# Diabetes mellitus among tuberculosis patients: a cross sectional study from Pakistan.

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## Abstract

**Background:** The co-occurrence  of  diabetes mellitus (DM) and tuberculosis (TB) is largely associated with  high frequency of morbidity.

**Objective:** To determine  the prevalence of DM among TB patients and describe the  socio-demographic and behavioral factors associated with  TB-DM co-occurrence  .

**Methods:** We enrolled 500 TB patients  from September, 2014 to August 2015 at four major public sector hospitals of Lahore, Pakistan. A questionnaire was used to collect information regarding associated socio-demographic and behavioral  factors of the patients. We monitored the fasting blood sugar of each patient by using a semi automated clinical chemistry analyzer followed by an HbA1c level check of all hyperglycemic patients.

**Results:** The  prevalence  of  TB-DM co-occurrence  was  14.8%. The  prevalence  of TB-DM was higher (62.2%) among males. The  >57 year age group had the highest proportion of patients (35.1%),  with co-existent TB-DM. Most were illiterate (73.0%) and  unemployed (48%). Moreover, among the 74 patients positive for TB-DM had a history of smoking. Age and education level were significantly associated with DM-TB  while gender, occupation and smoking were not associated.

**Conclusion:** The study revealed a 14.8% prevalence of  DM among TB patients. This was associated with several socio-demographic factors, including age, unemployment, literacy  and polluted environment. Thus, poor and unhealthy lifestyles were the factors associated with  DM among immunologically compromised individuals due to TB.

**Keywords:** Tuberculosis (TB), diabetes mellitus (DM), socio-demographic and behavioral factors.

## Introduction

Diabetes mellitus (DM) is one of  the most common diseases prevalent in low and middle income countries (LMICs) that are already facing problems due to various endemic infections like tuberculosis (TB) and malaria. The co-occurance of  DM-TB is largely associated with higher frequency of  morbidity, especially among LMICs that are facing epidemics of communicable and non-communicable diseases[1]. According to the WHO, 371 million people are living with DM worldwide  while 80% of them are living in LMICs. Moreover, these LMICs  also bear 90% burden of  worldwide TB patients.[2] Several studies have reported that TB and DM are co-incident and may serve as pre-disposing risk factors for each other.  In TB endemic areas,  patients are particularly  prone to DM when  compared to healthy population[3]. Similarly,  other studies have reported DM as a risk factor for TB. It is also reported that patients with TB-DM co-occurrence usually do not respond to anti-TB therapy thus resulting in higher mortality.[4] Therefore, it is essential to study the prevalence of  both diseases  in order to understand the factors associated with their co –occurrance.[5]

Pakistan ranks fifth among 22 high burden TB countries and  ranks fourth among 27 high burden drug resistant

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TB countries[6]. The World Health Organization (WHO) reported an estimated incindence of 275 cases per 100,000 persons and prevalence of 342 cases per 100,000 population[7,8]. In case of diabetes mellitus, the WHO has reported 4.3 million affected individuals in Pakistan and it is included among the top ten countries with highest DM incidence and it is expected that this figure will reach 14.5 million by the end of year 2025.[9] Therefore the Nation, having such a high burden of these two diseases, is at an increased risk of developing diabetes among TB infected patients. The exact mechanism of their inter-linkage is not clearly understood, but some studies suggested that reduced alveolar macrophage activity in TB patients is the main reason making them prone to DM[10]. On the other hand, diabetic patients have weak cellular immunity, kidney problems and alveolar angiopathy that ultimately make the conditions favorable for TB infection.[2,4]

Poverty and unhygienic life styles are the serious issues being faced by LMICs like Pakistan. These issues are making the situation more complicated and result in the co- occurrence of complex diseases like TB and DM. Therefore, there is an urgent need to develop some strategies regarding their control and prevention. Developing and effective strategy to address the issue needs sufficient information about the prevalence and spread of such diseases. The present study aimed to determine the frequency of DM among TB patients visiting four major hospitals of Lahore, Pakistan. It also determined the socio-demographic and behavioral factors associated with TB-DM co-occurrence.

## Materials and methods

The present study was carried out at four major public sector hospitals of Lahore Metropolitan including Mayo hospital, Gulab Devi hospital, Services hospital and Infectious diseases hospital during a one year time period (September, 2014 to August, 2015). This cross sectional study received ethical approval from the board of ethics, Institute of Public Health, Lahore. A pre-tested comprehensive questionnaire covering different demographic and medical aspects of the present study was used to collect the information from the participants. Informed consent was taken from all individuals who participated in this study. All the filled questionnaires were analyzed for participants' socio-demographic, clinical and behavioral risk factors for DM and TB.

Almost 500 TB patients meeting the inclusion criteria were enrolled in this study. Patients with tuberculosis were characterized as those having positive results for TB disease manifestation by clinical, radiological, microbiological and molecular examinations[11]. Microbiological confirmation was done by Zeihl Neelsen staining method[10] and culturing of Mycobacterium tuberculosis (MTB) was done on Lowen Stein Jensen (LJ) media by modified Petroff method[12]. Molecular confirmation was done using GeneXpert method.[13] All microbiological and molecular assays were carried out at biosafety level 2 Provincial TB Reference Lab, Institute of Public Health, Lahore.

All study participants were further subjected to fasting blood sugar level by semi automated clinical chemistry analyzer Microlab 300 according to manufacturer's protocol.[14] Patients having DM were categorized as those individuals who had fasting blood sugar level of higher than 126 mg/dl and HbA1C level >6.8 or if pre-diagnosed by physicians and fulfilling all criteria of American Diabetes Association to diagnose a patient with DM.[15] Patients who had fasting blood sugar level more than 126 mg/dl were tested twice for two consective days for further confirmation. HbA1c level of all patients was also monitored according to guidelines suggested by American Diabetes Association (2015). Elevated HbA1c level (>6.5%) is considered diagnostic marker for DM. HbA1c level was performed by Microlab-300 (ELITech Group) with randox reagent (Crumlin, County Antrim, United Kingdon) according to manufacturer's guidelines.[16]

Verification of the patient's particulars was done by comparing with the hospital data and the patients who had abnormal blood sugar level and elevated HbA1C level were further referred to the physicians for their treatment. Information about the identity of participating patients was not disclosed at any stage of the study thus all personal information of patients was kept confidential.
Statistical analysis, including, Chi square, odd ratios and p value were calculated using SPSS version17.0.

## Results
During the one year study period, a total of 500 patients diagnosed with TB were recruited for the present study. Among them, 140 patients were screened from Infectious diseases hospital, 126 from Mayo hospital, 80 from Services hospital and 170 from Gulab Devi hospital were enrolled in this study. Out of the 500 TB patients, 74 (14.8%) were found to be diabetic (Fig. 1).

# Fig.1. Overall prevalence of diabetes among TB patients
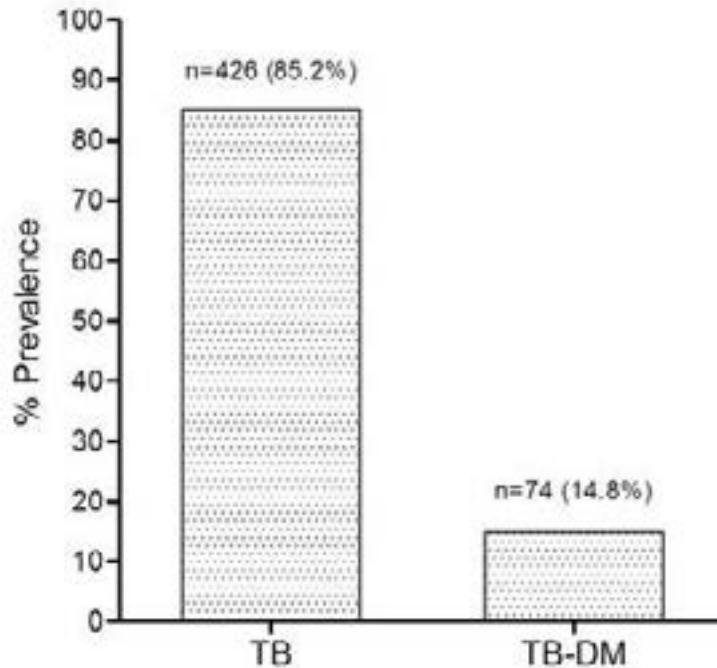


Among these 74 diabetic patients, 22 had been previously diagnosed with the disease, but their blood sugar level was <126 mg/dl at the time of data collection. The remaining 52 patients were diagnosed during this study due to high blood sugar level (>126 mg/dl) and elevated HbA1c level (>6.5%) and those were referred to the physician for further treatment.

Median age of the patients participating in the study was 38 years with the a range of 18–63 years. While the patients having DM mostly belonged to the age group of >57 years (n=26) only 4 patients were found in the 18-27 years age group as shown in Table 1.
Among 500 patients that fulfilled the inclusion criteria, 340 or 68% were male. Similarly, among the 74 with TB-DM co-occurrence, 62.16% (or 46) were male.
The statistical evaluation of socio-economic condition of the participants revealed that among the total participants, maximum number of patients (n=220; 51.6%) were illiterate and a similar trend was observed in the case of known diabetic patients where 54 (72.9%) individuals were illiterate (Table 1). Moreover, one of the socio-demographic factors studied was occupation of the participants that showed maximum co-incidence of TB-DM was spotted in house wives and unemployed individuals with the frequency of 32.43% each (n=24 each). Broadly a significant difference between TB-DM and TB was observed in the category of age groups and education (p≤0.05) while no significant difference was observed in the category of gender, occupation and smoking (p≥0.05)(Table 1).
Moreover, among diabetic patients, 27% (n=20) were known for their smoking history while the majority of these patients were non-smokers having frequency of 73% (n=54). Almost similar trend of smoking was observed in case of non-DM patients with TB.

## Table 1

| Variables | TB-DM (n=74) n (%) | TB (n=426) n (%) | Odd ratio (OR) | 95% Confidence Interval | | *pvalue |
|---|---|---|---|---|---|---|
| | | | | Lower | Upper | |
| **Gender** | | | - | | | **0.24** |
| Male | 46 (62.1) | 294 (69) | 0.737 | **.442** | **1.232** | 0.243 |
| Female | 28 (37.8) | 132 (30.9) | - | - | | - |
| **Age groups (Yrs)** | | | - | 40 | | **0.000** |
| 18-27 | 4 (5.4) | 148 (34.7) | 0.02 | 25.6 | | 0.000 |
| 28-37 | 6 (8.1) | 72 (16.9) | 0.08 | 3.7 | | 0.054 |
| 38-47 | 16 (21.6) | 70 (16.4) | 0.22 | 1.1 | | 0.270 |
| 48-57 | 22(29.7) | 62 (14.5) | 0.35 | 10.3 | | 0.001 |
| >57 | 26 (35.1) | 74 (17.3) | .35 | 12.4 | | 0.000 |
| **Education** | | | - | 14.5 | | **0.005** |
| Higher Secondary | 2 (2.7) | 6 (1.4) | 0.33 | 0.63 | | 0.400 |
| Secondary | 2 (2.7) | 46 (107) | 0.04 | 4.75 | | 0.020 |
| Illiterate | 54 (72.9) | 220 (51.6) | 0.24 | 11.5 | | 0.000 |
| Middle | 0 (0) | 6 (1.4) | 0 | 1.05 | | 0.300 |
| Primary | 16 (21.6) | 148 (34.7) | 0.10 | 4.9 | | 0.026 |
| **Occupation** | | | - | 14.4 | | **0.070** |
| Businessman | 10 (13.5) | 58 (13.6) | 0.17 | 0.000 | | 0.980 |
| Butcher | 0 (0) | 2 (0.4) | 0 | 0.34 | | 0.550 |
| Housewife | 24 (32.4) | 98 (23) | 0.20 | 3.03 | | 0.080 |
| Labor | 8 (10.8) | 60 (14.1) | 0.13 | 0.57 | | 0.440 |
| Milkman | 2 (2.7) | 10 (2.3) | 0.2 | 0.03 | | 0.850 |
| None | 24 (32.4) | 94 (22) | 0.25 | 3.7 | | 0.052 |
| Private Employee | 6 (8.1) | 78 (18.3) | 0.07 | 4.09 | | 0.030 |
| Student | 0 (0) | 20 (4.6) | 0 | 3.6 | | 0.057 |
| Veterinarian | 0 (0) | 6 (1.4) | 0 | 1.05 | | 0.30 |
| **Smoking** | | | - | 0.43 | | **0.508** |
| Smokers | 20 (27) | 100 (23) | 1.20 | **.254** | **758** | 0.508 |
| Non-smokers | 54 (73) | 326 (77) | - | - | | - |

*p≤0.05= significant

## Discussion

LMICs are facing serious issues due to high burden of TB and emerging cases of multi-drug resistant tuberculosis (MDR TB). On the other hand DM has been declared as pandemic in the South Asian region. Furthermore the co-occurrence of these two diseases is creating further complication. This problem of DM-TB co-morbidity is mostly noticed in the LMICs because of endemic TB and DM caused by low socio-economic status and poor living[17]. In this study we determined the prevalence of DM among TB patients of in Lahore, Pakistan. We also determined socio-demographic, clinical and other factors associated with the the co-occurrence of TB and DM.

In the present study, out of 500 TB patients, 74 (14.8%) were recorded as diabetic. Of these, 22 patients were already known DM and due to taking medicine they had fasting blood sugar level <126 mg/dl at the time of data collection. The results of present study are similar to those of Amin et al. that reported co-occurrence of TB and DM in 14% patients of Peshawar, Pakistan[6]. Similarly, another study of Pakistani population conducted by Jabbar et al. in 2006 showed co-occurrence of TB and DM among 11.9% study participants[18].

Age of the patients participating in the present study ranged between 18-63 years while the median age was 38 years. However, most of the study participants who had co-occurrence of TB and DM belonged to the age group of >57 years with frequency of 35.13%. Qayyum et al., reported that 77.7% DM patients positive for TB tests were from age groups of 30-49 years[19]. However, in the present study this pattern is quite varied and highest incidence has been observed among >57 years age group individuals that may be due to weak immune system along with multiple ailments. A study based on Ethiopian population conducted by Amare et al. displayed almost similar association of age and disease as encountered in this study[20]. Therefore, these results predict that the chances of TB-DM leading to co-morbidity increase significantly with age of the patient.

Higher incidence of DM in old age patients was also reported by the study of Baghaei et al.[21]. Analysis of the gender-based distribution revealed that male participants (62.16%) were more affected by both of the diseases as compared to female (37.83%). Similar results were reported by Patel et al. during his study conducted in Indian population that majority patients of TB-DM were male (73.68%) while female were the minority (26.32%).[9] Moreover, similar results were obtained from another study conducted in Pakistan by Jabbar et al. revealed that 60.21% male patients out numbered the female participants (39.78%) in terms of TB-DM co-incidence[18]. The perevelnce of higher ratio of TB-DM may be due to the case that male are exposed to the outer environment more as compared to female and encountered by multiple infections.

The socio-demographic factors being studied in this research included education and occupation. The results revealed that majority of the study subjects (72.97%) were illiterate followed by those of primary class (21.62%). While in terms of occupation, majority of the patients (48%) were not doing any jobs and comprised of house wives and unemployed persons (24% each). The results of present study are in agreement with those of Siddiqui et al. who described maximum prevalence of TB among illiterate and unemployed individuals with the frequencies of 29.60% and 20.4% respectively.[22] Therefore, the study suggests that there is a strong correlation between disease manifestation and the status of employment along with literacy.

In the present study, we also studied the relation of smoking with TB-DM. We found the frequency of smoking was 27% and 23% in TB patients with and without DM respectively. Similar results were reported in Ethiopian population in the study conducted by Qayyum et al. where he found 28.57% frequency of smoking among DM-TB patients[20]. However, in the study of Siddiqui et al., 48.80% patients exhibited smoking that is a comparatively higher frequency of smoking observed than that in the present study.[22]

The present study indicated 14.8% prevalence of DM among TB patients that may serve as pre-disposing factor leading to the latent tubercle infection. Our study showed a significant relation between diabetes and different age groups, especially in old age group. Furthermore, the study revealed an augmenting impact of old age, sex, literacy and employment on the co-occurrence of TB-DM. Therefore, various socio-economic factors as well as behavioral aspects like smoking strongly influence such complicated diseases and there is need of awareness and education among common people to avoid such un healthy habits.

The study also revealed that 14.8% DM-TB prevalence in patients which confirms the fact that people with TB, must be appropriatly screened for DM.

**Conflict of interest**
The authors declare no conflict of interest.

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