PREVALENCE OF DIABETES AMONG TUBERCULOSIS PATIENTS ATTENDING A TERTIARY CARE HOSPITAL

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DECLARATION

I hereby humbly declare that the thesis work entitled " **Prevalence of diabetes among tuberculosis patients attending a tertiary care hospital**", a requirement for the degree of Master of Philosophy (MPhil) in Epidemiology and Biostatistics under the Faculty of Biological Sciences, University of Dhaka(DU), was carried out by me under the guidance of Prof. M A Hafez, Professor and Head, Department of Biostatistics, Bangladesh Institute of Health Sciences, under DU for the session 2011-2012.

This work has not been submitted elsewhere for any other purpose.

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CERTIFICATE

This is to certify that Dr. Afsana Habib Sheuly has completed her thesis work entitled "**Prevalence of diabetes among tuberculosis patients attending a tertiary care hospital**" in the Bangladesh Institute of Health Sciences (BIHS), under Dhaka University, Dhaka under my guidance and supervision as a partial fulfillment of the requirements for the degree of MPhil (Epidemiology and Biostatistics) course, session 2011-2012.

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The undersigned certify that they have carefully read and examined the student on this thesis and being satisfied, recommended to the Faculty of Biological Sciences, University of Dhaka for acceptance of this thesis titled "Prevalence of diabetes among tuberculosis patients attending a tertiary care hospital" by Dr. Afsana Habib Sheuly in partial fulfillment of requirements for the degree of Master of Philosophy in Epidemiology and Biostatistics.

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Date of Approval:

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Dedicated to My Respected Parents & My Beloved Family

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List of Contents

List of Tables

List of Figures

List of Abbreviation

AIDS	Acquired Immunodeficiency Syndrome
BIHS	Bangladesh Institute of Health Sciences
BMI	Body Mass Index
BUHS	Bangladesh University of Health Sciences
CI	Confidence Interval
DM	Diabetes Mellitus
DOTs	Direct Observed Treatments Short Course
DBP	Diastolic Blood Pressure
EPTB	Extra-Pulmonary Tuberculosis
GDM	Gestational Diabetes Mellitus
HIV	Human Immunodeficiency Virus
HbA1C	Glycated Hemoglobin
IDDM	Insulin-Dependent Diabetes Mellitus
IDF	International Diabetes Federation
IGRAs	Interferon-Gamma-Release Assays
IPD	Inpatient Department
LADA	Latent Autoimmune Diabetes of Adults
MDG	Millennium Development Goals
MDR TB	Multiple Drug Resistant Tuberculosis
MTB	Mycobacterium Tuberculosis
NIDCH	National Institute of Diseases of the Chest and Hospital
NIDDM	Non-Insulin Dependent Diabetes Mellitus
NTRL	National Tuberculosis Reference Laboratory
OGTT	Oral Glucose Tolerance Test
OR	Odds Ratio
PTB	Pulmonary Tuberculosis
SEA	South East Asia
SPSS	Statistical Package for the Social Sciences
SBP	Systolic Blood Pressure
TB	Tuberculosis
USA	United States of America
UK	United Kingdom
WHO	World Health Organization
WC	Waist Circumference

ABSTRACT

Diabetes mellitus (DM) is recognized as highly associated with tuberculosis (TB). In Bangladesh both diabetes and tuberculosis are major public health problems. Although the prevalence of TB and diabetes in Bangladesh are high, little is known about the association between the two diseases in the country. The aim of the study was to determine the prevalence of diabetes among tuberculosis patients attending tertiary care hospital and to see the association between them.

In this cross-sectional study 350 eligible TB patients participated who are selected by purposive sampling technique and study was done for 1 year from 1st June, 2014 to 31st May, 2015. OGTT was done for those without previous history of DM and diagnosis was based on WHO criteria. Fasting and 2 hours after breakfast plasma glucose was done for previously known DM patients. A pretested questionnaire was used to collect information on socio-demographics, habitual risk factors. Anthropometric measurements with details of current treatment regimen of TB and DM were recorded.

Out of 350 TB patients 70(20%)[CI 16%-24%] were found to have diabetes , of them 46 (19.4%) were male and 24 (21.2%) were female. and median age was 46 yrs (21-70). For PTB, out of 175, 47 (26.9%) were found diabetic and for EPTB, of the 175, 23(13.1%) were diabetic, (p=<0.001). Family history of DM were significantly higher among DM group compare to non-DM group (p=<0.001). On Pearson correlation coefficient, a significant correlation was found between age and DM (r=0.327, p=0.001). On Binary logistic regression, family history of DM had 2.8 times more chance to developed DM (p=0.002; Odds ratio 2.812) and PTB had 2.9 times chance to developed DM (p=0.005; Odds ratio 2.973) after adjusting age, BMI, treatment category variables.

The study demonstrates that diabetes mellitus is common among tuberculosis patients attending a tertiary care hospital in Bangladesh. The significant predictor associated with diabetes mellitus among tuberculosis patients was pulmonary TB.

CHAPTER 1: INTRODUCTION

1.1 Background

1.2 Rationale

1.3 Research Question

1.4 Objectives of the study

1.5 Conceptual framework

1.6 List of key variables

1.7 Operational Definitions

1.8 Limitations of the study

1.1 Background

Tuberculosis (TB) remains a considerable global public health concern, mainly affecting poor and vulnerable populations [1]. Every year, more than 9 million people are infected with TB and close to 2 million die from it. Diabetes, a chronic metabolic disease that is increasing globally, including in many settings with a high burden of TB, is associated with higher risks of TB [2] and adverse TB treatment outcomes [3]. The increase in the number of people with diabetes may further complicate care and control of TB, especially in the many areas with high burden of both diseases [4, 5].

The World Health Organization (WHO) suspects that TB control is being undermined by the growing number of TB patients with diabetes mellitus in the world, which currently stands at an estimated 285 million but is anticipated to reach about 438 million by 2030.[2,3] and among them 80% of prevalent cases will occur in the developing world [6,7]. The increase is mainly driven by changes in diet and levels of physical activity [8]. In the poorest countries, diabetes is more common among the better-off, but economic development quickly reverses this trend so that people from lower socioeconomic groups are more affected by diabetes; squeals are worse among the poor in all countries [9]. People from lower socioeconomic groups are therefore more vulnerable to both diseases [10].

Intensified discussions and research over the past decade have focused on the links between TB and diabetes [11, 12]. Theoretically, diabetes and TB may complicate each other at many levels. Conceivably, people with diabetes may be more easily infected by TB than non-diabetic people leading to a higher risk of latent TB infection, but the evidence remains weak [13, 14]. TB infection may progress at a faster rate in people with diabetes than in those without diabetes [2,15,16]. The clinical presentation of TB in people with diabetes may be altered and change the sensitivity and specificity of conventional diagnostic algorithms. Among those with active TB, diabetes may adversely affect TB treatment outcomes by delaying the time to microbiological response, reducing the likelihood of a favorable outcome, and increasing the risk of relapse or death [3]. Diabetes may also accelerate the emergence of drug-resistant TB, especially multidrug resistant TB (defined as strains of TB resistant to both rifampicin and isoniazid) among those receiving TB treatment,

although the evidence is limited [17]. Conversely, TB may trigger the onset of diabetes, and worsen glycemic control in existing diabetes. Finally, TB medications may interfere with the treatment of diabetes through drug interactions, and diabetes may interfere with the activity of certain anti-TB medicines [18].

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. Many studies reported that subjects with diabetes were at threefold higher risk of developing TB. In addition, studies that screened for DM among TB patients reported a wide range of DM prevalence among TB patients, ranging from 1.9% to as high as 35% [19, 20]. Studies conducted in regions with dual burden have reported that the prevalence of DM ranged from 14-40% [21, 22] among TB patients. A study conducted in 2011 in Tamil Nadu, India reported the prevalence of diabetes mellitus among the tuberculosis patients was 25.3% and another study in 2012 reported the prevalence rate of diabetes is 44% among the TB patients of Kerala, India. A case control study conducted in Bangalore, South India, during 2001-2003, reported that chronic disease particularly diabetes was a significant risk factor for developing TB. The prevalence rates of diabetes in TB and non-TB subjects were 22.2% and 15.9% respectively [23]. Based on secondary analysis of countrywide data, another research group estimated that 18.4% of subjects with PTB also have DM in India [24]. A retrospective analysis of 2 years data on TB subjects from Saudi Arabia in 1998 revealed that 27% had DM [25]. Another study from Taiwan reported 16.9% of DM among TB patients [26]. All these reports indicate that routine screening for DM among TB patients should be encouraged in areas with high TB burden. Alisjahbana et al. [21] reported prospective data from a cohort of patients with TB in Indonesia, where the prevalence of confirmed DM among patients with TB is 14.8% compared with 3.2% in general population.

In Bangladesh, both diabetes and tuberculosis are major public health problems. The prevalence of diabetes has been increasing in recent years and around 5.5 million people in Bangladesh are estimated to have diabetes [27]. Regional surveys conducted in urban and semi-urban populations showed a high prevalence of diabetes (6.8%-

10.5%) [28,29]. In rural Bangladeshi populations the prevalence of diabetes which was 3.8% in 1999-2000 [30], had increased to 8.5% by 2004-2005 [31]. WHO listed 10 countries to have the highest numbers of people with diabetes in 2000 and 2030 [8]. Bangladesh appears in the list for both 2000 and 2030 with India, Pakistan, China, Japan, USA and others. Likewise, TB also continues to be a major public health problem in Bangladesh. With over 300000 new TB cases and 65,000 TB deaths annually the country occupies the 6th position in the list of 22 high burden countries in the world [32]. Although the prevalence rates of TB and diabetes in Bangladesh are high, little is known about the association between the two diseases in the country. As diabetes may impair the response to TB treatment, it is very important to assess to what extent it is present in Bangladeshi TB patients in order to ensure their proper management.

In view of this situation, we therefore plan to carry out an epidemiological study to determine the prevalence of diabetes in our population of patients with tuberculosis and to identify other risk factors associated with DM among tuberculosis patients

1.2 Rationale

Screening for DM in TB patients could improve DM case detection and early treatment and indirectly lead to better TB specific treatment outcomes [6]. In 2013, the International Diabetes Federation (IDF) estimated that about 382 million people worldwide have diabetes mellitus (DM). 80% of these people live in the low and middle income countries where tuberculosis (TB) is highly prevalent [7]. Currently, both TB and DM are of great public health importance globally, especially in South East Asia (SEA) due to the converging epidemics of both communicable and non-communicable diseases. Recent evidence advocates for bi-directional screening and care of TB and DM patients.

The global burden of diabetes mellitus (DM) and tuberculosis (TB) is huge. Nearly one-third of world's population is infected with Mycobacterium tuberculosis and about 10% of them are at risk of developing active form of the disease in their lifetime depending upon the interaction of the epidemiological triad [33, 34]. Available reports suggest that 95% of patients with TB live in the low- and middle-income countries and more than 70% of patients with DM also live in the same countries, especially in South East Asia. Bangladesh, the nation with a high number of TB cases in the world, is also undergoing epidemic growth in DM rates. The estimated prevalence of DM in Bangladesh in 2012 was 5.5 million and this is projected to increase to 11.1 million by 2025 [27]. Tuberculosis also continues to be an important contributor to overall disease burden and death in Bangladesh: with an estimated 300,000 new cases and 65,000 deaths each year, Bangladesh ranks 6th in the world in tuberculosis disease burden.

The association between DM and TB is well documented and there is substantial evidence to support the fact that diabetes is an important risk factor for TB [19]. Conversely, it is also possible that TB can induce glucose intolerance and also deteriorate glycemic control in subjects with diabetes [19, 20]. Although the prevalence rates of TB and diabetes in Bangladesh are high, little is known about the association between the two diseases in the country. As diabetes may impair the response to TB treatment, it is very important to assess to what extent it is present in Bangladeshi TB patients in order to ensure their proper management. To the best of

our knowledge there is lack of appropriate studies on the prevalence of diabetes in our population of patients with tuberculosis. In the above context, question arises as to " What is the magnitude of the Diabetes among TB cases? What are the risk factors?"

This would be the attempt to estimate the prevalence of diabetes among TB patients in Bangladesh. In the above context, we are attempting to carry out an epidemiological study to determine the prevalence of diabetes in our population of patients with tuberculosis attending tertiary care hospital and to identify other risk factors associated with DM among tuberculosis patients.

1.3 Research Question

1. What is the prevalence of diabetes mellitus among Tuberculosis patients?

2. Does risk of DM vary with type 0f TB ie. PTB & EPTB?

3. Which factor(s) influence TB patients to have DM?

1.4 Objectives of the study

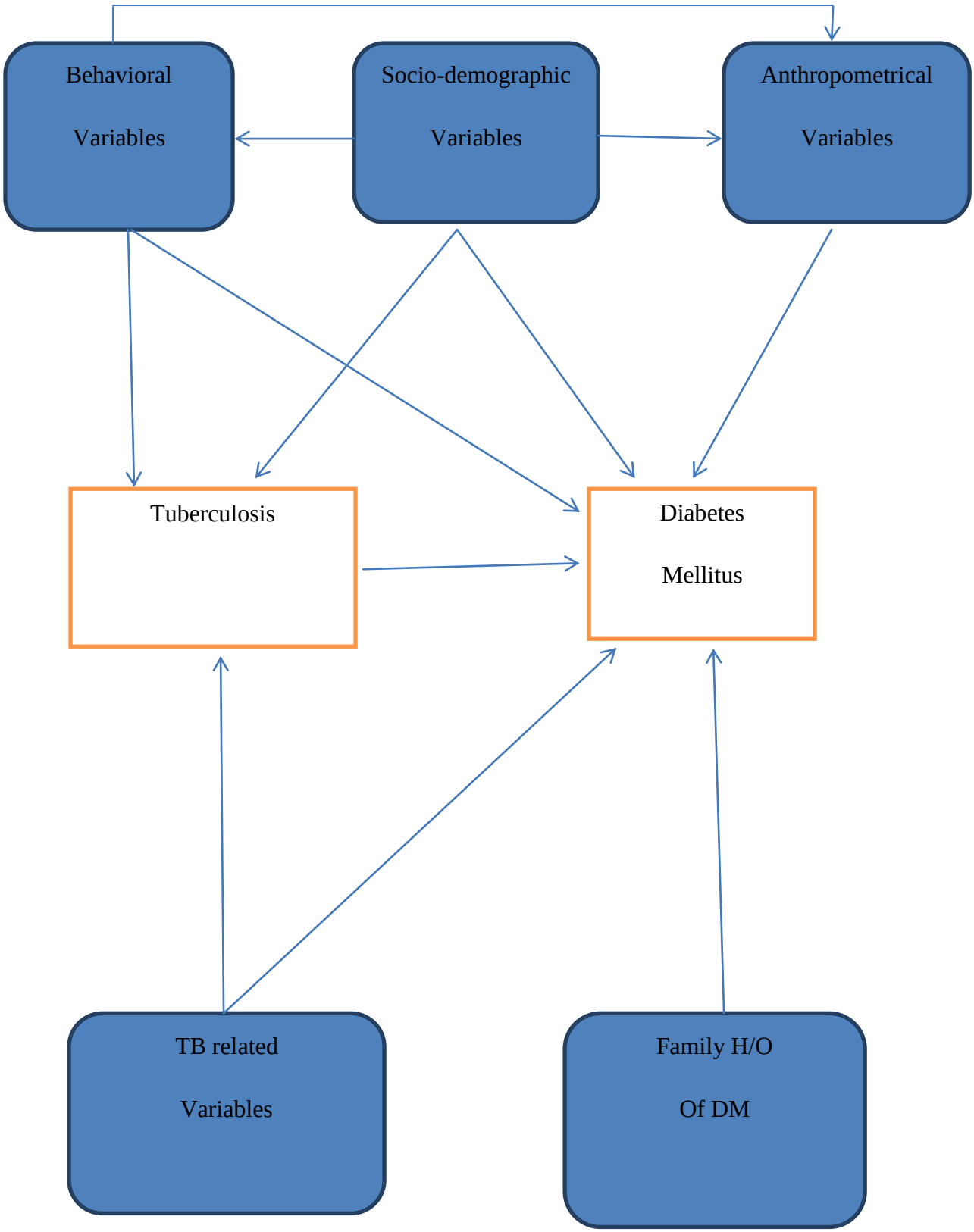
1.4.1 General Objectives

To find out the prevalence of diabetes mellitus and its associated factors among tuberculosis patients.

1.4.2 Specific Objectives

- To find out the proportion of TB patients suffering from diabetes mellitus.
- To compare the proportion of diabetes mellitus among pulmonary tuberculosis and extra-pulmonary tuberculosis patients.
- To find association between diabetes mellitus and tuberculosis.
- To identify the factors influencing TB patients to have diabetes mellitus.

1.5 **Conceptual framework of association of TB and DM:**



1.6 List of key variables

Socio-demographic Variables-

- Age in years grouped as into

  i.< 25

  ii.25-34

  iii.35-44

  iv.45 & above
- Sex
- Occupation grouped as into

  i.Service

  ii.Business

  iii.Housewife

  iv.Day laborer

  v.Others
- Educational status
- Monthly family income
- Family size
- Type of residence

Anthropometrical variables-

- Height
- Weight
- Waist Circumference

Behavioral variables-

- Smoking
- Other forms of tobacco use

Clinical variables-

- Blood pressure

TB related variables -

- Type of TB
- Category of treatment
- Family history of TB
- Place of taking anti TB drugs
- Adherence to treatment

DM related variables

(for those patients who already diagnosed with diabetes)

- Duration of diabetes
- Type of treatment
- Family history of DM

Biochemical variables-

- OGTT(oral glucose tolerance test)

1.7 Operational Definitions

i. Diabetes mellitus

Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period[35] Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications[36].

In my study, I have taken study participants as diabetes mellitus whose fasting blood sugar was ≥ 7.0 mmol/l and 2 hours after glucose ≥ 11.1 mmol/l.

ii.Pulmonary tuberculosis

Most commonly tuberculosis infection involves lung (in about 90% of cases)[37,38], which is known as pulmonary tuberculosis. Symptoms may include chest pain and a prolonged cough producing sputum. About 25% of people may not have any symptoms (i.e. they remain "asymptomatic")[37].

iii. Extra pulmonary tuberculosis

When Tuberculosis infection occurs other than lungs it is termed as extra pulmonary tuberculosis.

iv. Tertiary care hospital

A **tertiary referral hospital** (also called **tertiary hospital**, **tertiary referral center**, or **tertiary care center**, or tertiary center) is a hospital that provides tertiary care, which is health care from specialists in a large hospital after referral from primary care and secondary care. Beyond that general definition, there is no precise narrower or more formal definition, but tertiary centers usually include the following:

- a major hospital that usually has a full complement of services including pediatrics, obstetrics, general medicine, gynecology, various branches of surgery and psychiatry or
- a specialty hospital dedicated to specific sub-specialty care (pediatric centers, Oncology centers, psychiatric hospitals). Patients will often be referred from smaller hospitals to a tertiary hospital for major operations, consultations with sub-specialists and when sophisticated intensive care facilities are required.

v. Impaired fasting glucose

Impaired fasting glucose (IFG), more commonly known as **pre-diabetes** refers to a condition in which the fasting blood glucose level is consistently elevated above what is considered normal levels.

WHO criteria: fasting plasma glucose level from 6.1 mmol/l (110 mg/dL) to 6.9 mmol/l (125 mg/dL)[39,40,41,42].

vi. Impaired glucose tolerance

Impaired glucose tolerance (IGT) is a pre-diabetic state of hyperglycemia that is associated with insulin resistance and increased risk of cardiovascular pathology.

According to the criteria of the World Health Organization and the American Diabetes Association, impaired glucose tolerance is defined as:

- two-hour glucose levels of 140 to 199 mg per dL (7.8 to 11.0 mmol/l) on the 75-g oral glucose tolerance test. A patient is said to be under the condition of IGT when he/she has an intermediately raised glucose level after 2 hours, but less than would qualify for type 2 diabetes mellitus. The fasting glucose may be either normal or mildly elevated[43,44,45].

1.8 Limitations of the study

The limitation of the study was that plasma glucose tests were done at two hospitals in two different machines as it was more convenient. So some machine error might present there.

Although the study adjusted for some of the confounding factors, the role of residual confounding factors for the association between DM and TB cannot be ruled out. In addition, due to the cross sectional nature of the study, the temporality between the TB and DM could not be ascertained.

Another limitation of this study include the fact that the study was conducted within a hospital setting and may therefore not truly represent the true prevalence of the conditions in the community.

CHATER 2: LITERATURE REVIEW

2.1 Introduction

2.2 Definition of Diabetes mellitus

2.3 Signs and symptoms of DM

2.4 Complications of DM

2.5: Types of DM

2.6: Diagnosis of DM

2.7: Prevention of DM

2.8: Management of DM

2.9: Epidemiology of DM

2.10 Pulmonary tuberculosis

2.11 Extra pulmonary tuberculosis

2.12 TB Symptoms

2.13 Causes of TB

2.14 Diagnosis of TB

2.15 Treatment and prevention of TB

2.16 Risk factors for TB

2.17 Public health Scenario of TB

2.18 Epidemiology

2.19 Growing double burden of tuberculosis and diabetes mellitus

2.20 Treatment and screening of TB DM

2.21 Disease management

2.1 Introduction

People with diabetes have more risk to develop tuberculosis (TB) than those without diabetes. Globally every year tuberculosis, an infectious disease affects 9.4 million people and kills 1.7 million[46].

TB is a major public health problem in many low- and middle-income countries, also with rapidly rising number of people with diabetes . Regions, such as Africa and Asia that are most heavily affected by tuberculosis are also those that have some of the highest numbers of people with diabetes , and will experience the biggest increases by 2030.

2.2 Definition of Diabetes mellitus

Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period[35] Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications[36] Acute complications include diabetic ketoacidosis and nonketotic hyperosmolar coma[47] Serious long-term complications include cardiovascular disease, stroke, kidney failure, foot ulcers and damage to the eyes[36]

2.3 Signs and symptoms of DM

polydipsia (increased thirst), and polyphagia (increased hunger)[48] Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes.

Several other signs and symptoms may develop on the onset of diabetes, although they are not specific to the disease. In addition to the known ones above, they include blurry vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermatomes.

2.4 Complications of DM

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20), but may be the first symptom in those who have otherwise not diagnosed before.

Among the long-term complications, major one is relates to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease[49] and about 75% of deaths in diabetics are due to coronary artery disease[50] Other "macro vascular" diseases are stroke, and peripheral vascular disease.

The primary micro vascular complications of diabetes include damage to the eyes, kidneys, and nerves[51] Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and blindness[51] Damage to the kidneys, known as diabetic nephropathy, can lead to tissue scarring, urine protein loss, and eventually chronic kidney disease, sometimes requiring dialysis or kidney transplant[51] Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes[51] The symptoms can include numbness, tingling, pain, and altered pain sensation, which can lead to damage to the skin. Diabetes-related foot problems (such as diabetic foot ulcers) may occur, and can be difficult to treat, occasionally requiring amputation. Additionally, proximal diabetic neuropathy causes painful muscle wasting and weakness.

There is a link between cognitive deficit and diabetes. Compared to those without diabetes, those with the disease have a 1.2 to 1.5-fold greater rate of decline in cognitive function[52]

2.5 Types of DM

There are mainly three types of diabetes namely as follows

- **Type 1 DM** results from the body's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown[36] .

- **Type 2 DM** begins with insulin resistance, a condition in which cells fail to respond to insulin properly [36] This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The primary cause is excessive body weight and not enough exercise [36]
- **Gestational diabetes**, is the third main form and occurs when pregnant women without a previous history of diabetes develop a high blood glucose level [36]

Other types

- Prediabetes indicates a condition that occurs when a person's blood glucose levels are higher than normal but not high enough for a diagnosis of type 2 DM. Many people destined to develop type 2 DM spend many years in a state of prediabetes.
- Latent autoimmune diabetes of adults (LADA) is a condition in which type 1 DM develops in adults. Adults with LADA are frequently initially misdiagnosed as having type 2 DM, based on age rather than etiology
- Other forms of diabetes mellitus include congenital diabetes, which is due to genetic defects of insulin secretion, cystic fibrosis-related diabetes, steroid diabetes induced by high doses of glucocorticoids, and several forms of monogenic diabetes.

2.6: Diagnosis of DM

Glycated hemoglobin and Glucose tolerance test
WHO diabetes diagnostic criteria edit[53]

Condition	**2 hour glucose**	**Fasting glucose**	**HbA_{1c}**	
Unit	mmol/l(mg/dl)	mmol/l(mg/dl)	mmol/mol	DCCT %
Normal	<7.8 (<140)	<6.1 (<110)	<42	<6.0
Impaired fasting glycaemia	<7.8 (<140)	≥ 6.1(≥110) &<7.0(<126)	42-46	6.0–6.4
Impaired glucose tolerance	≥7.8 (≥140)	<7.0 (<126)	42-46	6.0–6.4
Diabetes mellitus	≥11.1 (≥200)	≥7.0 (≥126)	≥48	≥6.5

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following:[54]

- Fasting plasma glucose level ≥ 7.0 mmol/l (126 mg/dl)
- Plasma glucose ≥ 11.1 mmol/l (200 mg/dl) two hours after a 75 g oral glucose load as in a glucose tolerance test
- Symptoms of hyperglycemia and casual plasma glucose ≥ 11.1 mmol/l (200 mg/dl)
- Glycated hemoglobin (HbA_{1C}) ≥ 48 mmol/mol (≥ 6.5 DCCT %)[55]

According to the World Health Organization people with fasting glucose levels from 6.1 to 6.9 mmol/l (110 to 125 mg/dl) are considered to have impaired fasting glucose [55]. people with plasma glucose at or above 7.8 mmol/l (140 mg/dl), but not over 11.1 mmol/l (200 mg/dl), two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance. Of these two prediabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus, as well as cardiovascular disease [56].

2.7 Prevention of DM

There is no known preventive measure for type 1diabetes [36]. A person having normal body weight, physical exercise, and following a healthful diet can often prevent type 2 diabetes [36]. Dietary changes known to be effective in helping to prevent diabetes include a diet rich in whole grains and fiber, and choosing good fats, such as polyunsaturated fats found in nuts, vegetable oils, and fish [57]. Limiting sugary beverages and eating less red meat and other sources of saturated fat can also help in the prevention of diabetes [57]. Active smoking is also associated with an increased risk of diabetes, so smoking cessation can be an important preventive measure as well [58].

2.8 Management of DM

Diabetes mellitus is a chronic disease, for which there is no known cure. Management concentrates on keeping blood sugar levels as close to normal ("euglycemia") as possible, without causing hypoglycemia. This can usually be accomplished with a

healthful diet, exercise, and use of appropriate medications (insulin in the case of type 1 diabetes; oral medications, as well as possibly insulin, in type 2 diabetes).

2.9 Epidemiology of DM

At 2013, 382 million people have diabetes worldwide [59]. Type 2 makes up about 90% of the cases [60,61] This is equal to 8.3% of the adult population [52] with equal rates in both women and men [61].

In 2014, the International Diabetes Federation (IDF) estimated that diabetes resulted in 4.9 million deaths [62]. The World Health Organization (WHO) estimated that diabetes resulted in 1.5 million deaths in 2012, making it the 8th leading cause of death [63]. The discrepancy between the two estimates is due to the fact that cardiovascular diseases are often the cause of death for individuals with diabetes; the IDF uses modelling to estimate the amount of deaths that could be attributed to diabetes [64]. More than 80% of diabetic deaths occur in low and middle-income countries [65].

Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in more developed countries. The greatest increase in rates was expected to occur in Asia and Africa, where most people with diabetes will probably live in 2030[66]. The increase in rates in developing countries follows the trend of urbanization and lifestyle changes, including a "Western-style" diet. This has suggested an environmental (i.e., dietary) effect, but there is little understanding of the mechanism(s) at present [67].

2.9 Definition of Tuberculosis

Tuberculosis, **MTB**, or **TB** (short for *tubercle bacillus*), in the past also called **phthisis**, **phthisis pulmonalis**, or **consumption**, is a widespread, and in many cases fatal, infectious disease caused by various strains of mycobacteria, usually *Mycobacterium tuberculosis* [68] Tuberculosis typically attacks the lungs, but can also affect other parts of the body. It is spread through the air when people who have an active TB infection cough, sneeze, or otherwise transmit respiratory fluids through the air [69]. Most infections do not have symptoms, known as latent tuberculosis.

About one in ten latent infections eventually progresses to active disease which, if left untreated, kills more than 50% of those so infected.

2.10 Pulmonary tuberculosis

Most commonly tuberculosis infection involves lung (in about 90% of cases) [37,38], which is known as pulmonary tuberculosis. Symptoms may include chest pain and a prolonged cough producing sputum. About 25% of people may not have any symptoms (i.e. they remain "asymptomatic") [37]. Occasionally, people may cough up blood in small amounts, and in very rare cases, the infection may erode into the pulmonary artery or a Rasmussen's aneurysm, resulting in massive bleeding[70,71] Tuberculosis may become a chronic illness and cause extensive scarring in the upper lobes of the lungs. The upper lung lobes are more frequently affected by tuberculosis than the lower ones [70]. The reason for this difference is not entirely clear [68]. It may be due either to better air flow [68], or to poor lymph drainage within the upper lungs [72] .

2.11 Extrapulmonary tuberculosis

When Tuberculosis infection occurs other than lungs it is termed as extra pulmonary tuberculosis.

In 15–20% of active cases, the infection spreads outside the lungs[73]. These are collectively denoted as "extrapulmonary tuberculosis"[74]. Extrapulmonary TB occurs more commonly in immunosuppressed persons and young children. In those with HIV, this occurs in more than 50% of cases [74]. Notable extrapulmonary infection sites include the pleura (in tuberculous pleurisy), the central nervous system (in tuberculousmeningitis), the lymphatic system (in scrofula of the neck), the genitourinary system (in urogenital tuberculosis), and the bones and joints (in Pott disease of the spine), among others. When it spreads to the bones, it is also known as "osseous tuberculosis"[75], a form of osteomyelitis[68]. Sometimes, bursting of a tubercular abscess through skin results in tuberculousulcer [76]. An ulcer originating from nearby infected lymph nodes is painless, slowly enlarging and has an appearance of "wash leather"[77]. A potentially more serious, widespread form of TB is called

"disseminated" TB, commonly known as miliarytuberculosis[70]. Miliary TB makes up about 10% of extrapulmonarycases[78].

2.12 TB Symptoms

Symptoms of TB disease include:

- a bad cough that lasts 3 weeks or longer
- pain in the chest
- coughing up blood or sputum
- weakness or fatigue
- weight loss
- no appetite
- chills
- fever
- sweating at night

2.13 Causes of TB

The main cause of TB is *Mycobacterium tuberculosis*, a small, aerobic, nonmotile bacillus[70].

2.14 Diagnosis of TB

Active tuberculosis

Diagnosing active tuberculosis based merely on signs and symptoms is difficult[79], as is diagnosing the disease in those who are immunosuppressed[80]. A diagnosis of TB should, however, be considered in those with signs of lung disease or constitutional symptoms lasting longer than two weeks [80]. A chest X-ray and multiple sputum cultures for acid-fast bacilli are typically part of the initial evaluation [80]. Interferon-γ release assays and tuberculin skin tests are of little use in the developing world [81,82]. IGRA have similar limitations in those with HIV [82].

A definitive diagnosis of TB is made by identifying *M. tuberculosis* in a clinical sample (e.g., sputum, pus, or a tissue biopsy). However, the difficult culture process

for this slow-growing organism can take two to six weeks for blood or sputum culture [83]. Thus, treatment is often begun before cultures are confirmed [84].

Nucleic acid amplification tests and adenosine deaminase testing may allow rapid diagnosis of TB [79]. These tests, however, are not routinely recommended, as they rarely alter how a person is treated [84]. Blood tests to detect antibodies are not specific or sensitive, so they are not recommended [85].

Latent tuberculosis

The Mantoux tuberculin skin test is often used to screen people at high risk for TB [80]. Those who have been previously immunized may have a false-positive test result [86]. The test may be falsely negative in those with sarcoidosis, Hodgkin's lymphoma, malnutrition, or most notably, in those who truly do have active tuberculosis[68].Interferon gamma release assays (IGRAs), on a blood sample, are recommended in those who are positive to the Mantoux test [84]. These are not affected by immunization or most environmental mycobacteria, so they generate fewer false-positive results [87]. However, they are affected by *M. szulgai*, *M. marinum*, and *M. kansasii* [88]. IGRAs may increase sensitivity when used in addition to the skin test, but may be less sensitive than the skin test when used alone[89].

2.15 Treatment and prevention of TB

Treatment is difficult and requires administration of multiple antibiotics over a long period of time. Social contacts are also screened and treated if necessary. Antibiotic resistance is a growing problem in multiple drug-resistant tuberculosis (MDR-TB) infections. Prevention relies on screening programs and vaccination with the bacillus Calmette-Guérin vaccine.

2.16 Risk factors for TB

A number of factors make people more susceptible to TB infections. The most important risk factor globally is HIV; 13% of all people with TB are infected by the virus [90]. This is a particular problem in sub-Saharan Africa, where rates of HIV are high [91,92]. Of people without HIV who are infected with tuberculosis, about 5–10%

develop active disease during their lifetimes [93], in contrast, 30% of those co infected with HIV develop the active disease[93].

Tuberculosis is closely linked to both overcrowding and malnutrition, making it one of the principal diseases of poverty [37]. Those at high risk thus include: people who inject illicit drugs, inhabitants and employees of locales where vulnerable people gather (e.g. prisons and homeless shelters), medically underprivileged and resource-poor communities, high-risk ethnic minorities, children in close contact with high-risk category patients, and health-care providers serving these patients [94].

Chronic lung disease is another significant risk factor. Silicosis increases the risk about 30-fold [95]. Those who smoke cigarettes have nearly twice the risk of TB compared to nonsmokers [96].

Other disease states can also increase the risk of developing tuberculosis. These include alcoholism [37] and diabetes mellitus (three-fold increase) [97].

Certain medications, such as corticosteroids and infliximab (an anti-αTNF monoclonal antibody), are becoming increasingly important risk factors, especially in the developed world [37].

2.17 Public health Scenario of TB

The World Health Organization declared TB a "global health emergency" in 1993[37], and in 2006, the Stop TB Partnership developed a Global Plan to Stop Tuberculosis that aims to save 14 million lives between its launch and 2015[98]. A number of targets they have set are not likely to be achieved by 2015, mostly due to the increase in HIV-associated tuberculosis and the emergence of multiple drug-resistant tuberculosis [37]. A tuberculosis classification system developed by the American Thoracic Society is used primarily in public health programs [99].

2.18 Epidemiology

In 2007, the prevalence of TB per 100,000 people was highest in sub-Saharan Africa, and was also relatively high in Asia [100].

Roughly one-third of the world's population has been infected with *M. tuberculosis* [101], with new infections occurring in about 1% of the population each year [102]. However, most infections with *M. tuberculosis* do not cause TB disease [103], and 90–95% of infections remain asymptomatic [104]. In 2012, an estimated 8.6 million chronic cases were active [105]. In 2010, 8.8 million new cases of TB were diagnosed, and 1.20–1.45 million deaths occurred, most of these occurring in developing countries [98,49] Of these 1.45 million deaths, about 0.35 million occur in those also infected with HIV[106].

Tuberculosis is the second-most common cause of death from infectious disease (after those due to HIV/AIDS) [70]. The total number of tuberculosis cases has been decreasing since 2005, while new cases have decreased since 2002[24]. China has achieved particularly dramatic progress, with about an 80% reduction in its TB mortality rate between 1990 and 2010[106]. The number of new cases has declined by 17% between 2004–2014 [107]. Tuberculosis is more common in developing countries; about 80% of the population in many Asian and African countries test positive in tuberculin tests, while only 5–10% of the US population test positive [68]. Hopes of totally controlling the disease have been dramatically dampened because of a number of factors, including the difficulty of developing an effective vaccine, the expensive and time-consuming diagnostic process, the necessity of many months of treatment, the increase in HIV-associated tuberculosis, and the emergence of drug-resistant cases in the 1980s [37].

In 2007, the country with the highest estimated incidence rate of TB was Swaziland, with 1,200 cases per 100,000 people. India had the largest total incidence, with an estimated 2.0 million new cases [108]. In developed countries, tuberculosis is less common and is found mainly in urban areas. Rates per 100,000 people in different areas of the world were: globally 178, Africa 332, the Americas 36, Eastern Mediterranean 173, Europe 63, Southeast Asia 278, and Western Pacific 139 in 2010[106]. In Canada and Australia, tuberculosis is many times more common among the aboriginal peoples, especially in remote areas [109,110,111]. In the United States Native Americans have a fivefold greater mortality from TB [112], and racial and ethnic minorities accounted for 84% of all reported TB cases[113].

The rates of TB varies with age. In Africa, it primarily affects adolescents and young adults[113]. However, in countries where incidence rates have declined dramatically (such as the United States), TB is mainly a disease of older people and the immunocompromised (risk factors are listed above)[68,114]. Worldwide, 22 "high-burden" states or countries together experience 80% of cases as well as 83% of deaths [115].

2.19 Growing double burden of tuberculosis and diabetes mellitus

The growing prevalence of diabetes poses a challenge for TB control as uncontrolled diabetes leads to a greater risk of developing TB. A recent study showed that countries that saw an increase in diabetes prevalence also had a significant increase in the number of people with TB [116]. This suggests that increasing diabetes prevalence could make attainment of the Millennium Development Goals on tuberculosis more difficult to achieve.

These trends reflect the important links between the diseases. Several studies have looked at the association between diabetes and tuberculosis in developed countries [117] and found that people with diabetes are around 2.5 times more likely to develop tuberculosis [118]. These findings were also true of developing regions including Africa where one study found that the prevalence (%) of diabetes was twice as high in people with tuberculosis than in people without tuberculosis [116].

Map 4.2 shows estimates of the proportion of tuberculosis attributable to diabetes. In countries where the burden of diabetes is relatively high, for example Mexico, Egypt, Saudi Arabia and the United States of America, it is a significant contributor to the number of cases of tuberculosis. However, where rates of tuberculosis are high and diabetes is relatively low, diabetes contributes to a smaller proportion of the TB burden.

2.20 Treatment and screening of TB DM

Not only does diabetes contribute to a person's risk of developing tuberculosis, but it also makes it more difficult to treat those who have both diseases. A review looking at

the impact of diabetes on tuberculosis treatment found that people with diabetes are more likely to fail treatment and more likely to die during treatment compared to those without diabetes [119].

The link between tuberculosis and diabetes requires interventions that address both diseases. For example, screening for tuberculosis in people with diabetes and screening for diabetes in people with tuberculosis could offer opportunities to increase detection and prevent diabetes or tuberculosis-related complications.

A recent review showed that when people with diabetes were checked for tuberculosis, more people were found to have previously undiagnosed TB than in the general population. This was also true of people who had tuberculosis, and were checked for diabetes, in which many more were found to have previously undiagnosed diabetes than in the general population [120].

People with diabetes who have good glucose control are less likely to develop tuberculosis [121,122]. In addition, tuberculosis treatment leads to decreasing blood glucose levels [120], suggesting that integrated management of tuberculosis in people with high blood glucose could lead to better diabetes control.

2.21 Disease management

Effective management of both diseases requires the same elements including early detection, providing guided standard treatment, and having an effective drug supply. The same principles can be applied to both diseases and help many people affected by tuberculosis and diabetes. Setting standards on these simple priorities could lead to effective detection and treatment for diabetes as has been seen in global tuberculosis control.

CHAPTER 3: METHODOLOGY

3.1. Study Design

3.2. Study area

3.3. Study period

3.4. Study population

3.5 Inclusion criteria

3.6 Exclusion criterion

3.7 Sampling technique and sample size

3.8 Data collection tools and technique

3.9 Data processing

3.10 Ethical consideration

3.1. Study Design

A **cross sectional study** was conducted to see the prevalence of diabetes mellitus among tuberculosis patients and as well as the factors influence tubercusis patients to have diabetes.

3.2. Study place

The study was conducted in two tertiary care hospitals which are specialized for Tuberculosis treatment. The institutes were as follows :

i. National Institute of Diseases of the Chest and Hospital(NIDCH), Mohakhali, Dhaka

National Institute of Diseases of the Chest and Hospital (NIDCH) is a state supported research institute and hospital in Bangladesh. It was established in 1955 as *TB Hospital*. In 1962 it was upgraded as *National Chest Diseases Institute*. The hospital has 600 functioning bed, proposed bed 660.The institute runs postgraduate training for the students of Diploma in Tuberculosis and Chest Diseases (DTCD), Doctor of Medicine (MD, Chest), FCPS, MS. It also provides undergraduate teaching in tuberculosis for the students of different medical colleges.The objectives of the institute are :

- To provide diagnosis and treatment facilities for tuberculosis and chest diseases.
- To conduct postgraduate courses and training facilities for DTCD, MD (Chest), MS (Thoracic Surgery), FCPS (Pulmonary), FCPS (Thoracic Surgery).
- To provide specialized training facilities for the chest specialists, nurses, medical technologists and field workers.
- To conduct research activities in the field of chest diseases.
- To provide surgical treatment of chest diseases.
- To provide and co-ordinate management of the avian influenza, pandemic H1N1.

ii. National Centre for Tuberculosis & Research (NCTBR),Shamoli, Dhaka

It is a 250 bed specialized tuberculosis government hospital. The hospital provides outdoor services and DOTs facilities through their organization.Indoor services not yet started.

3.3. Study period

Study was conducted for 1 year time from 1st june 2014 to 31st may, 2015.

3.4. Study population

The study population consisted of all confirmed consecutive TB patients undergoing treatment at inpatient departments as well as at DOTs centers of the concerned hospitals during the study period.

3.5. Inclusion criteria

- Both pulmonary and extra-pulmonary TB cases under DOTs register for treatment and also inpatients {PTB cases confirmed with sputum smear for acid fast bacilli(AFB) and X-ray, and extra pulmonary cases confirmed with culture of specimen from the site and or histological evidence}.
- Age: 18 years and above.
- Sex: both male and female
- Physically able and willing to participate

3.6.Exclusion criterion

- Very sick or very old patients

3.7. Sampling technique and sample size

A total of 350 TB patients, among them 175 pulmonary TB and 175 extra pulmonary TB patients was investigated from inpatients department and DOTs center.

1. Prevalence of DM among TB patients:

For prevalence of diabetes mellitus among TB patients sample size was calculated using the formula: $n=\frac{z^2q}{r^2p}$

Where , z=1.96(95% confidence interval)

p=prevalence of diabetes among tuberculosis patient: 25.3% [117]

q=(100-25.3)% =74.7%

r= relative error 25% of prevalence

Sample size was 290

2.For comparing proportion of PTB and EPTB:

For comparison among pulmonary and extra- pulmonary patients sample size calculation was done by

$n= \{z_{1-\alpha/2}\sqrt{[2p(1-p)]}+z_{1-\beta}\sqrt{[p_1(1-p_1)+p_2(1-p_2)]}\}^2/(p_1-p_2)^2$

Where,

Prevalence of diabetes in pulmonary TB patients (p_1)=27.2% ; [118]

Prevalence of diabetes in extra pulmonary TB patients (p_2)=14.8%; [118]

z = 1.96 (95% confidence interval)

power 80%

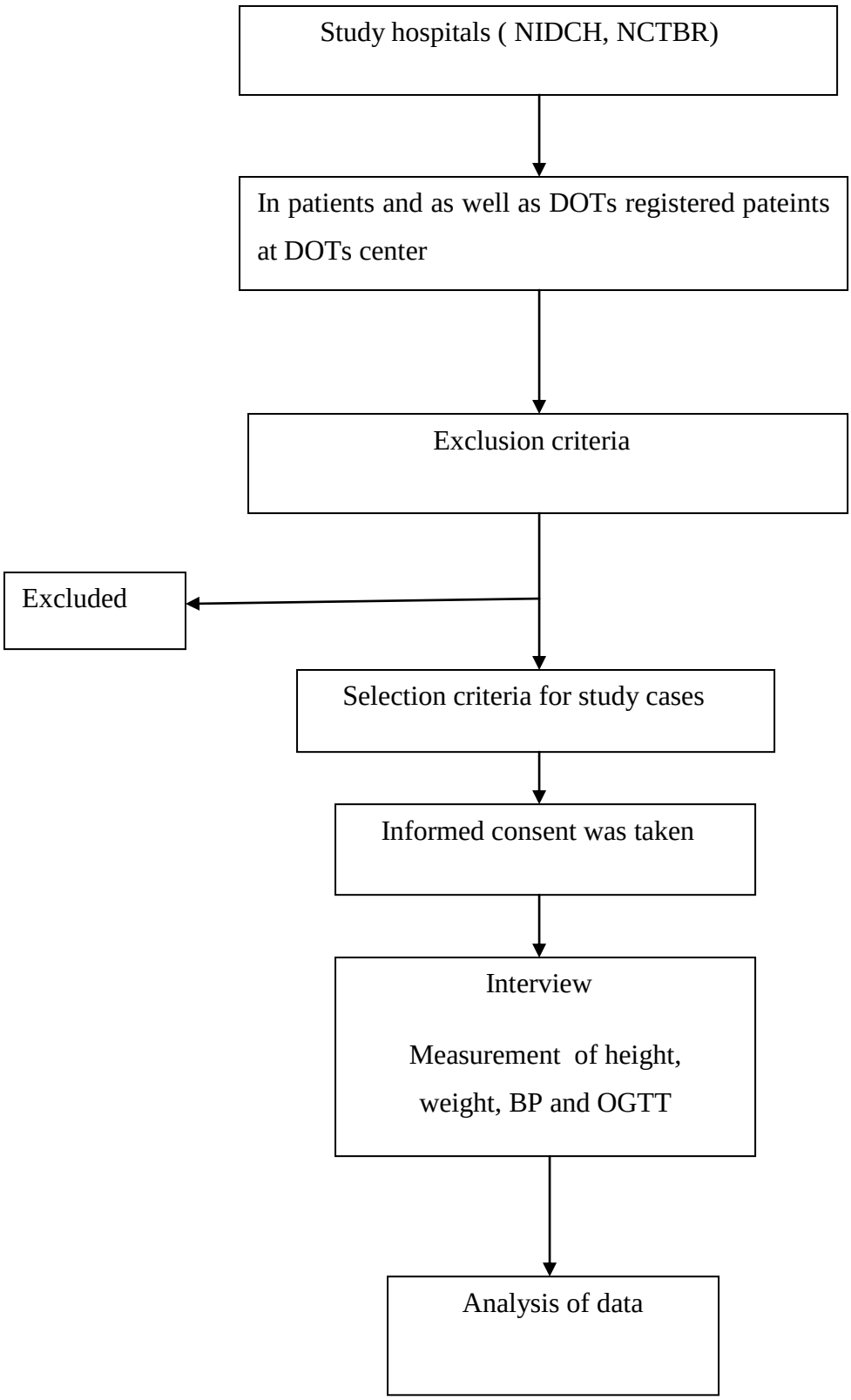
The sample size was 104 in each pulmonary and extra-pulmonary group.

Finally the sample size was 175 for each pulmonary TB and extra pulmonary TB for the sub population – male /female and, hospital registered inpatient and DOTs registered. Final sample size was arrived at using adjustment for 10% nonresponse rate.

The samples were selected purposively from all consecutives patients who fulfilled the inclusion criteria of the study attending the hospital during study period.

Figure: 1

Sample technique and patient selection flowchart:



3.8. Data collection tools and technique

After receiving informed consent, data was collected by three different phases. All the participants was invited to finish all of these three phases.

3.8.1 Interviewer administered interview schedule

Separate semi-structured pre-tested interview schedule and check list was used for interviewing the subjects to collect information regarding socio-demographics and habitual risk factors like smoking and other forms of tobacco use; family history of TB and DM, educational and occupational status, and monthly income. Type of TB, category of treatment were also recorded. Patients already diagnosed with diabetes were interviewed to elicit and record information on duration of diabetes, type of treatment, and type of DM and family history of DM.

3.8.2 Anthropometric and clinical parameters

A trained investigator recorded anthropometric (H/W and WC) measurement by standard procedure. BMI (weight in kg/ height in m^2) was calculated. Two blood pressure measurements was taken using sphygmomanometer with the subject in sitting posture, and average of the two readings was recorded.

Anthropometric measurements such as weight, height, were taken from the respondents. Body weight in light cloths was measured to the nearest 0.1 kg using a Soehenle mechanical weighing scale(Soehenle-Waagen GmbH &Co.KG,Wilhelm-Soehenle-Strabe 2,D-71540 Murrhard/Germany) and the height was taken to the nearest 0.5 cm using a steel tape with subjects, standing upright on a flat surface without shoes, keeping feet together and knee straight. Body Mass Index(BMI) was calculated as the ratio of weight in kilograms over height in meters squared,[weight/height (kg/m^2)].

The International Classification of adult underweight, normal, overweight and obesity according to BMI

Classification	BMI(kg/m^2)	
	Principal cut-off points	**Additional cut-off points**
Underweight	**<18.50**	**<18.50**
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	**18.50 - 24.99**	**18.50 - 22.99**
		23.00 - 24.99
Overweight	**≥25.00**	**≥25.00**
Pre-obese	25.00 - 29.99	25.00 - 27.49
		27.50 - 29.99
Obese	**≥30.00**	**≥30.00**
Obese class I	30.00 - 34.99	30.00 - 32.49
		32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49
		37.50 - 39.99
Obese class III	≥40.00	≥40.00

Source: Adapted from WHO,1995, WHO, 2000 and WHO 2004

For waist circumference subjects stood erect with abdomen relaxed, arms at the sides, feet together and their weight equally divided over both legs. The lowest rib margin and the iliac crest in the mid-axillary line was located and marked. Then a tape was placed horizontally midway between the two points to measure waist circumference to the nearest centimeter.

Measurement of blood pressure

Two readings of blood pressure were taken from each respondent by trained data collectors. First measurement was recorded after the respondent has rested for 15 minutes. Second measurement was recorded after at least 3 minutes following the first measurement. Both measurements were taken in upright sitting position on the right arm using normal cuffs for adults fitted with standard sphygmomanometer (Model UA-767,A & D Company Limited, Tokyo, Japan), placing the stethoscope bell lightly over the brachial artery.

3.8.3.Biochemical parameters

Collection of blood samples

Fasting blood was collected between 7.00 – 8.00 am. Venous blood (10 ml) was taken by venipuncture with subject sitting comfortably in a chair in a quiet room . Then the patient was given a mixture of 75g of glucose in 250-300 ml of water and advised to the drink in 5 min. Patient was advised not to smoke, not to take any food and to take rest for 2 hours. Then blood sample was taken 2h after glucose load. Blood sample was poured into test tubes containing sodium fluoride (6 mg/ml of whole blood). After 10-15 minutes blood sample was centrifuged for 1 minutes at 3000 rpm to obtain plasma. Fasting and 2h plasma glucose was measured on the same day.

Analytical methods and lab analysis

- Plasma glucose (fasting and 2 hours after 75g glucose) was measured by Glucose Oxidase (GOD-PAP) method (Randox Laboratories Ltd., UK).

3.9. Data processing

Data was processed with Microsoft office Excel 2010 version and SPSS version 17.0. Data was cleaned, edited and verified daily to exclude any error or inconsistency.

Data analysis

Descriptive statistics like Mean (SD), Median (Range), Percentage etc, was calculated.

Inferential statistics

For association and identification of factors Chi-squared test and logistic regression analysis was used. Odds Ratio (OR) and CI for OR was also calculated to define the nature of relationship.

3.10. Ethical consideration

Ethical approval was obtained from the ethical review committee of Bangladesh University of Health Sciences(BUHS).International ethical guidelines for biomedical research involving human subjects were followed throughout the study(Written informed consent (Annex no) was taken at the time of enrolling the interview. Illiterate participant given their consent with fingerprints. In consent form, the title, aim of study, data collection procedures, required time for data collection, confidentiality and anticipated use of the result of this study was written in plain and simple Bangla and it was briefed to each respondent before data collection. All respondents were informed that they were free to leave or to refuse to take part in this study at any time. The personal information given by the respondents was kept totally confidential. The information given by the respondents were analyzed using code number so that nobody can identify them.

CHAPTER 4: RESULTS

A total 350 diagnosed Tuberculosis patients who were eligible for the study and were interviewed. Among them 175 were Pulmonary tuberculosis patients and 175 were Extra-pulmonary tuberculosis patients.

4.1 Socio-demographic characteristics of the study subjects

Table 1 and table 2 shows the detailed socio-demographic characteristics of the study subjects.

Age and Sex

The mean±SD age of the study subjects was 36.3±12.0 years. Among them 237 were male and 113 were female. Women were comparatively younger than men. The mean age of male was 38±1 years and the mean age of female was 33±1 years; ($p<0.001$). In this study,75 (21.4%) subjects were aged less than 25 years among them 40(16.9%) were male and 35 (31.0%) were female and 124(35.4%) subjects aged 26 to 35 years among which 79 (33.3%) were male and 45(39.8%) were female. Among all participants 70 (20.0%) subjects were aged 36 to 45 years and 49(20.7%) were male participants and 45 (39.8%) were female. Among them 45 and above years subjects were 81 (23.1%); 69 (29.1%) were male and 12 (10.6%) were female.

Gender differentiations

There was no significant gender difference between extra pulmonary and pulmonary subjects (p=0.732). Among EPTB men were 120 (68.6%) and women were 55 (31.4%). Among PTB subjects men were 117 (66.9%) and women were 58 (33.1%).

There was significant difference between mean age of extra pulmonary subjects and pulmonary subjects (35.7±11.1, 36.8±12.9, p<0.004). Among EPTB subjects aged less than 25 years were 36(20.6%), aged 26 to 35 years were 63 (36.0%), aged 36 to 45 years were 40 (22.9%) and aged more than 45 years were 36 (20.6%).Among PTB subjects less 25 years age group was 39 (22.3%) in number, 26 to 35 years age group was 61 (34.9%), 36 to 45 years age group was 30 (17.1%) and more than 45 years age group was 45 (25.7%).

Occupation

Majority of men were employed than women (p<0.001).

EPTB and PTB had significant difference (p<0.002) regarding profession. Among EPTB subjects 56 (32.0%) were service holders while 33 (18.9%) PTB subjects were service holders. 49 (28.0%) EPTB and 34 (19.4%) PTB subjects were involved in business. Among EPTB the number of house wife was 30 (17.1%) while that in PTB was 42 (24.0%). Among EPTB 17 (9.7%) was day laborer and among PTB 25 (14.3%) in number.

Smoking status of the respondents

Among all study participants 146 (41.7%) subjects gave positive history of smoking and other type of tobacco use (battle leaf chewing). Female subjects have less positive smoking and smokeless tobacco history than male subjects [19 (16.8%)vs. 127 (53.6); p<0.001].

Among EPTB participants 61 (34.9%) had positive smoking and tobacco use history, while that in the PTB subjects was 85(48.6%).There was significant difference regarding this issue among EPTB and PTB group(p<0.009).

Family history of DM

Among 350 study participants, 84 (24.0%) subjects had positive family history of Diabetes Mellitus and of whom 60 (25.3%) were male and 24 (21.2%) were female.

There was significant difference between men and women regarding having positive family history of DM; ($p<0.001$). There was no difference regarding positive family history of DM among EPTB and PTB group ($p=0.617$). Among EPTB 44 (25.1%) subjects had positive DM family history and 40 (22.9%) among PTB subjects.

Table 1 Socio-Demographic characteristics of the study subjects (Men vs. Women)

Characteristics	Total (n=350)	Men (n=237)	Women (n=113)	p-value (men vs. women)	x^2 value
Age groups(years)					
Up to 25	75(21.4)	40(53.3)	35(46.7)		
26-35	124(35.4)	79(63.7)	45(36.3)		
36-45	70(20.0)	49(70.0)	21(30.0)		
45 & above	81(23.1)	69(85.2)	12(14.8)		
Mean±SD	36.30±12.09	38±12	33±10		
Occupation					
Service	89(25.4)	66(74.2)	23(25.8)	**0.001**	200.936[a]
Business	83(23.7)	81(97.6)	2(2.4)		
House wife	72(20.6)	-	72(100)		
Day Laborer	42(12.0)	36(85.7)	6(14.3)		
Others(student, farmers, unemployed, etc.)	64(18.3)	54(84.4)	10(15.6)		
Monthly family income(BDT*)					
Median(Range)	15000(2000-80000)				
up to 10000	130(37.1)	96(73.8)	34(26.2)		
10001-15000	78(22.3)	45(57.7)	33(42.3)		
15001-20000	57(16.3)	35(61.4)	22(38.6)		
> 20000	85(24.3)	61(71.8)	24(28.2)		
Smoking status					
Yes	146(41.7)	127(87.0)	19(13.0)	**0.001**	42.555[a]
No	204(58.3)	110(53.9)	94(46.1)		
Family history of DM					
Yes	84(24.0)	60(71.4)	24(28.6)	0.404	0.697[a]
No	266(76.0)	177(66.5)	89(33.5)		

*Results were expressed as number (percentage) and mean±SD) and median range, comparison done by chi-square test for categorical variables, significant at p-value<0.05- *BDT= Bangladeshi Taka*

Table 2 Socio-Demographic characteristics of the study subjects (Extra pulmonary vs. Pulmonary)

Characteristics	Total n=350(%)	Extra Pulmonary n=175(%)	Pulmonary n=175(%)	p-value (EPTB vs. PTB)	x^2 Value
Gender					
Male	237(67.7)	120(50.6)	117(49.4)	0.732	0.118[a]
Female	113(32.3)	55(48.7)	58(51.3)		
Age groups(years)					
≤ 25	75(21.4)	36(48.0)	39(52.0)		
26-35	124(35.4)	63(50.8)	61(49.2)	0.461	2.581[a]
36-45	70(20.0)	40(57.1)	30(42.9)		
≥45	81(23.1)	36(44.4)	45(55.6)		
Mean±SD	*36.30±12.0*	35.78±11.1	36.82±12.9		
Occupation					
Service	89(25.4)	56(62.9)	33(37.1)		
Business	83(23.7)	49(59.0)	34(41.0)		
House wife	72(20.6)	30(41.7)	42(58.3)	**0.002**	17.241[a]
Day laborer	42(12.0)	17(40.5)	25(59.5)		
Others (students, farmers, unemployed, etc..)	64(18.3)	23(35.9)	41(64.1)		
Smoking status					
Yes	146(41.7)	61(41.8)	85(58.2)	**0.009**	6.769[a]
No	204(58.3)	114(55.6)	90(44.1)		
Family history of DM					
Yes	84(24.0)	44(52.4)	40(47.6)	0.617	0.251[a]
No	266(76)	131(49.2)	135(50.8)		

comparison done by chi-squared test for categorical variables, significant at p-value<0.05

Educational status

The educational status of all study subjects showed in detailed in table 3 and table 4.

Total 22 (6.3%) were illiterate and 328 (93.7%) were literate subjects. Comparatively male subjects were more educated [225 (94.9%) vs. 103 (91.2%); p=0.007]. Among educated subjects 316 (90.3%) went through general education system and rest 12 (3.4%) went through madrassa education system. There was significant difference among EPTB and PTB subjects about educational status (p<0.001).Among EPTB 174 (99.4%) was educated and among PTB subjects 154 (88.0%) was educated; of them 167 (95.4%) EPTB subjects went through general education system while 7 (4.0%) went through madrasa education system. Among them, total study years less than 5 years was 32 (18.3%), 6 to 10 years 31 (17.7%), 10 to 15 years 62 (35.%) and more than 15 years 49 (28.0%).

Among PTB subjects 149 (85.1%) went through general education system and 5 (2.9%) through madrasa system. Among them, total study years less than 5 years was 49 (28.0%), 5 to 10 years 35(20.0%), 10 to 15 years 55 (31.4%) and more than 15 years 15 (8.6%).

Table 3 Educational information of the study subjects (Men vs. Women)

Characteristics	Total (n=350)	Men (n=237)	Women (n=113)	p-value (men vs. women)	x^2 Value
Educational status					
Illiterate	22(6.3)	12(5.1)	10(8.8)		
Literate	328(93.7)	225(94.9)	103(91.2)		
System of education(n=328)					
General	316(90.3)	215(90.7)	101(89.4)		
Madrasa	12(3.4)	10(4.2)	2(1.8)	0.172	1.862[a]
Total study Years(n=328)					
1-5	81(23.1)	53(22.4)	28(24.8)		
6-10	66(18.9)	41(17.3)	25(22.1)		
10-15	117(33.4)	86(36.3)	31(27.4)		
>15	64(18.3)	45(19.0)	19(16.8)		

Results were expressed as number (percentage), comparison done by chi-square test, significant at p-value<0.05

Table 4 Educational information of the study subjects (EPTB vs. PTB)

Characteristics	Total (n=350)	Extra pulmonary (n=175)	Pulmonary (n=175)	p- value (EPTB vs. PTB)	x^2 Value
Educational status					
Illiterate	22(6.3)	1(.6)	21(12.0)		
Literate	328(93.7)	174(99.4)	154(88.0)		
System of education(n=328)					
General	316(90.3)	167(95.4)	149(85.1)		
Madrasa	12(3.4)	7(4.0)	5(2.9)	**0.001**	19.401[a]
Total study years(n=328)					
1-5	81(23.1)	32(18.3)	49(28.0)		
6-10	66(18.9)	31(17.7)	35(20.0)		
10-15	117(33.4)	62(35.4)	55(31.4)		
>15	64(18.3)	49(28.0)	15(8.6)		

Results were expressed as number(percentage) and, comparison done by chi-squared test, significant at p-value<0.05

Tuberculosis related all information were showed in table 5 and table 6.

Family history of TB

Among the total participants 92 (26.3%) subjects had positive family history of Tuberculosis and there was difference between male and female subjects($p<.001$). Among them 43 (18.1%) men had positive family history of TB and 49 (43.4%) women had so. Among EPTB subjects 42(24.0%) had positive TB family history and 50 (28.6%) PTB subjects had positive TB family history, there was no significant difference between them ($p=0.331$).

TB Treatment category of the respondents

The proportion of treatment category and type of TB was similar between male and female ($p=0.023$) and ($p=0.732$).

Table 5 Tuberculosis related information of the study subjects (Men vs. Women)

Characteristics	Total (n=350)	Men (n=237)	Women (n=113)	p-value (men vs. women)	x^2 Value
Treatment category					
Category 1	241(68.9)	166(70.0)	75(66.4)	0.023	7.503[a]
Category 2	16(4.6)	15(6.3)	1(.9)		
Category 3	93(26.6)	56(23.6)	37(32.7)		
Family history of TB					
Yes	92(26.3)	43(18.1)	49(43.4)	**0.001**	25.116[a]
No	258(73.7)	194(46.7)	64(24.8)		

Results were expressed as number (percentage),comparison done by chi-square test, significant at p-value<0.05

Table 6 Tuberculosis related information of the study subjects (EPTB vs. PTB)

Characteristics	Total (n=350)	Extra pulmonary (n=175)	Pulmonary (n=175)	p- value (EPTB vs. PTB)	x^2 Value
Family history of TB					
Yes	92(26.3)	42(45.7)	50(50.3)	0.331	0.944[a]
No	258(73.7)	133(51.6)	125(47.4)		
Treatment category					
Cat 1	241(68.9)	166(68.9)	75(31.1)	**0.001**	111.159[a]
Cat 2	16(4.6)	3(18.8)	13(81.3)		
Cat 3	93(26.6)	6(6.5)	87(93.5)		

Results were expressed as number(percentage), comparison done by chi-squared test, significant at p-value<0.05

Table 7 and table 8 showed the anthropometrical and clinical characteristics of the study patients.

BMI

The mean BMI(Kg/m^2) of study subjects was18.8±3.3.There was no significant difference between men and women[18.6±3.1vs. 19.3±3.7; p=0.061].Among total 350 respondents 157 (44.9%) had BMI <18.5(underweight), 178 (50.9%) of the subjects had BMI 18.5-24.99 (normal) and the BMI of 15 (4.3%) was 25-29.99 (overweight).

BMI was significantly differ in EPTB and PTB groups (19.9±3.0, 17.7±3.2, p<0.003).Among EPTB subjects according to BMI 51 (29.1%) were underweight, 115 (65.7%) were normal and 9 (5.1%) were overweight. Among PTB subjects 106 (60.6%) were underweight, 62 (35.4%) were normal and 7 (4.0%) were overweight.

Waist circumference

The mean waist circumference(centimeter) of total subjects was 30.7±4.0and there was no difference between male and female(p=0.212).

Waist circumference was significantly differ in EPTB and PTB groups (32.7±3.8, 28.7±3.2, p<0.002).

Blood pressure

The mean systolic blood pressure (mm of Hg) among EPTB group was 112.7±14.5 and mean diastolic blood pressure (mm of Hg) was 109.5±14.6. The mean systolic blood pressure among PTB was 109.5±14.6 and mean diastolic blood pressure was 70.2±10.7.Among these two groups there was no difference in both systolic blood pressure(p=0.881) and diastolic blood pressure(p=0.133).

Gender difference was not noted in systolic blood pressure (p=0.163) but in diastolic blood pressure there was difference (p<0.001).

Table 7 Anthropometric and clinical characteristics of the study subjects (Men vs. Women)

Characteristics	Total (n=350)	Men (n=237)	Women (n=113)	p- value (men vs. women)	t value
BMI(kg/m²)					
Underweight	157(44.9)	125(52.7)	49(43.4)	0.066	-1.734
Normal	178(50.9)	108(45.6)	52(46.0)		
Overweight	15(4.3)	4(1.7)	11(9.7)		
Obese	-	-	-		
Mean±SD	18.88±3.35	18.66±3.11	19.34±3.77		
Waist Circumference(cm)	30.75±4.097	31±4	30±4	0.212	3.416
Blood Pressure(mm Hg)					
Systolic	111.13±14.6	113.12±13.8	106.95±15.5	0001	3.744
Diastolic	70.93±9.9	72.32±9.2	68.01±10.7	0.001	3.869

Results were expressed as number(percentage) and mean±SD, comparison done by t-test for continuous variables, significant at p-value<0.05

Table 8 Anthropometric and clinical characteristics of the study subjects (Extra pulmonary vs. Pulmonary)

Characteristics	Total (n=350)	Extra pulmonary (n=175)	Pulmonary (n=175)	p-value (EPTB vs. PTB)	t value
BMI(kg/m²)				0.483	-6.674
Underweight	157(44.9)	51(29.1)	106(60.6)		
Normal	177(50.6)	115(65.7)	62(35.4)		
Overweight	16(4.6)	9(5.1)	7(4.0)		
Obese	00	00	00		
Mean±SD	18.88±3.3	19.99±3.0	17.76±3.2		
Waist Circumference(cm)	30.75±4.097	32.74±3.8	28.75±3.2	**0.002**	-10.415
Blood Pressure(mm Hg)					
Systolic	111.13±14.6	112.74±14.5	109.51±14.6	0.881	-2.065
Diastolic	70.93±9.9	71.63±9.0	70.22±10.7	0.133	-1.325

Results were expressed as number(percentage) and mean±SD), , comparison done by t-test for continuous variables, significant at p-value<0.05

Diabetes related information of the TB patients which were taken during interview were detailed in table 9.

Information Of known DM respondents

Among total 350 respondents 52 (14.9%) was known case of diabetes mellitus. Among which 31 (13.1%) were men and 21 (18.6%) were women. Again among 52 known DM respondents 40 (11.4%) had registered diabetic guide book and 30 (8.6%) used insulin and 22 (6.3%) used oral drugs for treatment of DM and all were type 2 DM.There was no type 1 DM patient.

Table 9 Diabetes related information of known DM subjects

Known case of TB	Total (n=350)	Men (n=237)	Women (n=113)
Known case of DM (n=350)	52(14.9)	31(13.1)	21(18.6)
History of having registered diabetic book of known DM respondents(n=52)	40(11.4)	21(21)	19(16.8)
Type of treatment of known DM cases(n=52)			
Insulin	30(8.6)	16(6.8)	14(12.4)
Oral Medication	22(6.3)	15(6.3)	7(6.2)
Type of DM of known DM cases(n=52)			
Type 2	52(14.9)	31(13.1)	21(18.6)

Results were expressed as number(percentage)

4.2 Prevalence of Diabetes and Pre-diabetes among TB patients

Prevalence of diabetes among tuberculosis patients were given in table 10 and prevalence of pre-diabetes in table 11.

Out of 350 TB patients, 70 (20.0%) had prevalence of diabetes and prevalence of diabetes was almost same in men compared to women [19.4 vs. 21.2]. Diabetes was newly detected in 5.9% (n=18) and previously known diabetes was 14.9% (n=52) among all 350 TB patients who were attending a tertiary care hospital. Among TB patients who had diabetes men were 19.4% (n=46) and women were 21.2% (n=24). Among them 13.1% (n=23) Extra-pulmonary TB and 26.9% (n=47) Pulmonary TB patients had diabetes. Diabetes was significantly high among pulmonary TB patients than extra-pulmonary TB patients ($p<0.0001$).The prevalence of pre-diabetes was 28.3% (n=99) in total among all TB patients of whom 67.7% (n=67) were men and 32.3% (n-32) were women. 19.5% (n=34) extra-pulmonary TB and 37.1% (n=65).

The isolated Impaired Fasting Glucose (IFG) was 6.9%(n=24), isolated Impaired Glucose Tolerance(IGT) was 16.9% (n=59) and both IFG and IGT were 4.6% (n=16).There was difference between extra-pulmonary TB and pulmonary TB and also men and women in the different categories of pre-diabetes.

Table 10 Prevalence of diabetes mellitus among TB patients

Variables	Total (350)	Extra-pulmonary (175)	Pulmonary (175)	Men (237)	Women (113)
DM	70(20.0) [16%-24%]	23(13.1) [12%-15%]	47(26.9) [20%-33%]	46(19.4) [14%-24%]	24(21.2) [14%-29%]

Results were expressed as number (percentage), [95% Confidence Interval]

Table 11 Prevalence of pre diabetes among tuberculosis patients

Variables	Total (350)	Extra-pulmonary (175)	Pulmonary (175)	Men (237)	Women (113)
Pre-DM	99(28.3) [23%-33%]	34(19.5) [14%-25%]	65(37.1) [30%-44%]	67(67.7) [62%-74%]	32(32.3) [24%-41%]
IFG	24(6.9) [4%-10%]	14(8.0) [4%-12%]	10(5.7) [2%-9%]	17(7.17) [4%-10%]	7(6.2) [2%-11%]
IGT	59(16.9) [13%-21%]	15(8.6) [4%-13%]	44(25.1) [19%-31%]	37(15.6) [11%-20%]	22(19.5) [12%-27%]
IFG & IGT	16(4.6) [2%-7%]	5(2.9) [.5%-5%]	11(6.3) [3%-10%]	13(5.5) [3%-8%]	3(2.7) [.2%-6%]

Results were expressed as number(percentage)), [95% Confidence Interval]

Table 12 Prevalence of DM, Pre-DM and Non-DM regarding sex difference among tuberculosis patients

Sex group	Characteristics	PTB (n=175)	EPTB (n=175)	Total (n=350)	p value	x^2 value
Male **(237)**	DM	31(26.4)	15(12.5)	46(19.4)		
	Pre-DM	43(36.8)	24(20.0)	67(28.3)		
	Non-DM	43(36.8)	81(67.5)	124(52.3)	**0.001**	22.564[a]
Female **(113)**	DM	16(27.6)	08(14.5)	24(21.2)		
	Pre-DM	22(37.9)	10(18.2)	32(28.3)		
	Non DM	20(34.5)	37(67.3)	57(50.5)	**0.002**	12.166[a]

Results were expressed as number(percentage) and comparison done by chi-squared test, significant at p-value<0.05

Table 13 Prevalence of DM, Pre-DM and Non-DM regarding Occupational difference among tuberculosis patients

Occupational group	Characteristics	PTB (n= 175)	EPTB (n=175)	Total (n=350)	p value	x^2 value
Service	DM	10(30.3)	06(10.7)	16(18.0)		
(89)	Pre-DM	14(42.4)	14(25.0)	28(31.5)	**0.002**	12.062[a]
	Non DM	09(27.3)	36(64.30	45(50.5)		
Business	DM	10(29.4)	06(12.2)	16(19.3)		
(83)	Pre-DM	10(29.4)	09(18.4)	19(22.9)	0.032	6.900[a]
	Non-DM	14(41.2)	34(69.4)	48(57.8)		
House wife	DM	14(33.3)	07(23.3)	21(29.2)		
(72)	Pre-DM	12(28.6)	06(20.0)	18(25.0)	0.297	2.431[a]
	Non-DM	16(38.1)	17(56.7)	33(45.8)		
Day laborer	DM	03(12.0)	00(00)	03((7.1)		
(42)	Pre-DM	09(36.0)	02(11.8)	11(26.2)	0.043	6.302[a]
	Non-DM	13(52.0)	15(88.2)	28(66.7)		
Others(students,farmers,	DM	10(24.4)	04(17.4)	14(21.9)		
Unemployed, etc..)	Pre-DM	20(48.8)	03(13.0)	23(35.9)		
(64)	Non-DM	11(26.8)	16(69.6)	27(42.2)	**0.003**	11.945[a]
Total		41(100)	23(100)	64(100)		

Results were expressed as number(percentage) and comparison done by chi-squared test, significant at p-value<0.05

Table 14 Prevalence of DM, Pre-DM and Non-DM regarding different age group among tuberculosis patients

Age group	Characteristics	PTB (n=175)	EPTB (n=175)	Total (n=350)	P value	x^2 value
< 25	DM	02(5.1)	00(00)	02(2.7)		
	Pre-DM	15(38.5)	05(13.9)	20(26.7)	0.015	8.422[a]
	Non DM	22(56.4)	31(86.1)	53(70.7)		
25-34	DM	10(16.4)	05(7.9)	15(12.1)		
	Pre-DM	28(45.90)	14(22.3)	42(33.9)	**0.002**	12.887[a]
	Non-DM	23(37.7)	44(69.8)	67(54.0)		
35-44	DM	13(43.3)	05(12.5)	18(25.7)		
	Pre-DM	06(20.0)	08(20.0)	14(20.0)	**0.009**	9.340[a]
	Non DM	11(36.7)	27(67.5)	38(54.3)		
45 & above	DM	22(48.9)	13(36.2)	35(43.2)		
	Pre-DM	16(35.5)	07(19.4)	23(28.4)	0.015	8.462[a]
	Non DM	07(15.6)	16(44.4)	23(28.4)		

Results were expressed as number(percentage) and comparison done by chi-squared test, significant at p-value<0.05

Table 15 Prevalence of DM, Pre-DM and Non-DM regarding Educational status among tuberculosis patients

Educational groups	Characteristics	PTB (n=175)	EPTB (n=175)	Total (n=350)	p Value	x^2 value
Literate	DM	39(25.3)	22(12.6)	61(18.6)		
(328)	Pre-DM	58(37.7)	34(19.5)	92(28.0)	**0.001**	31.158[a]
	Non-DM	57(37.0)	118(67.8)	175(53.4)		
Total		154(100)	174(100)	328(100)		
Illiterate	DM	08(38.1)	01(100)	09(40.9)		
(22)	Pre-DM	07(33.3)	00(00)	07(31.8)	0.469	1.513[a]
	Non-DM	06(28.6)	00(00)	06(27.3)		
Total		21(100)	01(100)	22(100)		

Results were expressed as number(percentage) and comparison done by chi-squared test, significant at p-value<0.05

Figure 2: Prevalence of DM among TB Patients

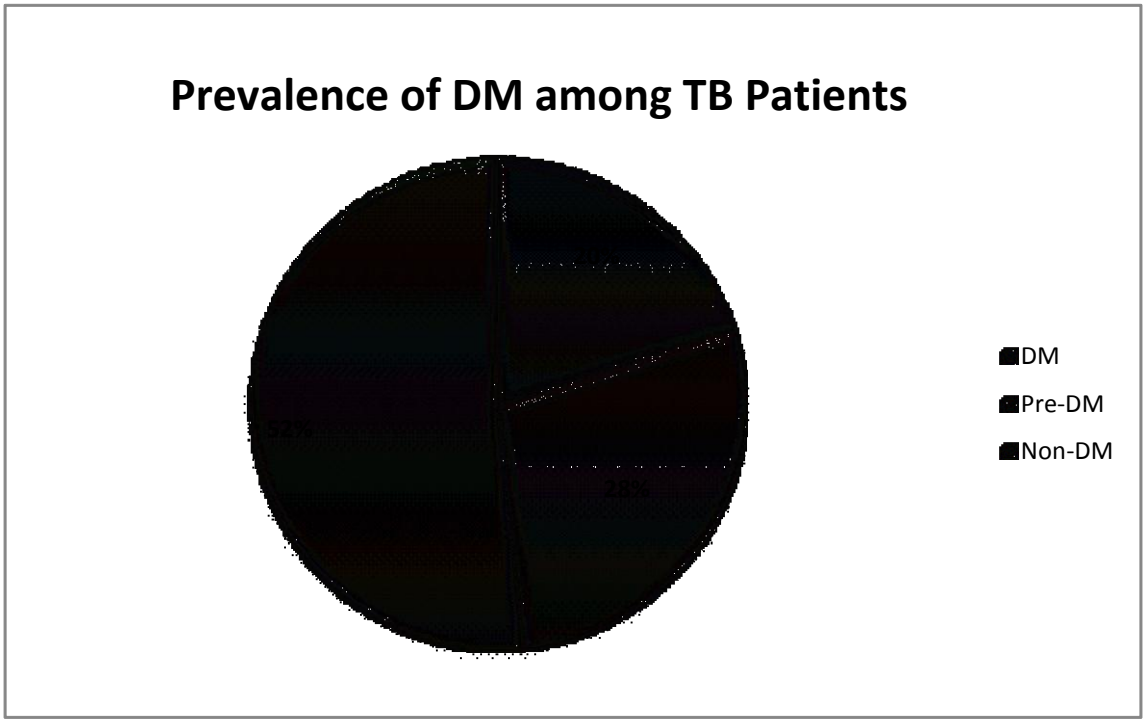
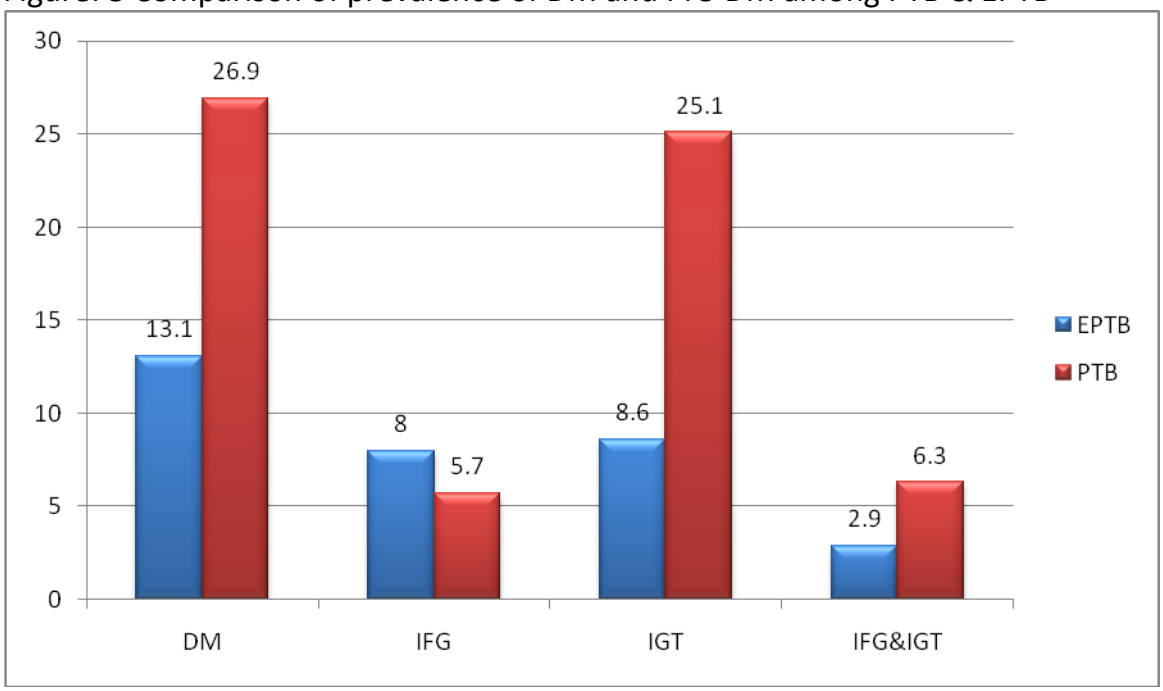


Figure: 3 Comparison of prevalence of DM and Pre-DM among PTB & EPTB



4.3 Characteristics of TB Patients as per Stages of Glucose Intolerance

Table 16 shows the comparison of the study characteristics among patients with normoglycemia, pre-diabetes and diabetes. TB patients with diabetes were older than the subjects with pre-diabetes and normoglycemia (45±10 vs. 36±13 vs. 33±11 years, $p<0.001$).Mean BMI of patients with diabetes was higher when compared to patients with pre-diabetes and normoglycemia(19.5±3.8 vs. 18.3±3.5 vs. 18.9±3.0, $p= 0.083$). Mean waist circumference was does not significantly differ in these three groups. TB patients with diabetes had a higher systolic blood pressure in comparison with normoglycemia and pre-diabetes ($p<0.001$) and TB with DM patients also had higher diastolic pressure than other two groups ($p=0.003$). As expected, fasting and 2 hours after glucose plasma glucose levels were statistically significant among these three groups ($p<0.001$). Type of tuberculosis had significant role in these groups ($p<0.001$) whereas treatment category had not significant effects among them($p=0.020$).

Table 16 Comparison of study characteristics among TB patients with normoglycemia, prediabetes and diabetes

Variables	Non DM	Pre diabetes	Diabetes	p- value
N,M:F	181,124:57	99,67:32	70,46:24	
Age(years)	33±11	36±13	45±10	**0.001**
BMI(kg/m^2)	18.91±3.01	18.37±3.53	19.53±3.81	0.083
Waist circumference(cm)				
Men	32±4	31±5	31±3	0.121
Women	30±4	29±3	31±5	
Blood pressure(mm Hg)				
Systolic	109.12±14.0	109.95±14.4	118.00±14.9	**0.001**
Diastolic	70.50±9.2	69.24±11.7	74.41±7.8	**0.003**
Plasma glucose				
Fasting	4.77±.73	5.65±5.65	8.39±2.65	**0.001**
After 2 hrs	6.31±.88	8.86±1.32	13.35±5.41	**0.001**
Type of TB				
Extra - pulmonary	118(65.2)	34(34.3)	23(32.9)	**0.001**
Pulmonary	63(34.8)	65(65.7)	47(67.1)	
Treatment category				
Category 1	137(75.7)	59(59.6)	45(64.3)	0.020
Category 2	9(5.0)	3(3.0)	4(5.7)	
Category 3	35(19.3)	37(37.4)	21(30.0)	

Results were expressed as n(%) and mean±SD),comparison done by one-way ANOVA test

4.4 Risk factors associated with Diabetes and pre-diabetes among TB Patients

On Pearson correlation coefficient, a significant correlation was found between age and DM ($r=0.327$, $p<0.001$). On binary logistic regression analysis (Table 21) showed that family history of DM and presence of PTB were significantly associated with diabetes among tuberculosis patients. On Binary logistic regression, family history of DM had 2.8 times chance to developed DM ($p=0.002$; Odds ratio 2.812) and PTB had 2.9 times chance to developed DM ($p=0.005$; Odds ratio 2.973) after adjusting age, BMI, treatment category variables.

On other hand Pearson correlation coefficient analysis showed that increasing age significantly associated with pre-diabetes($r=0.144$,$p=0.016$).On binary logistic regression showed presence of PTB had 3.3 times more chance to developed pre-diabetes other than EPTB patients($p<0.001$,OR=3.328).

Table17 Determinants of DM and Pre-DM by students' t-test

Variables	t/p
DM	
Age	7.55/.0001
BMI	1.811/.071
Systolic Blood pressure	4.492/.001
Diastolic Blood pressure	3.333/.0001
Pre-DM	
Age	1.9450/.053
BMI	-1.3640/.174
Waist Circumference	-2.009/0.045

The results were expressed as parametric test, students' t -test for measure the level of significance($p<0.05$)

Table 18 Association of DM with age and BMI among the study subjects

Variables	Fasting Blood Sugar		2 hrs After Glucose	
	r	**p**	**r**	**P**
Age	0.327	<0.001	0.270	0.001
BMI	0.125	0.019	0.042	0.429

The level of significance at p<0.05; r = correlation coefficient

Figure 4: Correlation among age and fasting blood sugar level of the respondents

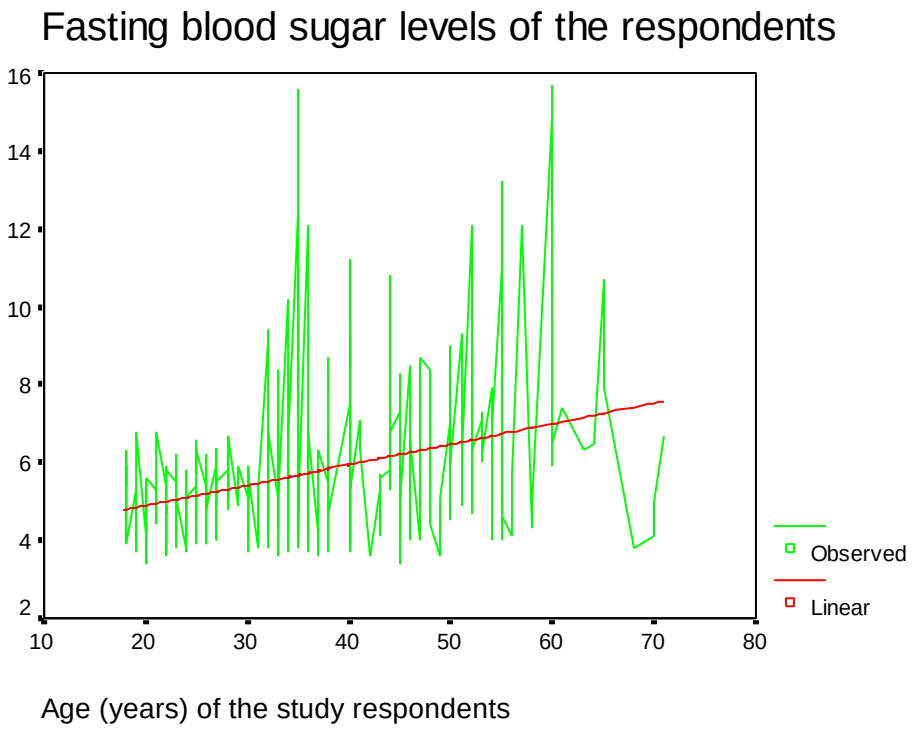


Figure 5: Correlation among age and blood sugar level after2 hours of the respondents

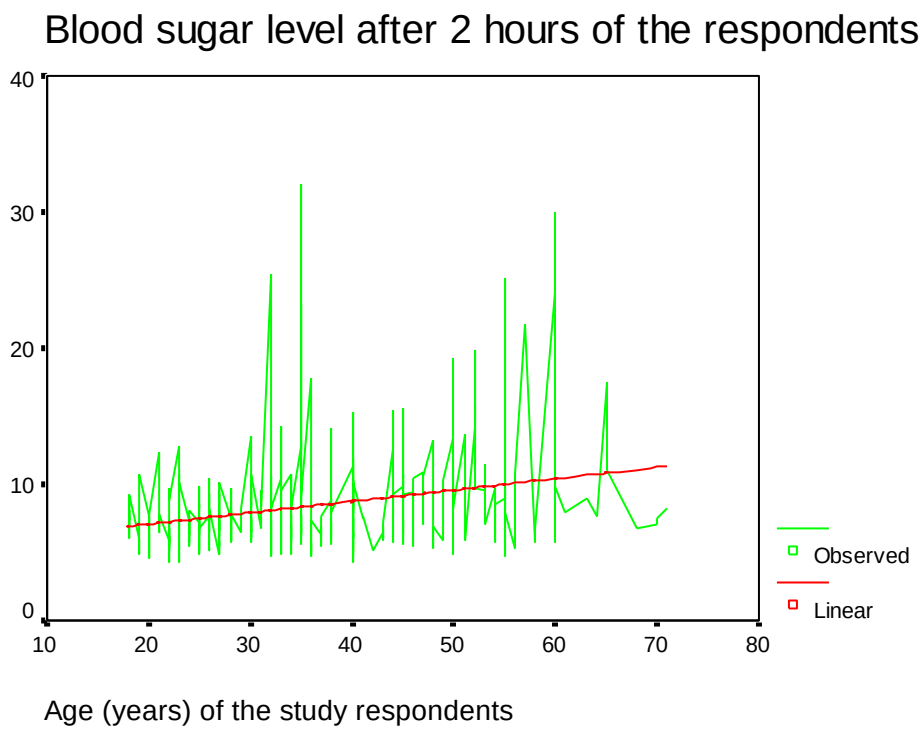


Table 19 Association of Pre-DM with age, WC and BMI among the study subjects

Variables	Fasting Blood Sugar		2 hrs After Glucose	
	r	**p**	**r**	**p**
Age	0.144	0.016	.081	.178
BMI	-0.041	0.493	-.060	.318
WC	0.001	0.984	-.155	.009

The level of significance at p<0.05; r= correlation coefficient

Table 20 Determinants of DM by Binary logistic regression analysis (Diabetes vs. Non-diabetes; dependent variable)

Variables	B	P value	Wald	Odds Ratio (OR)	95% CI for OR	
					Lower	Upper
Age	-0.080	**0.001**	37.797	0.924	0.900	0.947
Family history of DM						
No	Reference					
Yes	1.034	**0.002**	9.544	2.812	1.459	5.420
Type of TB						
EPTB	Reference					
PTB	1.090	**0.005**	7.872	2.973	1.389	6.366
Treatment category						
Category 1	Reference					
Category 3	-0.146	0.705	0.143	0.864	0.405	1.842
BMI	-0.083	0.089	2.901	0.920	0.836	1.013
Constant	4.800	0.001	19.087	121.475		

Reference group,β for standardized regression coefficient, Pre-DM was taken as dependent variable, whereas non-diabetes was taken as independent variable, significant at p-value<0.05, level of confidence interval 95%

Table 21 Determinants of Pre-DM by Binary logistic regression analysis (Pre-Diabetes vs. Non-diabetes; dependent variable)

Variables	β	P value	Wald	Odds Ratio (OR)	95% CI for OR	
					Lower	Upper
Age	0.024	0.041	4.183	1.024	1.001	1.048
Family history of DM						
No	Reference					
Yes	0.338	0.337	0.920	1.402	0.703	2.797
Type of TB						
EPTB	Reference					
PTB	1.202	**0.001**	13.129	3.328	1.737	6.377
Treatment category						
Category 1	Reference					
Category 3	0.337	0.327	0.962	1.401	0.714	2.751
BMI	0.029	0.542	0.372	1.029	0.939	1.128
Constant	-2.599	0.017	5.687	0.074		

Reference group,β for standardized regression coefficient, Pre-DM was taken as dependent variable, whereas non-diabetes was taken as independent variable, significant at p-value<0.05, level of confidence interval 95%

CHAPTER 5: DISCUSSION

The present study showed the prevalence of DM and pre-diabetes were 20% and 28.3% respectively among TB patients attending a tertiary care hospital. There was no significant gender difference between extra pulmonary and pulmonary subjects (p=0.732).In the current study, amongst those with DM,5.1% were newly detected DM cases and 14.9% were known cases of DM. A case control study conducted in Bangalore, South India, during 2001– 2003 reported that chronic disease particularly diabetes was a significant risk factor for developing TB. The prevalence rates of diabetes in TB and non-TB subjects were 22.2% and 15.9% respectively [123]. Based on secondary analysis of countrywide data, another research group estimated that 18.4% of subjects with PTB also have DM in India [124]. A retrospective analysis of 2 years data on TB subjects from Saudi Arabia in 1998 revealed that 27% had DM [125]. Another study from Taiwan reported 16.9% of DM among TB patients [126]. All these reports indicate that routine screening for DM among TB patients should be encouraged in areas with high TB burden. Type 2 DM was the most frequent type of DM encountered among the study participants with DM-TB co-infection . A similar observation has been documented in most similar studies [127-129]. This could probably be due to the higher proportions of people with type 2 DM compared to type 1 DM in most general populations.

The mean age of the patients with TB and DM was higher than in those with TB alone. This is similar to the study in the United States [130]. This may be related to the fact that Type 2 DM is seen more frequently in the older age group, the fact that this study was conducted largely among adults with TB may also be a factor. In our study majority of the patients were presumed to have Type 2 DM with only 25% of the patients studied being 30 years and below.

The association between DM and TB is well documented and there is substantial evidence to support the fact that diabetes is an important risk factor for TB [131].Previously there were no data from this area on the prevalence of both diagnosed and undiagnosed DM among TB patients. In Asia and the Middle East, the documented prevalence varies from 9.5%-44% [132-138] and 11.9%-27% [139-141] respectively. A multi centre study done in Texas, USA and Mexico reported

prevalence of 39% and 36% respectively [142]. Conversely, it is also possible that TB can induce glucose intolerance and also deteriorate glycemic control in subjects with diabetes [143]. A study conducted in 2011 in Tamil Nadu, India reported the prevalence of diabetes mellitus among the tuberculosis patients was 25.3% and another study in 2012 reported the prevalence rate of diabetes is 44% among the TB patients of Kerala, India. Alisjahbana et al. [144] reported prospective data from a cohort of patients with TB in Indonesia, where the prevalence of confirmed DM among patients with TB is 14.8% compared with 3.2% in general population. A nationwide INDIAB study [145] conducted in the general population of Tamil Nadu, South India, showed that the prevalence rates of diabetes and pre-diabetes were 10.4% and 8.3% respectively, substantially lower in comparison with the estimated prevalence of DM and pre-diabetes in the current study among TB patients conducted in the same period.

In the present study, among the TB patients identified with diabetes, almost 75% of them had been diagnosed with diabetes previously. It is known that long-term diabetes can impair the innate and adaptive immune responses necessary to counter the proliferation of TB [24]. This might be one of the reasons for the higher number of DM cases among the TB patients in the current study. In addition, the TB subjects also had the common risk factors associated with diabetes.

In this study age, positive family history of DM were the common risk factors associated with diabetes among TB patients like general population. But BMI, sedentary occupation and income status were not seen like general population in the current study.TB patients with DM were older than TB patients without DM(45 yrs vs.33 yrs).In the binary logistic regression analysis regarding age p=0.001.Among total TB patients most of them 44.9% were underweight, few overweight. Mean BMI of TB patients without DM was 18.9 whereas that of TB DM patients was 19.5 and mean waist circumference were almost same in both groups.

Positive family history of DM was significantly associated with DM with an odd ratio 2.812.Presence of Pulmonary TB was also associated with DM with odd ratio 2.973.Age, positive family history of DM and presence of PTB were risk factors associated with pre-diabetes among TB patients.

Association of DM with PTB in this study was similar to that of the findings of Stevenson et al. [146] This higher association was not seen with extra-pulmonary TB. The preponderance of development of DM among urban TB patients as reported by Stevenson et al. [146] was not noted in this study.

TB treatment outcome among TBDM patients is still not clear. Few studies reported that TB treatment outcome amongst DMTB subjects was good compared with non-DMTB subjects with the existing treatment [147,148] whereas a study among Indonesian TB patients reported poor TB treatment outcome among DMTB subjects[149].

Besides other factors, the association between DM and TB can be attributed to poor glycemic control and lack of non-specific antibody production due to deficiency in innate and adaptive immune mechanism amongst subjects with diabetes. These were the facilitating factors for the resurgence of past infections and incidence of new TB cases among DM subjects.In our study 11.4% were having regular diabetic treatment with registered diabetic book and 8.6% were on insulin and 6.3% were on oral medication.

An earlier report stated that prevalence of diabetes might be overestimated in TB since TB can cause transient hyperglycemia [150]. Thus, over-diagnosis might take place if tested for glucose prior to initiation of TB treatment. Majority of our study subjects were screened for DM by OGTT after 3 weeks of initiation of TB treatment. Ideally, glucose screening for DM diagnosis may be more appropriate after TB treatment has taken effect. Considering the growing trend in prevalence of diabetes and huge burden of latent TB infection amongst Bangladeshi population, it is necessary to focus on diagnosis of latent TB infection and screening for DM and ensuring good metabolic control amongst those diagnosed with DM. The role of possible chemoprophylaxis for subjects with DM and latent TB needs to be carefully considered and evaluated given the magnitude of the burden.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion

The prevalence of DM in patients with TB in our study was 20% [CI 16%-24%]and pre-diabetes 28.3%.The high association between TB and dysglycemia (about half of TB cases with diabetes and pre-diabetes) and around a third of DM cases amongst people with TB were newly detected.

Moreover, those with TB DM were more likely to have the pulmonary form of TB and getting treatment category 3.The TB patients with DM had less control of DM so it a challenge to control TBDM in Bangladesh as it's a double burden for the country.

In the light of findings of the study and the prevalence of DM among TB patients appears to be higher than DM in general population and prevalence of DM appears to be higher in PTB patients than EPTB patients. So does tuberculosis plays as an risk factor for DM can be determined by a case-control or a cohort study.

6.2 Recommendations

In the hospital settings for diagnosis of DM , RBS is the first choice of investigations. The confirmatory test for DM is done for the patients who are getting category 3 treatment. So sometimes diagnosis of DM may skip and which may cause treatment failure to TB patients. So Routine and confirmatory screening of DM among all TB patients should be done in all DOTs center and hospitals.

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Annex 1

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সম্মতিপত্র

আসসালামুআলাইকুম,
আমিবাংলাদেশ ইনষ্টিটিউট আব হেলথ্সাইন্সএরএকজনশিক্ষর্থী।.“**Prevalence of diabetes among tuberculosis patients attending a tertiary care hospital”**শীর্ষকএকটিগবেষণার তথ্য সংগ্রহেরজন্য আমিএখানেএসেছি। আপনারঅংশগ্রহন ও সুচিন্তিত উত্তর এই যক্ষা রোগীদের মধ্যে ডায়াবেটিসেরউপস্থিতিজানতেগবেষণায়সহায়কহবে। এই সাক্ষাৎকারসম্পন্নকরতেআনুমানিক ২০-৩০ মি: সময়প্রয়োজন। সংগ্রহীত তথ্য শুধুমাত্রগবেষণারকাজেব্যবহৃতহবে। সাক্ষাৎকারেঅংশগ্রহনকরা্ঐচ্ছিক, আপনিইচ্ছাকরলে যে কোনমুহুর্তে সাক্ষাৎকারদিতে অসম্মতিবানাকরতেপারেন। সকল তথ্যেও গোপনীয়তারক্ষাকরাহবে।

সাক্ষৎকারপ্রদানকারীরসাক্ষর

Questionnaire

Prevalence of Diabetes among tuberculosis patients attending a tertiary care hospital

SL No

Date

Name of the institute:
Type of Tuberculosis: 1.pulmonary Tb 2. Extra-pulmonary TB
Treatment category: 1.category 1 2.category 2 3.category 3
Status of patient: 1.DOT registered
2.Inpatients:a.registeredb.not registered
Contact no:……..

Part-A: Socio-demographic Information

Question	Coding Categories (Encircle appropriate response)	Answer (Write code no.)
I.What is your name? আপনারনামকি? II.where do you live(address) আপনি কোথায় থাকেন (ঠিকানা)		
A.1. What is your age? আপনারবয়স কত?	Age in completed years	
A.2. Gender(by observation) লিঙ্গ	1=Male 2= Female	

A.3.what is your marital status? আপনার বৈবাহিকঅবস্থা কি?	1= Married 2= Unmarried 3= Widow/Widower 4= Others(specify…….)	☐
A.4.i. which system of education have you followed? আপনিপড়াশুনার কোনপদ্ধতিঅনুসারনকরেছেন?	0= No education 1= General 2= Madrasa	☐
A.4.ii.How many years have you studied? আপনি কত বছরপড়াশোনাকরেছেন?	1= 1-5 yrs. 2= 6-10 yrs. 3= 10-15 yrs. 4= > 15 yrs.	☐
A.5.What do you do? আপনার পেশাকি?	1= Service 2= Business 3= House wife 4=Day laborer 5=Others (specify…….)	☐
A.6. What is your monthly family income? আপনরপরিবারেরমাসিকআয় কত?	Tk…….	…….
A.7. How many family member you have including you? আপনারপরিবারেরসদস্য সংক্ষা কত, আপনিসহ?	Total No……	☐☐
A.8. What is the type of your house? আপনারবসতবাড়ীরধরনকি?	1= Building 2=Semi-pacca 3= Tin shed 4= Mud 5= Others…….. (pl. mention)	☐

Part-B: Information Related to Tuberculosis and Diabetes

B.1. Do you have any family history of TB? আপনারপরিবারেরকারোযক্ষাআছে/ছিল?	1= Yes 2= No	☐
B.2. How many tablets you are taking every day? আপনিপ্রতিদিনকয়টিট্যাবলেটখান?	In numbers……	☐☐
B.3. During treatment have you ever forget to take medicine? চিকিৎসাচলাকালীনআপনিকিকখনও ঔষধখেতে ভুলে গেছেন?	1= yes 2= No	☐
B.4. Where you take medicine? আপনি কোথায়ঔষধ সেবনকরেন?	1= home 2=DOT center 3= Others(specify……)	☐
B.5. Do you have any family history of DM? আপনারপরিবারেরকারোডায়াবেটিস রোগআছে?	1= Yes 2= No	☐
B.6.Are you suffering from any type of Diabetes? আপনিকি কোনোধরনেরডায়াবেটিস রোগেভুগছেন?	1= Yes 2= No	☐

B.7. If yes have you any registered diabetic book? আপনারকি কোননিবন্ধনবইআছে?	1= Yes 2= No	☐
B.8.How many days/years you are suffering from diabetes? আপনি কত দিন/বছরধরেডায়াবেটিস রোগেভুগছেন?	1=less than 5 yrs 2= 6- 10 yrs 3= 11-15 yrs 4=16-20 yrs 5=more than 20 yrs	☐
B.9.What type of treatment you are taking? আপনিডায়াবেটিসেরজন্য কিধরনেরচিকিৎসাগ্রহনকরেছেন?	1= Insulin 2= Oral drugs 3= Diet 4= Others (specify……)	☐
B.10. Type of Diabetes suffering from? কোনধরনেরডায়াবেটিস?	1= Type 1 2= Type 2	

Part- C: Physical and Behavioral variables-

Information related to behavioral variables:

C.1. Do you smoke or take others form of tobaccos? আপনিকিধূমপানঅথবাঅন্য কোনোতামাকজাত দ্রব্য গ্রহনকরেন?	Yes =1 No =2	☐
C.2. If yes name the specific form of tobacco? যদি করে থাকেন, নির্দিষ্ট তামাকজাত দ্রব্যেরনামটিবলুন ।	Specify……..	…….
C.3. If smoker how many sticks you are taking per day? যদি ধূমপায়ীহন, তাহলেপ্রতিদিনকতটিসিগারেটখান?	In numbers…….	☐☐☐

Physical Measurement:

C.4.Height উচ্চতা Record participant's height in cm	In Centimeters(cm):…….	☐☐☐
C.5.Weight ওজন Record participant's weight in kg	In kilograms(kg):……	☐☐☐
C.6. Waist circumference in centimeters কোমরেরমাপ	In centimeters…….	☐☐☐

C.7.i.Blood pressure রক্তচাপ Reading 1 (record first measurement after the participant has rested for 15 minutes. Wait 3 minutes before taking second measurement)	Systolic (mm hg):……. Diastolic(mm hg):…….	☐☐☐ ☐☐☐
C.7.ii.Reading 2 Record second measurement	Systolic(mm hg):……. Diastolic(mm hg):……	☐☐☐ ☐☐☐
C.8. During the past two weeks, have you been treated for raised blood pressure with drugs (medication) prescribed by a doctor or other health worker? গত দুইসপ্তাহেআপনিকি উচ্চ রক্তচাপেরজন্য কোনোঔষধ খেয়েছেন (ডাক্তার অথবাস্বাস্থ্যকর্মীরপরামর্শ মতে)	Yes =1 No =2	☐
C.9.Could you please mention the name of drug or type of drug (sedative or anti-hypertensive) you are taking? আপনিকি্ঔষধেরনামঅথবাকিধরনেরঔষধ (ঘুমেরঅথবা উচ্চরক্তচাপের) খেয়েছেনবলতেপারেন ।	Name of drug:…… Type of drug:……	……. ……..

Part-D: Biochemical observations

Observations	**Results**
D.1.(for those who are already diagnosed as diabetic): a.Fasting blood sugar b. 2 hours after breakfast blood sugar	 ……mmol/L ……mmol/L
D.2.(for those other than known diabetic): a.Fasting blood sugar b. 2 hours after glucose blood sugar	……mmol/L ……mmol/L

Interviewer signature …….....

Annex 2: Work Plan for MPhil Thesis

Sl .No.	Activity detail	1-2 months	3-4 months	5-6 months	7-8 months	9-10 months	11-12 months
1	Title selection and approval						
2	Introduction and Rationale						
3	Literature review						
4	Questionnaire Development, Training of the Data collector and Pilot study						
5	Data collection						
6	Data processing and data analysis						
7	Report writing and submission						