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## REVIEW ARTICLE

# THE RELATIONSHIP BETWEEN DIABETES MELLITUS AND TUBERCULOSIS IN REVIEW OF PREVALENCE, DIAGNOSTICS AND PREVENTION

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### Abstract

Tuberculosis (TB) is a bacterial infection caused by *M. tuberculosis*, also known as *Mycobacterium tuberculosis*. There is a bidirectional relationship between TB and diabetes, and they both impact the presentation of each other. Diabetes is being increasingly recognized as a risk factor for TB. The expected rise in diabetes cases in developing countries having the brunt of tuberculosis would increase the influence of diabetes on TB in the coming future. The impact and relationship between TB and diabetes will vary across different regions of the world depending on the incidence and prevalence of each condition. Patient education is so important in understanding the disease nature (both TB and diabetes), duration of treatment, side effects of drugs, and complications of disease as well as the promotion of healthy lifestyle choices

The objective of this review is to determine the prevalence, diagnostic and prevention strategy between diabetes mellitus and tuberculosis. The selected studies were identified using Pub Med database. The identified studies define lifestyle as important risk factor that may worsen the progression of the disease. This article also discussed about the prevalence of tuberculosis-diabetes mellitus over a span of 8 years.

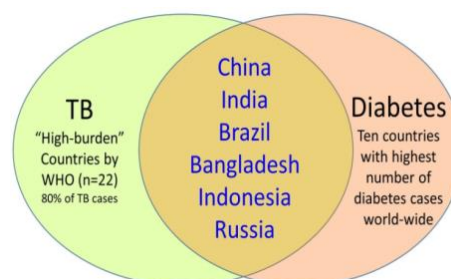
**Keywords:** Diabetes mellitus, risk factors, tuberculosis.

## INTRODUCTION

Tuberculosis is a contagious infection that affects lung most efficiently and can also transport through the blood or lymphatic system, TB bacteria can infect almost any part of the body, including lymph nodes, joints, kidneys, and bone. Tuberculosis can spread by droplets of bacteria released into the air by an infected person who coughs, sneezes, talks or sings<sup>1,2</sup>. Nowadays, TB has become the most prevalent infectious disease in the world. TB is by far the 7<sup>th</sup> leading cause of the death worldwide, and experts predict that if the disease is not well controlled, it could become the world's leading cause of death by 2020 as mentioned in Figure 1.

People infected with TB will show symptoms of cough, fever, chest pain, loss of appetite, weight loss and others<sup>3</sup>. TB can affect other parts of the body and shows symptoms that depend on the part it affects. For example, it can lead to meningitis if TB affected the brain or infection with the liver or kidney can cause filtration dysfunction, causing blood to enter the urine. People with immune deficiencies caused by the disease are most likely to develop TB. For instance, when a

person is infected with HIV, it suppresses the immune system, preventing it from usually suppressing TB bacteria<sup>4,5</sup>. Furthermore, people with diabetes, certain cancers, malnutrition, kidney disease, cancer treatments such as chemotherapy or many others can have an increased risk to get TB. TB is common in particular geographic regions, ethnic groups, or age groups<sup>6</sup>. However, it can affect all age groups and all parts of the world. People with diabetes are three times more likely to develop TB. In the interaction between TB and diabetes, the effect of diabetes on TB is more life-threatening.



**Figure 1.** Countries with the highest burden of diabetes mellitus and TB.

**Table 1: Studies assessing the effect of diabetes mellitus on treatment failure and death in patients treated for TB.**

Characteristics	Treatment Failure			Mortality				
	Year	2003	2007	2002	2003	2008	2009	2009
Location	Egypt	Indonesia	Maryland, USA	Congo	Sao Paulo, Brazil	Maryland, USA	Taiwan	
Setting	TB treatment centres	Outpatient clinics	Outpatient clinics	University hospital	Urban	TB patients in three countries	Teaching hospital	
Type of study	Case-control study assessing risk factors for treatment failure, matched for sex and centre	Prospective cohort study of new pulmonary TB patients	Retrospective cohort study of culture-confirmed TB patients	Case-control study using chart review	Retrospective study of all TB-related deaths using death certificates, surveillance data, hospital records	Retrospective cohort study of culture-positive TB patients	Retrospective study of culture-positive pulmonary TB patients	
Participants (n)	119 cases, 119 controls	634 cases	139 cases	32 cases, 100 controls	416 cases	297 cases	217 cases	

**Table 2: Review on several characteristics comparing article 1 and article 2.**

Characteristics	Article 1 <sup>2</sup>	Article 2 <sup>1</sup>
Prevalence of Diabetes Mellitus and TB	<p><b>The global prevalence of Diabetes Mellitus:</b> The number of diabetes patients was 171 million in 2000. It is predicted to increase 214.04% to 257.31% by 2030 which is 366 million to 440 million, with three-quarters of diabetes patients living in low-income countries</p> <p><b>The global prevalence of Tuberculosis:</b> N/A</p> <p><b>Prevalence of TB-Diabetes Mellitus:</b> Higher in low-income and middle-income countries.</p>	<p><b>The global prevalence of Diabetes Mellitus:</b> The number of people who are suffering from Diabetes Mellitus among adults has increased by 20% in less than 30 years, and Diabetes Mellitus is predicted to reach 642 million worldwide by 2040 with most (80%) of the patients living in low and middle-income countries where TB is also endemic.</p> <p><b>The global prevalence of TB:</b> N/A</p> <p><b>Prevalence of Tuberculosis-Diabetes Mellitus:</b> Higher in low- and middle-income countries where TB and Diabetes Mellitus are endemic.</p>
Countries having high incidence of TB and Diabetes Mellitus	South Africa, Swaziland, Uganda, Kenya, Cabo Verde The Gambia, Nigeria, Zimbabwe, Western Sahara, Ethiopia, Cambodia, Taiwan.	China, India, Brazil, Bangladesh, Indonesia and Russia.
Type of study	Chest radiograph survey, retrospective cohort, cross-sectional study, longitudinal cohort study, case-control study, population-based cohort and matched case-control study.	Retrospective-based cohort
Diabetes Mellitus as a risk factor for TB	Diabetes Mellitus patients are more likely to develop multidrug-resistant TB than those without Diabetes Mellitus.	Diabetes Mellitus increases the risk of Tuberculosis by three-fold. Co-occurrence of Diabetes Mellitus with other host characteristics can further synergise TB risk among Diabetes Mellitus patients, as suggested for Diabetes Mellitus plus smoking, micro and macro vascular complications of DM, and even their social environment.

\*N/A=Not available

Therefore, the World Health Organization (WHO) defines diabetes as a risk factor for TB<sup>7</sup>. The main reason for the prevalence of TB in diabetic patient is because the bacteria can grow and multiply easily in the high-sugar environment and often lack vitamins A and B, thus weaken the resistance of respiratory tract, which is conducive to the infection and development of the bacteria. Infected patients with TB, due to symptoms of poisoning and the consumption of nutrients, affect the normal play of islet, causing islet cell malnutrition and atrophy, leading to diabetes<sup>8</sup>. Diabetes is closely related to TB. In recent years, diabetes has been significantly increased with TB, which has become a clinical concern. When the two

diseases coexist, the TB is complicated and difficult to treat. As the incidence of diabetes and TB continues to increase, the prevalence of TB has gradually increased. Therefore, objective of this study was to better understand the relationship between diabetes and tuberculosis prevalence, diagnosis and prevention<sup>9</sup>.

## METHODS

By using PubMed database, the author has found 3842 articles with the keywords of Tuberculosis and Diabetes which is ("tuberculosis"[MeSH Terms] OR "tuberculosis"[All Fields]) AND ("diabetes mellitus"[MeSH Terms] OR ("diabetes"[All Fields]

AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields]). The articles published are selected for last ten 10 years, which was from January 2009 to July 2019. The articles that have been chosen are published in the year 2010 and 2017, respectively. All article type such as clinical trial and review are included. The articles chosen are written in English. Among them, the author has chosen two articles which are most related to the topic. The chosen articles are based upon prevalence, diagnostics and prevention of TB and diabetes mellitus<sup>10</sup>.

## DISCUSSION

In the introduction, we mentioned that the existence of diabetes and TB is mutual. From the literature reviews that we choose, we also found that the TB rate in patients with diabetes was 23.5%, while the incidence of diabetes in patients with tuberculosis was 12.4%<sup>11,12</sup>. However, there was a low uptake of a diagnostic evaluation for TB and confined to the patients that had evident symptoms of TB. So, only diabetic patients suspected of TB will be actively referred. Several programs have also been proposed to screen early TB-diabetes mellitus<sup>13</sup>. Doctors must be well-trained that the diabetic patients receive routine TB screening to carry out other diabetes-associated complications. Moreover, user-fees for the X-ray limit the number of screenings. Based on this problem, cost-free or subsidised will reduce the financial burden, encourage patients to undergo screening and increase the uptake of TB testing. Screening for diabetes in TB patients is best done at the start of TB treatment and registration. The laboratories or at the provider clinics provide these tests with the assurance of interventions to obtain data on diabetes screening as part of the TB surveillance system<sup>14,15</sup>. Integrated delivery units provide a solution for diabetes screening, TB diagnosis and TB-diabetes mellitus treatment in a facility that can capture data with supporting systems and monitoring results. The results of the study indicate that patients with TB-diabetes mellitus have a higher risk of adverse diabetes mellitus outcomes, including delayed mycobacterial clearance, relapse and re infection, treatment failure, and even death<sup>16</sup>. Two factors are prime suspects, poor glucose control and differences in antibiotic levels of plasma anti-mycoplasmal bacteria. Based on the problems stated, we can bring out another question: How to prevent the development of diabetes mellitus in a patient with diabetes<sup>17</sup>. Therefore, for patients diagnosed with diabetic TB, the control of blood glucose and effective anti-tuberculosis drugs are the key points and difficulties in the treatment of this disease, as well as the key to prevent the emergence of drug-resistant diabetes mellitus<sup>18</sup>. Active control of blood glucose is the key to the treatment of diabetic TB<sup>19</sup>. Meanwhile, early diagnosis of TB, early adequate and reasonable anti-TB treatment, strengthens blood glucose monitoring during treatment, and timely evaluation of the treatment effect by reviewing chest radiographs and sputum bacteria. For people with poor glycaemic control, they should consider an appropriate extension of course to 1 year or

more. If it progresses to multidrug-resistant TB (Mdr-tb), it is more contagious, more difficult to treat, and the failure rate and mortality are higher. It is essential to develop an appropriate and effective treatment plans for Mdr-tb, and also strengthen the management of patients. These methods are essential to interrupt its transmission<sup>20</sup>.

## CONCLUSIONS

The high prevalence of diabetes mellitus in low- and middle-income countries where TB is endemic has become one of the issues that should be targeted by the related department. Prevalence, diagnostics and prevention of TB and diabetes mellitus are the topics that needed to be emphasized. Upon the high prevalence of diabetes mellitus and TB, the author has mentioned some actions which are necessary for preventing the occurrence of TB and diabetes mellitus that will be stated below<sup>17</sup>. Furthermore, the author has also stated the relationship between diabetes mellitus and TB. People who are suffering from chronic diseases such as diabetes mellitus will have a weaker immune system<sup>6</sup>. Therefore, they are more likely to progress from latent to active TB. In the research, it was found that the risk of TB is related to the severity of diabetes mellitus. Patients who needed more than 40 units of insulin per day have a double chance to develop TB than those with lower doses<sup>21</sup>. There are several precautions that are needed to be taken note by TB-diabetes mellitus patients. Poorly controlled diabetes can lead to several complications, including increased susceptibility to infection. For example, infection caused by *Mycobacterium tuberculosis* (Mtb). Therefore, diabetes patients need to have regular diabetes control<sup>22</sup> including strict control on their diet and carry out a healthy lifestyle such as exercise regularly and sleep according to time. Besides, the author has also mentioned that diabetes mellitus can increase the risk of successful LTBI in close contacts which can facilitate the progression from LTBI to TB<sup>23</sup>. In the article, the author has also mentioned that DM-diabetes mellitus patients have a higher frequency of lower lung lobe infiltrates where Mtb would implant during inhalation. One should further themselves from high infection area where Mtb are endemic. As the fact infections are the cause of worsening diabetic control. First, overlapping toxicities when treating TB and diabetes mellitus must be handled carefully to avoid subsequent action to the patients<sup>3</sup>. As an example, isoniazid is a drug which is used to treat active TB infections. However, it might cause peripheral neuropathy. Therefore, pyridoxine should be given at the same time to avoid such incidence<sup>24</sup>. In addition, rifampicin is a potent inducer, which is a host of metabolising enzymes can accelerate the metabolism of drugs given with rifampicin. It can cause hyperglycaemia when treated with oral hypoglycaemic drugs directly or indirectly and leading to reduced treatment effects. Other treatment such as rosiglitazone and repaglinide should also be paid more attention when treating with rifampicin. This is because rifampicin can reduce the plasma concentrations of the

mentioned drugs by 54% and 31% respectively<sup>25</sup>. TB is an infectious disease which can be transmitted through the air. Thus, one needs to be cautious when exposing to a high risk area. Wearing a mask would be an ideal way to prevent infection. As a conclusion, TB-diabetic patients need to pay more attention to their lifestyle. All the risk factors should be avoided to prevent any incidences or to worsening of the disease. Campaign and social media are the easiest and effective way of reducing the prevalence of TB and diabetes mellitus.

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## AUTHOR'S CONTRIBUTION

**Celine T:** writing original draft, methodology. **Yee CJ:** investigation, formal analysis, conceptualization. **Aslam MS:** review, supervision. Final version of manuscript is approved by all authors.

## DATA AVAILABILITY

Data will be made available on request.

## CONFLICT OF INTEREST

No conflict of interest associated with this work.

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