diagnosed by using X-ray and in Dessie, Northeast Ethiopia, it was diagnosed among TB suspected diabetic patients , so these may over estimated the magnitude of TB among diabetics.

The socio-demographic characteristics of diabetic patients and other behavioral and clinical risk factors for TB outcome were also investigated. Several studies have shown that socio-economic status, gender and age are a risk factor for active TB occurring (8, 13, 36). The result of this study showed that the higher the age of the patients, the more likely it is that they will have TB infection if they are also diabetic. The majority of the patients who developed TB were older than 50 years of age and this was comparable to other age reports from Dessie, Northeast Ethiopia, and South India (10, 36). The possible reason for this may be due to a compromised host‟s immunity that increased susceptibility to TB due to increased age, and most diabetic patients were in the over 50 years age group as well.

Body mass index is one of the most important risk factor for the occurrence of TB among diabetics, as indicated by different studies (8, 41, 36). A study showed that body mass index less than 18kg/m^2 is one of the determining factors for the occurrence of TB among diabetic patients (35). This study indicated that diabetic patients whose body mass index is less than 18kg/m^2 were almost 28 times (AOR=27.6; 95%CI=1.7-442) more likely to develop TB than those who have normal body mass index. In contrast, a study from Dessie, Northeast Ethiopia reported that there was no a significant association between body

mass index and TB among diabetic patients, this discrepancy may be due to the difference in socio-demographic, behavioral and sample size.

Different studies showed that TB is more common among insulin dependent diabetes mellitus patients, for example in Ethiopia a facility based study showed that out 71 TB-DM patients 76.05% of the patients were had insulin dependent diabetes mellitus (12), and another population based study in Australia reported that RR of TB among insulin dependent DM patients was 2.16 (95%CI, 1.19 to3.39) and also its prevalence was 9.1/100,000/year 95%CI 7.6 to 10.9(23). The present study supports, this report with a prevalence rate of 8.3% and AOR (7, 95%CI, 1.1- 41.6) of TB among insulin dependent DM. The possible reason for this may be type-I diabetes mellitus occur at the early age of the patients and because of this they will have longer duration of DM, it affects the immunity status of the patients with this type of diabetes mellitus and also patients with type-I DM may have a poor glycemic control, and this poor glycemic control can leads to multiple complications, including vascular diseases, neuropathy, and increased susceptibility to infections like tuberculosis.

Regarding the duration of the DM, several studies outlined that the longer the duration, the higher risk of TB among diabetics (10, 41). In this study diabetic patients who had a duration of 6-10 years were 5 times (AOR=5.1; 95%CI=1-24) more likely to develop TB than from those who have less than five years duration of DM. This finding is also similar with the study done in Ethiopia (AOR=8.89; 95%CI=1.88-58.12) and Pakistan, Jabbar et.al (10, 41). This may be because of uncontrolled high levels of blood glucose for long periods of time could be another factor associated with the development of TB. In addition, in low-resource settings, early diagnosis and adequate glycemic control of DM is difficult, and this will probably further increase the proportion of diabetic patients developing TB.

7. STRENGTH AND LIMITATION

7.1. Strength

- ✓ Data collectors were trained and experienced health professional.
- ✓ The data collection tool (checklist) was checked against the patient‟s medical records before the data collection.
- ✓ Adjustments was done for possible confounders
- ✓ Careful data management and processing was used.

7.2. Limitation

- ❖ Under recording of
    - o Diabetic patients‟ behavioral, life style, socio-economic, educational level, marital status, occupational status and ethnicity, which may have been confounding factors in this setting.
- ❖ Incomplete medical records.
- ❖ Inability to reliable distinguish between type-I and type-II diabetes mellitus.
- ❖ Loss of medical records.

8. CONCLUSION

The overall magnitude of TB among diabetic patients was high in Tikur Anbessa Specialized Teaching Hospital. Pulmonary TB was the commonest form of TB among diabetics. Type-I DM, duration of DM, body mass index and age at time of DM diagnosis were independently associated for the development of TB among diabetics.

9. RECOMMENDATIONS

Based on the finding of this study the following important recommendations are forwarded for the respective bodies" such as clinicians, patients, health educators, policy makers, program implementers and researchers who will engage on TB and DM areas as of one main public health concern:

For organizations and institutions

- ✓ The ministry of health should have collaborate and initiate TB screening and treatment program for all diabetic patients in health institutions (collaboration of non-communicable diseases with communicable diseases).
- ✓ The ministry of health should have to develop guidelines which helps when and how to screen tuberculosis among diabetic patients.

For health workers

- ✓ All diabetic patients should be screened for tuberculosis at their diagnosis time and they should have regular follow up.
- ✓ Intensify detection of TB disease among diabetic patients.
- ✓ Prevent the occurrences of TB among DM patients by early diagnosis and by acting accordingly.
- ✓ Providing IEC and BCC towards modifiable risk factors such as smoking, alcohol use, weight control and diet.

Patients

- ✓ Awareness creation on the patients to make early diagnosis and treatment when they will have cough for more than two weeks, night sweating, chest pain and unusual weight loss.

For researchers

- ✓ Finally, it is better to conduct further large scale epidemiological studies with large sample size and advanced TB diagnostic technologies.

ANNEX

Annex 1: References

1. Global tuberculosis report Geneva: World Health Organization; 2014.
2. Global Tuberculosis Control Report 2013: World Health Organization; 2013.
3. International Diabetes Federation (IDF): Global Diabetes Plan 2011-2021.
4. International Diabetes Federation (IDF): Diabetes Blue Circle Symbol, 2006. http://www.diabetesbluecircle.org.
5. The International Union against Tuberculosis and Lung Disease and the World Diabetes Foundation: The growing threat of the double burden of diabetes and tuberculosis, Updated March 2014.
6. The International Union Against Tuberculosis and Lung Disease health solutions for the poor, Public Health Action,Vol-3 Supplement 1 November 2013.
7. USAID Health-Related Research and Development Progress Report, Report to Congress, December 2013.
8. Sulliva T, Ben Amor Y; The Co-management of tuberculosis and diabetes; Challenges and Opportunities in the developing World. PLoS Med.2012.9 (7):e1001269.
9. Baker, et al: The impact of diabetes on tuberculosis treatment Outcomes; A systematic review: BMC, Medicine 2011, 9:81. http://www.biomdcentral.com/174-7015/9/81.
10. Amare et al. Smear positive pulmonary tuberculosis among diabetic patients at the Dessie referral hospital, Northeast Ethiopia, 2013. Infectious Diseases of Poverty, 2:6.
11. Dooley KE, Chaisson RE92009): Tuberculosis and diabetes mellitus; convergence of two epidemics. Lancet Infect Dis 9:737-746.
12. Feleke Y, Abdulkadir J, Aderaye G: Prevalence and clinical features of tuberculosis in Ethiopian diabetic patients. East Afr Med J 1999, 76(7):361–364.
13. Nissapatorn V, Kuppusamy I, Jamaiah MY Fng, Rohehla M and Khairul Amuar A. Tuberculosis in Diabetic patients, a clinical perspective. Department of Parasitology, University of Malaya Medical Center, Kuala Lumpur: National Tuberculosis Center, Kuala Lumpur, Malaysia Vol-3(Supp 14)2005.
14. Lin Y, Li L, Mi F, Du J, et al. Screening patients with diabetes mellitus for tuberculosis in Chain. Trop Med Int Health. 2012:17:13028.
15. India Diabetes Mellitus-Tuberculosis study group. Screening of patients with diabetes mellitus for tuberculosis in India. Trop Med Int Health. 2013; 18:646.54.

16. Parvaneh B, Majid M,et al; Diabetes mellitus and tuberculosis facts and controversies. Journal of Diabetes and metabolic Disorders 2013, 12:58, http://www.jdmonline.com/content/12/1/58.
17. Sarah LB, Paul G. the impact of diabetes mellitus on tuberculosis and its threat to global tuberculosis control. „The tubercular diabetic". Clinical Medicine 2011, Vol-11, Nov 4:344-7
18. Perez A, Brown HS, Restrepo BI: Association between tuberculosis and diabetes in the Mexican border and non-border regions of Texas. Am J Trop Med Hyg 2006, 74(4):604-611.
19. Leung CC, Lan TH, Clan WM, et al. Diabetic Control and risk of tuberculosis: a cohort study. Am J Epidemiol 2008; 167:1486e94.
20. Young F, Wotton CJ, Critchley JA,et al. Increased risk of tuberculosis disease in people with diabetes mellitus: record-linkage study in a UK population. J Epidemiol Community Health, 24 November 2010.doi:10,1136/jech.2010.114595.
21. Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med 2008; 5:e152.
22. Kim SJ, Hong YP, Lew WJ, et al. Incidence of pulmonary tuberculosis among diabetics. Tuber Lung Dis 1995; 529e33.
23. Dobler CC, Flack JR, Marks GB: Risk of tuberculosis among people with diabetes mellitus; an Australian nationwide cohort study, BMJ Open 2012; e000666. (Accessed date Nov 30, 2014).
24. Broxmeyer L, Diabetes mellitus, tuberculosis and the mycobacteria two millennia of emigma, Med Hypotheses,2005,65(3);433-439.
25. Ponce- De-Leon A, Garcia-Garcia MdMdel. Tuberculosis and diabetes in Southern Mexico. Diabetic Care 27:1584-1590.
26. Matthew J Magee, Henry M Blumberg and KM Venkat Narayan: Commentary: Co-occurrence of tuberculosis and diabetes: new paradigm of epidemiological transition; International Journal of Epidemiology 2011; 40:428–431 doi:10.1093/ije/dyq268.
27. Stevenson CR, Forouhi NG, Rolglic G, Williams BG, Lauer JA at al. Convergence of the tuberculosis and diabete epidemics: renewal of old acquaintances. J Diabetes Metab Disord.2012; 11:28.doi:10.1186/2251-6581-11-28.
28. Baker MA Harries AD, Jeon CY, Hart JE, Kapur A, Lönnroth K, et al. The impact of diabetes on tuberculosis treatment outcomes: A systematic review. BMC Med. 2011; 9:81Pablos-Mendet A, Blustein J, Knirsch CA (1997). The role of Diabetes in the higher prevalence of Tuberculosis among Hispanics. Am J Public Health 87:574-579.

29. Singla R, Khan N, Al-Sharif N, Ai-Sayegh MO, Shaikh MA, et al(2006). Influence of diabetes on manifestations and treatment outcome of pulmonary TB patients. Int J Tuberc Lung Disc 10:74-79.
30. Root HF (1934). The Association of Diabetes and Tuberculosis: Epidemiology, Pathology, Treatment and Prognosis. N Engl J Med 1934; 210:1-13.
31. Boucot KR, Dillon ES, Cooper DA, Meier P. et al (1952). Tuberculosis among diabetics: the Philadelphia survey. Am Rev. Tuber 65:1-50.
32. Banerjee D, Bhattacharya R, Kaul D, Sharma P (2011). Diabetes and tuberculosis: analysis of a pyradox. Adv Clin Chem 53:139-153.
33. Jeon CY, Harries AD, Baker MA, et al. Bi-directional screening for tuberculosis and diabetes: a systematic review. Trop Med Int Health 2010; 15:1300-1314.
34. Restrepo BI, Camerlin AJ, Rahbar MH, Wang W, Restrepo MA, et al (2011). Cross-sectional assessment reveals high diabetes prevalence among newly diagnosed tuberculosis cases. Bull World Health Orga 89:352-359.
35. Zhang Q, Xiao H, Sugawara I: Tuberculosis complicated by diabetes mellitus at Shanghai pulmonary Hospital, Chain. Jpn J. Interct Dis…, 62,390-391, 2009.
36. Kumpatle S, Serkar A, Achante S, Sharath N, et al: Characteristics of patients with diabetes, Screened for tuberculosis in a tertiary Care hospital in India. International Union Against tuberculosis and Lung Disease. Health solution for the poor, public health action vol-3 supplement 1, 24 may 2013.
37. Perez-Navarro LM, Fuentes-Dominguez F, Morales-Ronur OJ, Zenteno-Cuevas R; Factors associated to pulmonary tuberculosis in patients with diabetes mellitus, Veracruz, Mexico. Gac Med Max, 2011 may-June: 219-25.
38. Diabetes mellitus increases the risk of active tuberculosis. A systematic review of 13 observational studies. Department of Epidemiology, Harvard School of Public Health ,Boston, Massachusetts, United States of America,2008.
39. Chi C. Leung ,Tai H. Lam , Wai M. Chan ,Wing W. Yew ,Kin S. Ho, et al. Diabetic Control and Risk of Tuberculosis: A Cohort Study, Hong Kong, People‟s Republic of China. Am J Epidemiol 2008: Vol. 167, No. 12 167:1486–1494.
40. Davies PD, Yew WW, Ganguly D, Davidow AL, Reichman LB, Dheda K, Rook GA: Smoking and tuberculosis: the epidemiological association and pathogenesis. Trans R Soc Trop Med Hyg 2006, 100(4):291–298.

41. Jabbar SF, Hussain L, Khan A: Clinical characteristics of pulmonary tuberculosis in adult Pakistani patients with co-existing diabetes mellitus. East Mediterr Health J 2006, 12(50):522–527.

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Annex 2: Data abstraction form

Check list form to assess the magnitude and factors associated with Tuberculosis among diabetics in Addis Ababa, Ethiopia.

Instruction: Circle/write the recorded information by reviewing the patients" medical record.

Section-1 Socio-demographic history			
		Card number	
Sr.no	Questions	Options/answers	Remark
101	Sex	1. Male	
		2. Female	
102	Age	_____(in years)	
103	Height	_____ meter	
104	Weight	_____kg	
105	BMI	_____kg/m^2	
106	Place of residence	1. Addis Ababa	
		2. Out of Addis Ababa	
Section-2 Clinical features of the diabetic patients			
201	Sero-status for HIV	1. Positive	
		2. Negative	
		3. Not known	
202	History of renal failure?	1. Yes	
		2. No	
		3. Not recorded	
203	History of organ transplantation?	1. Yes	
		2. No	
		3. Not recorded	
204	History for diagnosis of cancer?	1. Yes	
		2. No	
		3. Not recorded	
205	History of chemotherapy use?	1. Yes	

		2. No	
		3. Not recorded	
206	When did the DM diagnosis made?	_____(year in GC)	
207	Did the patient have family history of DM?	1. Yes	
		2. No	
		3. Not recorded	
208	Type of DM did the patient have?	1. Type-I	
		2. Type-II	
		3. Not recorded	
209	Medication the patient has been taking/ taken?	1. Oral hypoglycemic agents only	
		2. Insulin only	
		3. Not recorded	
2010	Mean Fasting blood sugar/HbA1c at each year	_____mg/dl and _____%g (2010)	
		_____mg/dl and _____%g (2011)	
		_____mg/dl and _____%g (2012)	
		_____mg/dl and _____%g (2013)	
		_____mg/dl and _____%g(2014)	
Section-3 Tuberculosis related history			
301	Did the patient have past history of TB treatment?	1. Yes	
		2. No	
		3. Not recorded	
		If the answer is yes skip to Q302&303	
302	What type of TB did the patient had?	1. Pulmonary TB	
		2. Extra-pulmonary TB	
		3. Disseminated TB	
		4. Not recorded	
303	What was the patients‟ treatment outcome?	1. Cured	
		2. Treatment completed	

		3. Defaulted	
		4. Treatment failure	
		5. Not recorded	
304	Have history of close contact with TB patients?	1. Yes	
		2. No	
		3. Not recorded	
305	Did the patient have a diagnosis of TB after his/her DM diagnosis?	1. Yes	
		2. No	
		If the answer is yes, answer question number 306 and 307	
306	How long after DM diagnosis?	_____years/months	
307	What type of TB was diagnosed?	1. Pulmonary	
		2. Extra pulmonary	
		3. Disseminated	
		4. Not recorded	
Section-4 Personal characteristics of diabetic patients			
401	Did the patient have history of smoking?	1. Yes	
		2. No	
		3. Not recorded	
402	Did the patient have history of alcohol use?	1. Yes	
		2. No	
		3. Not recorded	
405	Did the patient have history of both smoking and alcohol use?	1. Yes	
		2. No	
		3. Not recorded	

Thank You!!!

Declaration

I, the undersigned, declare that this thesis is my original work and has never been presented for a degree in this or any other university and all the sources of materials used for the thesis have been fully acknowledged.

Name: **Sisay Tiroro (Bsc, N)**

Signature: _____

Date: _____

Place Addis Ababa University School of public health

This thesis work has been submitted for the examination with my approval as a university advisor.

Name: **Fikre Enquiselassie (Msc, PhD, Associate prof.)**

Signature: _____

Date: _____