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Original Review Article

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

**Abstract:**

Tuberculosis (TB)is a bacterial infection caused by M. tuberculosis, also known as Mycobacterium Tuberculosis. 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 PubMed 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 (TB-DM) over a span of 8 years.

## 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 [1].Nowadays, Tuberculosis (TB) has become the most prevalent infectious disease in the world. Tuberculosis is by far the 7th 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.

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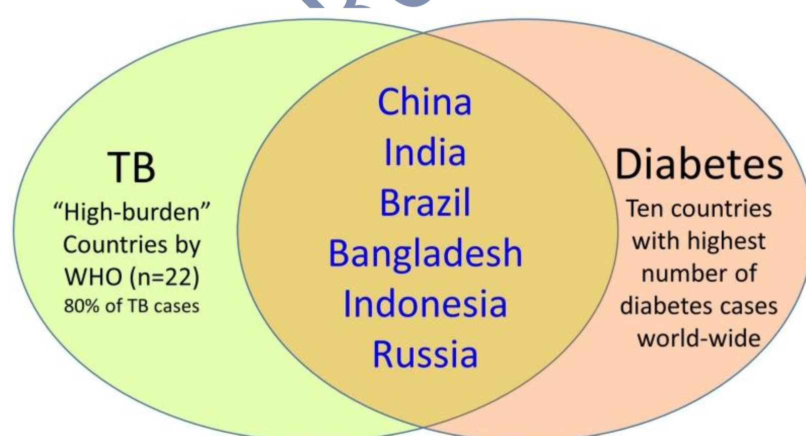


Figure 1 Countries with the highest burden of DM and TB

People infected with TB will show symptoms of cough, fever, chest pain, loss of appetite, weight loss and others. 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 AIDS, HIV suppresses the immune system, preventing it from usually suppressing TB bacteria.

Furthermore, people with diabetes, certain cancers, malnutrition, kidney disease, cancer treatments such as chemotherapy or many others can have an increased risk to get tuberculosis.Tuberculosis is common in particular geographic regions, ethnic groups, or age groups. However, it can affect all age groups and all parts of the world.

People with diabetes are three times more likely to develop tuberculosis. In the interaction between tuberculosis and diabetes, the effect of diabetes on tuberculosis is more life-threatening. Therefore, the World Health Organization (WHO) defines diabetes as a risk factor for tuberculosis[2]. The main reason for the prevalence of tuberculosis 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 tuberculosis, 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.

Diabetes is closely related to tuberculosis. In recent years, diabetes has been significantly increased with tuberculosis, which has become a clinical concern. When the two diseases coexist, the tuberculosis is complicated and difficult to treat. As the incidence of diabetes and tuberculosis continues to increase, the prevalence of tuberculosis has gradually increased, and research on the correlation between the two has increased. Therefore, our objective of this study is to better understand the relationship between diabetes and tuberculosis prevalence, diagnosis and prevention.

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**Methodology**

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 publishedare 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 2 articles which are most related to the topic. The chosen articles are based upon prevalence, diagnostics and prevention of Tuberculosis and Diabetes Mellitus.

| Database | Search Strategy | Results |
|---|---|---|
| Pubmed | Search field: All field<br>Search item: ("tuberculosis"[MeSH Terms] OR "tuberculosis") AND ("diabetes mellitus"[MeSH Terms] OR ("diabetes" AND "mellitus") OR "diabetes mellitus")<br>Limits used: English text only and published within the last 10 years (1997 to present). | 3842 |

**Literature review**

Table 1: Studies assessing the effect of diabetes mellitus on treatment failure and death in patients treated for tuberculosis (TB) [3]

| Characteri-stics | 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 clinic | 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 | Retrospect-ive study of culture-positive pulmonary TB patients |

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| 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[2] | Article 2[1] |
|---|---|---|
| Prevalence of Diabetes Mellitus and Tuberculosis | The global prevalence of Diabetes Mellitus:<br>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<br><br>The global prevalence of Tuberculosis:<br>N/A<br><br>Prevalence of Tuberculosis-Diabetes Mellitus:<br>Higher in low-income and middle-income countries. | The global prevalence of Diabetes Mellitus:<br>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.<br><br>The global prevalence of Tuberculosis:<br>N/A<br><br>Prevalence of Tuberculosis-Diabetes Mellitus:<br>Higher in low- and middle-income countries where Tuberculosis and Diabetes Mellitus are endemic. |
| Countries having high incidence of Tuberculosis | South Africa, Swaziland, Uganda, Kenya, Cabo Verde The Gambia, Nigeria, Zimbabwe, Western Sahara, Ethiopia, Cambodia, | China, India, Brazil, Bangladesh, Indonesia and Russia. |

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| and Diabetes Mellitus | Taiwan. | |
|---|---|---|
| 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 Tuberculosis | Diabetes Mellitus patients are more likely to develop multidrug-resistant Tuberculosis than those without Diabetes Mellitus. | Diabetes Mellitus increases the risk of Tuberculosis by three-fold.<br><br>Co-occurrence of Diabetes Mellitus with other host characteristics can further synergise Tuberculosis risk among Diabetes Mellitus patients, as suggested for Diabetes Mellitus plus smoking, micro and macrovascular complications of DM, and even their social environment. |

*N/A=Not available

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**Discussion**

In the introduction, we mentioned that the existence of diabetes and tuberculosis is mutual. From the literature reviews that we chose, we also found that the tuberculosis rate in patients with diabetes was 23.5%, while the incidence of diabetes in patients with tuberculosis was 12.4%[4]. However, there was a low uptake of a diagnostic evaluation for tuberculosis and confined to the patients that had evident symptoms of TB. So, only diabetic patients suspected of tuberculosis will be actively referred. Several programs have also been proposed to screen early TB-DM. Doctors must be well-trained that the DM 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. Low-cost diabetes testing is recommended, although the results may be slightly skewed, patients are more likely to agree that it is cheap. The laboratories or at the provider clinics provide these tests with the assurance of interventions to obtain data on DM screening as part of the TB surveillance system. Integrated delivery units provide a solution for DM-screening, TB diagnosis and TB-DM treatment in a facility that can capture data with supporting systems and monitoring results.

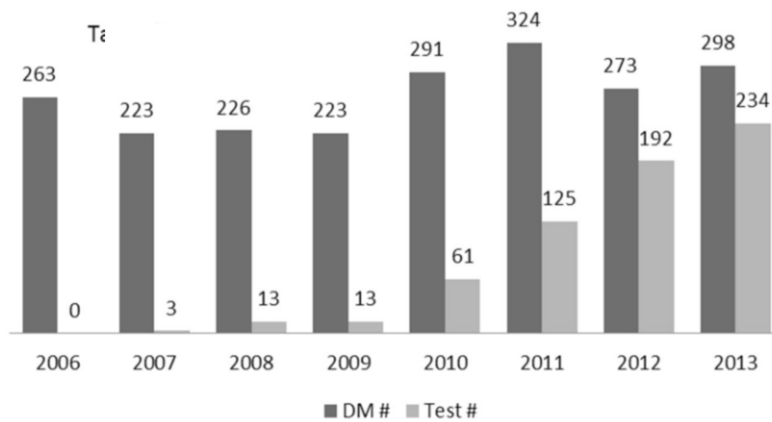


Figure 2 The prevalence of TB-DM among TB cases increased over 8 years

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The results of the study indicate that patients with TB-DM have a higher risk of adverse tuberculosis outcomes, including delayed mycobacterial clearance, relapse and reinfection, treatment failure, and even death[2]. Two factors are prime suspects, poor glucose control and differences in antibiotic levels of plasma anti - mycoplasma bacteria. Based on the problems stated, we can bring out another question: How to prevent the development of tuberculosis in a patient with diabetes?

Therefore, for patients diagnosed with diabetic tuberculosis, 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 tuberculosis. Active control of blood glucose is the key to the treatment of diabetic tuberculosis. Meanwhile, early diagnosis of tuberculosis, early adequate and reasonable anti-tuberculosis treatment, strengthening 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 tuberculosis (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.

**Conclusion**

The high prevalence of diabetes mellitus in low- and middle-income countries where tuberculosis is endemic has become one of the issues that should be targeted by the related

department. Prevalence, diagnostics and prevention of tuberculosis and diabetes mellitus are the topics that needed to be emphasized. Upon the high prevalence of diabetes mellitus and tuberculosis, the author has mentioned some actions which are necessary forpreventing the occurrence of tuberculosis and diabetes mellitus that will be stated below. Those actions need to be paid attention by related department so that the prevention for TB-DM can be controlled in well-manner.

Furthermore, the author has also stated the relationship between diabetes mellitus and tuberculosis. People who are suffering from chronic diseases such as diabetes mellitus will have a weaker immune system[6]. Therefore, they are more likely to progress from latent to active tuberculosis. In the research, it was found that the risk of tuberculosis is related to the severity of diabetes mellitus. Patients who needed more than 40 units of insulin per day havea double chance to develop Tuberculosis than those with lower doses.

There are several precautions that are needed to be taken note by TB-DM patients. Poorly controlled diabetes can lead to several complications, including increased susceptibility to infection. For example, infection caused by Mtb. Therefore, diabetes patients need to have regular diabetes control [7] 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. In the article, the author has also mentioned that DM-TB 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.

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As we know that infections are the cause of worsening diabetic control, but the drugs taken by diabetes patients to treat tuberculosis may also weaken the glycaemic control of the patients. In the article, the author has also brought up some facts that need to be taken serious. First, overlapping toxicities when treating tuberculosis and diabetes mellitus must be handled carefully to avoid subsequent action to the patients[3]. As an example, isoniazid is a drug which is used to treat active tuberculosis infections. However, it might cause peripheral neuropathy. Therefore, pyridoxine should be given at the same time to avoid such incidence.

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. For example, Sulfonylureas is an oral hypoglycaemic drug which is usually used for NIDDM patients. Other treatment such as rosiglitazone and repaglinide should also be paid more attention when treating with rifampicin. This is because rifampicin can reduce the concentrations of the mentioned drugs by 54% and 31% respectively.

Tuberculosis is an infectious disease which can be transmitted through the air [5]. Thus, one needs to be cautious when exposing to a high risk area. Wearing a mask would be an ideal way to prevent infection. However, the best preventing way is to avoid an area with the high spreading of tuberculosis, especially diabetes patients. They need to have full protection from tuberculosis in order to prevent any infection.

As a conclusion, TB-DM 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. The associated department should also educate the public on the prevention of diseases. Campaign and social media are the easiest and effective way of reducing the prevalence of tuberculosis and diabetes mellitus.

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