Screening of Tuberculosis in Diabetic Patients at a Tertiary Care Hospital in Hyderabad

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ABSTRACT

Aims and objectives: *To Study the prevalence of TB in diabetic patients in a tertiary care hospital in Hyderabad and describe demographic features, socio economic status of diabetic patients who are at risk of developing tuberculosis.*

Methodology: *Patient demographic details were obtained through a questionnaire. The sample size was 100 out of which 96 were enrolled for the study. All the patients with at least 3 TB symptoms were grouped as positive TB symptoms. They were subjected to further investigations (after obtaining their due consent)-random blood sugar and two sputum samples (spot-morning) were collected. Sputum samples were observed for AFB bacilli by Ziehl-Neelson staining using light microscopy. The other patients were grouped as negative TB symptoms.*

Results: *Out of the 100, 4 were excluded. 105 of the patients had positive TB symptoms. 60% of these patients had a random blood glucose level in the range of 171-210mg/dl.Gender, occupation, monthly income was not a major risk factor though age was and the age group at risk was 30-50. Family size and treatment was also a risk for developing TB symptoms. Symptoms were more prevalent in upper middle class. Family history of DM was not a factor for risk of TB. Past history and family history of TB did not affect the risk of developing TB.*

Conclusion: *It was found that the prevalence of TB symptoms was 10.4% among diabetics and prevalence of TB was 10%. TB symptoms were more prevalent with those on oral anti-hyperglycemic drugs.*

Key words: *Sputum, Demographic features, Blood sugar level, Symptoms for tuberculosis*

INTRODUCTION

The current world population is 7.2 billion[1]. This population is affected by a number of diseases both communicable and non-communicable. One of the major non-communicable diseases is diabetes mellitus. 235 million are affected by diabetes i.e. a global prevalence of 8.3%[2]. It has caused 5.1 million deaths in 2013 alone[2]. About 80% live in low and middle-income countries[2]. If these trends continue, by 2035 some 592 million people, or one adult in 10, will have diabetes[2]. The numbers are increasing in developing economies. There will be a 170% increase from 84 to 228 million, in the developing countries. Thus, by the year 2025, >75% of people with diabetes will reside in developing countries, as compared with 62% in 1995[9].

In the Indian scenario, with a population of 1.2 billion[3]there are nearly 65 million diabetics[2]. India has been infamously tagged as the 'Diabetic Capital of the World'. India currently faces an uncertain future in relation to the potential burden that diabetes may impose upon the country. By 2030, India's diabetes numbers are expected to reach 79.4 million[2].

Table 1: Diabetes Statistics in India

DIABETES IN INDIA	
Adult population	762 million
Diabetes Cases	65 million
National Prevalence	8.56%
Diabetes Related Deaths	1,065,052.93
Incidence of Type 1 Diabetes (per 1,00,000	3.00

Source: References 2,3

In India, Hyderabad, one of the major cities in this country has earned the ignominy of 'Diabetic capital of the world'. Out of the total population of Hyderabad, 16.6% suffer from Diabetes[4,5,6]. There are several factors to explain this high number in India. These include genetic, environmental like lifestyle changes leading to obesity[23]. Geographical distribution also plays an important role in this. Studies have shown that the prevalence was three times higher among the urban (8.2%) compared to the rural population (2.4%)[7]. Where on one hand these are the shocking figures of diabetes in India, on the other India is the highest TB burdened country with World Health Organization (WHO) statistics for 2011 giving an estimated incidence of 2.2 million cases of TB in India out of global incidence of 8.7 million cases[10,11]. It is estimated

that about 40% of the Indian population is infected with TB bacteria[11].

Diabetic patients are more susceptible to infections. Infectious processes may be the first manifestation of diabetes mellitus. This can be explained on the basis of increased sugar levels that provide a very favorable environment for the invading microorganisms to grow. Hyperglycemia decreases the ability of many types of immune cells to function properly (e.g., damage to the neutrophil function, depression of the antioxidant system, and humoral immunity)[23] resulting in reduced efficiency in fighting against these infectious agents[12,13,14]. Hence, microbes find an ambient environment in diabetics. Thus, diabetics are more prone for the infections caused by these.

One of them is TB. Tuberculosis contributes to co-morbidity in diabetic patients. Studies have shown that most of the TB infections in diabetics go unnoticed as many of the symptoms such as lethargy, weight loss, anorexia are shared by both these conditions[15,16,17,18]. Moreover, patients with diabetes are at a 2-3 times higher risk of contracting tuberculosis than those without diabetes.[19,20,21,22]

The aim of this study is to establish the relation between TB and diabetic mellitus. The duration of diabetes in this research is taken as a minimum of 5 years for the metabolic changes to occur. The patients will be enrolled on the basis of certain inclusion and exclusion criteria. The sputum samples of the patients with positive TB symptoms will be collected and tested for AFB (Acid Fast Bacilli). The findings so obtained will be recorded and analyzed.

ABBREVIATIONS
DM- Diabetes Mellitus
TB- Tuberculosis
AFB- Acid Fast Bacilli
OPD- Out Patient Department

METHOD:
Study Design: It is a cross-sectional study.
Study Site: This study was carried out at Apollo Institute of Medical Sciences Research General Hospital in Hyderabad.
Study Period: It was spread over two months i.e. from June-July 2014.
Sample Size: 100 diabetic patients coming to the OPD.

A Patient Demographic Chart questionnaire was to be filled in by the patients. Patients were enrolled for this study based on certain inclusion and exclusion criteria, which are as follows.

Inclusion criteria:
-Male/Female patients (>18 years).
-Diabetic patients (duration >5 years) coming to the OPD.

Exclusion criteria:
-Diabetic patients with HIV/Hepatitis.
-Patients on immunosuppressive drugs/steroids.
-Patients on antibiotics for the past 15 days.

Patients were considered diabetic solely based on their history and treatment for diabetes prescribed by a physician in the past. The patients who fulfilled the above criteria were enrolled. Patients were asked about their symptoms that brought them to the hospital. Based on these symptoms they were segregated into TB positive and TB negative symptoms. For a patient to have TB positive symptoms he/she should have at least 3 of the following symptoms.

- Persistent cough for > 2 weeks
- Coughing of blood
- Fever
- Loss of weight
- Night sweats
- Tiredness

The patients who did not have at least 3 of these symptoms or had any other symptoms were considered as TB negative symptoms. Patients with positive symptoms were investigated for TB. Their due consent was taken before taking their samples. The random blood sugar levels were tested using a glucometer. Two sputum samples (morning-spot) were then collected to observe AFB by light microscopy using Ziehl-Neelson staining.

The data collected was analyzed using Microsoft Excel.

Ethical Considerations
Before starting the study, ethical clearance was obtained from the Ethical Committee of Apollo Institute of Medical Sciences and Research. Due consent of the patients was taken before collecting their samples. Confidentiality of the patients was maintained. The patient tested positive for TB was given appropriate treatment by the physicians.

RESULTS
Out of the 100 diabetic patients who came to the OPD, 4 were excluded (one of them was on immunosuppressive drugs, 3 of them were on antibiotics.) Other 96 patients fulfilled the inclusion criteria and were enrolled for the study. Majority of the patients were >50 years of age (59.38%). The mean age was 57.76 years. There were 57 males (59.4%) and 39 females (40.6%). In terms of occupation, among the females 89.74% were homemakers whereas among the males majority were retired (38.5%) followed by self-employment(31.5%) and salaried (29.8%).

Around 87 patients were married (90.6%) and the remaining 9 were under the category of unspecified (9.4%). Coming to the family size, majority i.e. 85 were from nuclear family accounting for 84.3%. In terms of

literacy, 31 have graduated (32.29%), 27 are educated till higher school (28.12%), 15 till primary school (15.63%), 15 were post-graduates (15.63%) and 8 were illiterates (8.33%).

The monthly income of 48 (50%) was between Rs.10,000-15,000, 44 earned >15,000 rupees per month (45.83%) and 4 (4.17%) had a monthly income of 3,000-10,000.

The mean duration of diabetes was 12.28 years. The duration ranged from 5 years to 30 years. More than half had diabetes for <15 years (64.6%). 92 patients had Type 2 DM (95.84%). 2 had Type 1 (2.08%) and remaining 2 had gestational diabetes (2.08%). The treatment taken by these patients was varied. Majority (49) of them were on only oral tablets (51.04%). 55 patients had a family history of DM (55.21%).
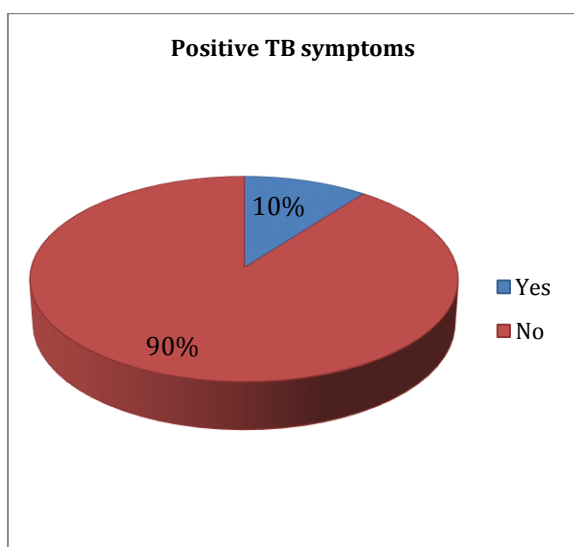

Fig. 2: Patients with positive TB symptoms

Overall, 5 patients had a past history of TB (5.21%) and 4 had a family history of TB (4.17%). 10 patients had positive TB symptoms (10.4%) i.e. they had at least 3 of the TB symptoms mentioned above. Remaining 86 had other symptoms (negative TB symptoms).

8 patients (80%) complained of persistent cough (>2 weeks). 7 had fever (70%). 9 of them complained of tiredness (90%). 4 had loss of weight (40%) and 4 had night sweats (40%).

Table 2. TB Symptoms as observed in 10 diabetic patients

TB Symptoms	Percentage (%)
Persistent Cough (>2 weeks)	80
Coughing of blood	0
Fever	70
Loss of weight	40
Night sweats	40
Tiredness	90

Observations and results seen in Positive TB symptoms:

7 patients were <50 years of age (70%) and 3 were >50 years (30%). 6 were males and 4 were females. In terms of occupation, 5 were salaried, 3 were homemakers, 1was retired and 1 self-employed.

Coming to literacy, 45% were graduates, 22% up to primary school and 22% up to higher school, 11% was illiterate and 1 a post graduate.

6 patients had a monthly income of >Rs. 15,000 and 4 had around 10,000-15,000. The duration of diabetes was <15 years in 9 patients and 1 had for > 15 years. All of them were on oral anti-hyperglycemics. 8 had a family history of DM and 1 had a family history of TB.

Comparison between positive TB and negative TB symptoms:

The patient demographic details between the two groups i.e. positive TB and negative TB symptoms were observed. Majority of patients with positive TB symptoms were in the age group of 30-50 years(70%) whereas majority of patients with negative TB symptoms were in the age group of 51-70 years (62.8%).
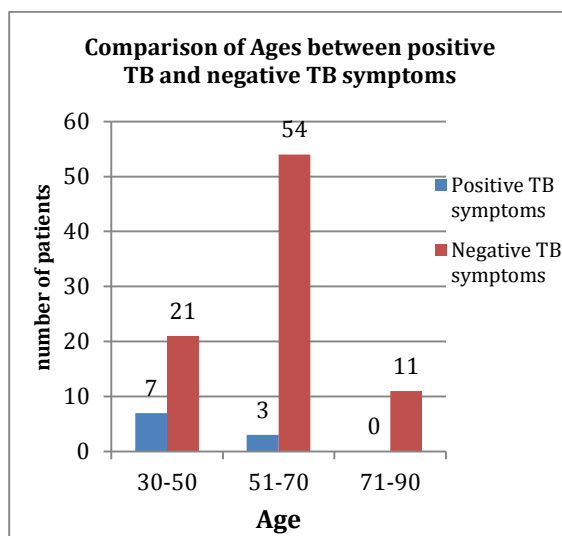

Fig. 3: Comparison of Ages between positive TB and negative TB symptoms

Majority were males in the both groups. The distribution was almost the same in both the groups. In terms of occupation, it was varied in both the groups. 50% of patients withpositive TB symptoms were salaried. More than half of the females were homemakers and majority of males were retired in those with negative TB symptoms.The education was also varied in both the groups. There was no major difference when the two were compared.Morethan half of the patients with positive TB symptoms (60%) had a monthly income of >Rs. 15,000. Almost 51.2% patients

with negative TB symptoms had monthly income between Rs. 10,000-15,000.

More than half of the patients with positive TB symptoms had diabetes for <15 years (90%). Similarly, 69.8% of patients with negative TB symptoms had diabetes for <15years.None of the patients with positive TB symptoms had a past history of TB. 5 patients (5.8%) with negative TB symptoms had a past history of TB. 80% of the patients with positive TB symptoms had a family history of DM. 52.3% of patients with negative TB symptoms had a family history of DM. On the other hand, only 1 patient with positive TB symptoms had a family history of TB and 3 patients (3.5%) with negative TB symptoms had a family history of TB.

Risk Factors associated with TB symptoms

Using Chi square test P values of several variables like age, gender, occupation, education, family size, monthly income, duration of DM, family history of DM, past history of TB and family history of TB were found out. A p-value of less than 0.05 was considered significant. According to this, age (p=0.001), family size (p=0.001) and treatment for diabetes (p=0.03) were significantly associated with TB symptoms. Other factors like gender (p value=0.96), occupation (p=0.11), education (p=0.92), monthly income (p=0.55), duration of diabetes (p=0.39), family history of DM (p=0.09), past history of TB (p=0.43), family history of TB (p=0.32) were not significantly associated with development of TB symptoms.

Table 3: Comparison between patients with positive TB and negative TB symptoms

Age	TB symptoms		p- value
	Yes	No	0.001
30 - 50	70	24.4	
51 - 70	30	62.8	
70 - 90	0	12.8	

Gender	TB symptoms		p-value
	Yes	No	0.96
Male	60	59.3	
Female	40	40.7	

Occupation	TB symptoms		p-value
	Yes	No	0.11
Homemaker	30	38.4	
Retired	10	23.3	
Salaried	50	17.4	
Self employed	10	20.9	

Family Size	TB symptoms		p-value
	Yes	No	0.001
Joint	50	11.6	
Nuclear	50	88.4	

Education	TB symptoms		p-value
	Yes	No	0.92
Illiterate	10	8.2	
Primary school	20	15.1	
Higher school	20	29.0	
Graduate	40	31.4	
Post graduate	10	16.3	

Monthly Income	TB symptoms		p-value
	Yes	No	0.55
3,000-10,000	0	4.6	
10,000-15,000	40	51.2	
>15,000	60	44.2	

Duration	TB symptoms		p-value
	Yes	No	0.39
5 - 15	90	69.8	
16 - 25	10	26.7	
26 - 30	0	3.5	

Treatment for diabetes	TB symptoms		p-value
	Yes	No	0.03
Diet and oral tablets	40	15.1	
Diet and insulin inj.	0	2.3	
Diet, exercise and oral tablets	10	0	
Diet, exercise, oral tablets and insulin inj.	0	1.2	
Exercise and insulin inj.	0	1.2	
Only oral tablets	50	51.2	
Only insulin inj.	0	17.4	
Oral tablets and insulin inj.	0	11.6	

Family History of DM	TB symptoms		p-value
	Yes	No	0.09
Yes	80	52.3	
No	20	47.7	

Past History of TB	TB symptoms		p-value
	Yes	No	0.43
Yes	0	5.8	
No	100	94.2	

Family History of TB	TB symptoms		p-value
	Yes	No	0.32
Yes	10	3.5	
No	90	96.5	

The two sputum samples (spot-morning) of patients with positive TB symptoms were collected and observed for AFB by Ziehl-Neelson staining using a light microscope. Out of these 10, only one patient was sputum positive (both morning and spot). Others were sputum negative.

The Random Blood Sugar levels were also tested using a glucometer.

RBS Levels (gm/dl)	No. Of patients
<170	10%
171-210	60%
211-250	10%
251-289	20%
>290	0

DISCUSSION

Earlier studies have established the link between TB and DM. Diabetes is one of the major factors for the development of TB[17,18,23,24,25]. In this study 10 patients had positive TB symptoms (10.4%) and out of this 10, 1 was tested positive for TB (10%). Thus, the prevalence was 10%. This is clearly more than what was what found out in a study in Ethiopia [18] where the prevalence was 6.2%. The higher rate observed in this study maybe because of the reason that there are higher rates of diabetes and TB in India. Though a study done in India in 2002[23] showed a prevalence of 6%, the prevalence was 27% by radiological findings. The prevalence rates were very low in Korea (2.12%).[27] A study in Tanzania observed a prevalence of pulmonary TB of 5.4%.[27]On the other hand the results of this study are in line with studies done in Pakistan where prevalence rates were 9.5% [25].

These differences arise due to a variation from region to region in the prevalence of TB among diabetes. Also, these rates are affected by the national prevalence of TB and diabetes in the respective countries. In the present study the patient's socio-demographic details were also observed. The major difficulty faced by the present study is the low sample size due to time constraints. Due to this, there was only one patient who was tested TB positive. The socio-demographic factors could not be compared between patients who were tested negative and those tested positive. Thus, the observations and results were restricted to just patients with positive TB symptoms and negative TB symptoms.

Majority of the patientswith positive TB symptoms were in the age group of 30-50. This relates to the findings seen in a study in Pakistan[25] where the prevalence was higher in the 4th and 5th decade. This is in contrast with the findings found in Australia where it was found that age did not modify the effect of DM on risk of TB[24]. TB symptoms were more prevalent in males. This result was consistent with the study in Pakistan[25] where there was a male predominance (77.22%).The education of the patient had no effect on the development of TB symptoms.

Majority of the patients were from upper middle class (>15,000 Rs. Monthly income). The present study had only included patients with diabetes for >5yrs. This criterion was used to see the risk of TB developing in patients after the metabolic changes have occurred in the body in response to diabetes.

Patients with positive TB symptoms had a duration ranging from 5-15 years.A similar finding was observed in study in Ethiopia[18] where high prevalence was observed among those who had DM for more than 10 years.It was found out that family size was a major risk factor for development of Tb symptoms.

The major symptoms were cough, fever and tiredness. This is almost similar to results in Pakistani study where the major symptoms were cough, fever and weight loss.[25]

A past history of TB had no correlation with a risk of developing TB. This is in contrast to what was found out in a study in Ethiopia[18] were there it was revealed that patients with a previous risk of TB were significantly associated with developing smear positive PTB. Family history of TB was not associated with development of TB. This is in line with the observations made by Ezunget al.[23].

More than half of the patients with a family history of DM had positive TB symptoms. Another finding observed in this study was the treatment taken by the patients for diabetes. All the TB positive symptom patients were on oral anti-hyperglycemic drugs. Hence, use of insulin was not associated with TB. This is in contrast with the results of the study in Australia where the risk is greater among those treated with insulin.[24]

60% of the patients with positive TB symptoms had random blood glucose level in the range of 171-210 gm/dl.

Limitations
The major limitation of this project was time and financial constraints. This study did not include several other risk factors associated with TB like smoking, alcohol consumption, BMI, other metabolic diseases (hypertension, obesity), and coronary heart disease. Further, more accurate and advanced investigations could have been employed like HbA1c levels, X-Ray and bacterial cultures to get specific and better results. More studies are suggested to be carried out to explore the problems in diabetes and TB patients, which are in high numbers in India and, by doing so the figures can be brought down.

A comparison could have been made with non-diabetic patients and also using just light microscopy (for AFB) cannot be considered a standard test for diagnosis of TB.

Suggestions
After seeing the results of this study, it is suggested to routinely screen diabetic patients for not only TB but various other infectious diseases so that the high prevalence of these in diabetics can brought down. Also, socio-demographic factors that have a risk of developing TB should be taken into account and patients falling under these categories should be screened separately. Awareness should be created among diabetics about the high risk of developing infectious diseases.

CONCLUSION
Diabetes (especially Type II) is an important risk factor for development of TB. Gender is not a major factor for development of TB symptoms. Patients in the age group of 30-50 were more prone to develop TB. TB symptoms were more prevalent with those on oral anti-hyperglycemic drugs. Family size was major risk factor for development of TB symptoms.

Education had no correlation with development of TB symptoms. So is the case with occupation and economic status of the patients. Family history of DM and family history of TB was not associated with development of TB symptoms. Even past history of TB did not affect the development of TB. Duration of diabetes was also not implicated as a risk factor of developing TB.On the other hand treatment taken for diabetes was a risk factor for TB. Persistent cough, fever and tiredness are the most common symptoms.

Overall, the prevalence of TB symptoms among diabetics was found to be10.4% and the prevalence of TB among diabetics was 10%.

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