Original Article

Diabetes Mellitus as a Risk Factor for Tuberculosis: A Community Based Case Control Study

Prashant R. Kokiwar, Arun K. Soodi Reddy

Department of Community Medicine, Malla Reddy Institute of Medical Sciences, Hyderabad, Telangana, India

Abstract

Background: Prevention of diabetes in the general population can help reduce the incidence of tuberculosis. Hence it is necessary to document that diabetes is strongly associated with tuberculosis as a risk factor. **Objective:** To study if diabetes is associated with tuberculosis compared to controls. **Materials and Methods:** A community based case-control study was carried out. 215 newly diagnosed cases of tuberculosis on treatment for not more than three months were selected randomly from the randomly selected tuberculosis unit. 215 neighbourhood controls were selected. They were matched for the age group of ± 10 years and sex. Fasting blood sugar (FBS) was estimated using a glucometer. **Results:** Tobacco chewing, residence and family history of TB were significantly more in cases ($P < 0.05$). Mean BMI was significantly lower in cases compared to controls. The proportion of TB cases among the known cases of diabetes was 67% compared to 33% in controls, which was statistically significant. Mean FBS was significantly higher in cases compared to controls ($P < 0.05$). The odds of cases being diabetic was 2.456 times more than those of controls. On binary logistic regression, diabetes was an independent risk factor for tuberculosis. Other independent risk factors were tobacco chewing, and family history of TB. **Conclusion:** Family history of tuberculosis, and tobacco chewing were positively associated with tuberculosis whereas body mass index was negatively associated with tuberculosis. Diabetes was significantly associated with tuberculosis.

Keywords: Diabetes, morbidity, mortality, prevalence, tuberculosis

Introduction

Tuberculosis is the second leading cause of mortality among the infectious diseases universally. Similarly same is true for diabetes also.[1] As per the global report from the World Health Organization (WHO) it has been stated that in 2015, new cases occurrence was to the tune of 10.4 million. Fourteen lakhs (1.4 million) people died from tuberculosis (TB) in the same year as per WHO.[2] The cases due to diabetes were to the tune of 415 million in the same year. Five million people died from diabetes.[3] Most of the cases of the diabetes as well as that of tuberculosis are from low and middle income countries. More prevalence of diabetes means a public health challenge for the control of tuberculosis. This is due to the fact that diabetes is a risk factor for tuberculosis. Not only that, it also affects the outcome of tuberculosis.[4,5]

On one side the incidence of diabetes is increasing and on the other side, the incidence of tuberculosis is decreasing. The average decrease in the incidence of tuberculosis is about 15% and currently it is around 18%. Even then, tuberculosis remains a global public health problem. The mortality due to tuberculosis in absolute numbers was 15 lakhs in the year 2014 and about 96 lakhs were struck by it. The problem is compounded by occurrence of multidrug-resistant TB (MDR-TB). Those with co-morbidities like diabetes and HIV suffer more morbidities and are at risk of mortality. Thus, these problems associated with tuberculosis are a challenge to our overall goal of elimination of tuberculosis by 2025 for India and by 2030 globally.[6,7]

At present, it has been estimated that there are 9.6 million new cases due to tuberculosis every year.[6] Among these, it has been stated that around one million have both tuberculosis and diabetes.[8,9]

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Address for correspondence: Dr. Prashant R. Kokiwar, Department of Community Medicine, Malla Reddy Institute of Medical Sciences, Hyderabad, Telangana, India.
E-mail: pkokiwar@gmail.com

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Prevention of diabetes in the general population can help reduce the incidence of tuberculosis. Hence it is necessary to document that diabetes is strongly associated with tuberculosis as a risk factor. With this background, this case control study was carried out to study the association between diabetes and tuberculosis.

Material and Methods

Community based case control study was carried out from January 2022 to June 2022. OpenEpi software was used to calculate the sample size. Alpha value was considered as 95%, the power of the study as 80% and it was decided to take 1:1 for cases and controls. Along with these parameters, the least extreme odds ratio to be detected as 2.65 (proportion of tuberculosis patients with diabetes as 13.6% and proportion of controls with diabetes as 5.6%),[10] the sample size was 215 in each group of cases and controls.

The study was being carried out in Medchal District. All TB patients here formed the reference population. Out of all the tuberculosis units (TU) in the Medchal District, Dundigal TU was selected randomly. This TU has a total population of 5,48,800. The estimated prevalence of TB in this TU is 180.39 per one lakh population. A total number of pulmonary tuberculosis patient's data was obtained from DTCO, Medchal for the Dundigal TU. From this total number, 215 TB patients were selected randomly as cases. The 215 neighbourhood controls were age and sex matched control of the TB patient. The control was selected only if he had no presumptive symptoms suggestive of TB like cough for more than two weeks, chest pain, hemoptysis, weight loss of more than 10% body weight in last three months. After visiting the house of a case, a third house to the right of the case house was taken and age and sex matched control was selected. If there are more than one eligible controls, in the selected house, then one was selected randomly by tossing the coin. If there are no eligible controls or the control person is not willing or not available in that house, then the immediate next house was searched and the procedure continued till the eligible control was found and was willing.

In the present study, age more than 30 years including both males and females, newly diagnosed tuberculosis cases (within last three months) were included as cases. It was ensured that controls are free of tuberculosis. They were matched for age (±10 years) and gender. They were from immediate neighbourhood of the cases. Patients or controls not willing to give the data or not willing to participate in the study, anyone having previous exposure to TB in preceding five years or having asthma or having diseases related to the pulmonary system were excluded.

Institutional Ethics Committee permission was obtained vide letter No. MRIMS-DHR-IEC-97/2021 dated 27/11/2021. District Tuberculosis Program Officer, Medchal was contacted and their permission for data access was obtained. The cases and controls were given the patient information sheet and their consent was taken.

The case definition for the present study was an incident tuberculosis case on treatment for not more than three months. Such 215 cases were selected randomly from the randomly selected TU. 215 controls who were in the neighbourhood of the selected cases were included. They were matched for age group of ± 10 years and sex.

After permissions and Ethics formalities the study was initiated. A list of all incident TB cases was obtained from the DTCO, Medchal in the Dundigal TU of Medchal District. From this list, 115 cases were randomly selected. They were visited and informed consent was sought.

Baseline characteristics like age, sex, education, occupation, income, addictions etc., were collected in the pre designed, pre tested, semi structured study questionnaire. They were informed one-day prior about the fasting blood sugar collection by glucometer. The glucometer used was "blood glucose monitoring system Model no. APG01 manufactured by Apollo Pharmacy." The next day early morning after ensuring fasting of 8-10 hours, and taking all aseptic precautions, the capillary blood sample was collected by skin prick method using a sterile needle. The glucometer is kept on with one strip and the blood drop is touched to the strip. Within one minute the glucometer gives the reading which was recorded in the questionnaire. The glucometer was standardized as suggested by WHO.

For proportions chi square test was used. *t* test was used for mean values. Two sided *P* value less than 0.05 was taken as statistically significant. Multivariable analysis was done using the binary logistic regression model. IBM Corp. Released 2011: IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp was used for data analysis.

Results

The total number of male was more than females even though the difference was not statistically significant. This may be due to more non-response from females. Only 12 were from rural areas. This is because, most of the area of the selected TU is now under the Greater Hyderabad Municipal Corporation area. Even though this finding is statistically significant here, but because of very low number of rural dwellers in this study, statistical significance needs to be interpreted with caution. Among the factors studied, being from rural area, being illiterate, having a family history of tuberculosis, smoking, tobacco chewing and known case of diabetes were found to be significantly associated with tuberculosis ($P < 0.05$) as seen from Table 1.

The mean body mass index, SBP, and DBP were significantly lower among the cases compared to the controls ($P < 0.05$). The mean fasting blood sugar was significantly higher in the cases compared to the controls ($P < 0.05$). The mean age and per capita income were similar in the two groups [Table 2].

Significant variables on univariable analysis were entered in the multiple logistic regression model. The predictive accuracy of model increased from 50% to 77.2% after entering the variables like residence, education, family history of TB, smoking, tobacco chewing, known case of diabetes, body mass index, SBP, DBP and FBG. These variables were able to explain 43.8% of the variation in tuberculosis (Nagelkerke R squared = 0.438). Hosmer Lemeshow test was not significant and the Omnibus test of model coefficients was significant which meant that the model was good for predicting tuberculosis. Out of these variables, only known cases of diabetes, SBP, tobacco chewing, family history of TB and BMI were significantly and independently associated with tuberculosis [Table 3].

Table 1: Risk factors of tuberculosis

Variables	Case	Control	*P*
Sex			
Female	72 (49.7%)	73 (50.3%)	0.919
Male	143 (50.2%)	142 (49.8%)	
Residence			
Rural	10 (83.3%)	2 (16.7%)	0.019
Urban	205 (49%)	213 (51%)	
Marital status			
Married	182 (48.5%)	193 (51.5%)	0.112
Unmarried or Widowed	33 (60%)	22 (40%)	
Education			
Illiterate	99 (62.7%)	59 (37.3%)	<0.001
Higher	36 (42.9%)	48 (57.1%)	
Primary or Secondary education	80 (42.6%)	108 (57.4%)	
Occupation			
Business or service	34 (56.7%)	26 (43.3%)	0.059
Home-maker	43 (56.6%)	33 (43.4%)	
Farmer/labor	105 (44.1%)	133 (55.9%)	
Not employed	33 (58.9%)	23 (41.1%)	
Contact with TB case			
Yes	1 (25%)	3 (75%)	0.315
No	214 (50.2%)	212 (49.8%)	
Family history of TB			
Yes	41 (95.3%)	2 (4.7%)	<0.001
No	174 (45%)	213 (55%)	
Smoking			
Yes	57 (64.8%)	31 (35.2%)	0.002
No	158 (46.2%)	184 (53.8%)	
Alcohol			
Yes	83 (53.5%)	72 (46.5%)	0.269
No	132 (48%)	143 (52%)	
Tobacco			
Yes	48 (85.7%)	8 (14.3%)	<0.001
No	167 (44.7%)	207 (55.3%)	
Known case of diabetes			
Yes	63 (67%)	31 (33%)	<0.001
No	152 (45.2%)	184 (54.8%)	

Discussion

In the present study we found that diabetes was a strong predictor of tuberculosis. Jeon and Murray[11] carried out a systematic review of observations studies in 2008. They included 13 studies which had 1,786,212 participants with 17,698 TB cases. They observed that the relative risk was 3.11, 95% CI 2.27–4.26. In the present study, the odds for development of tuberculosis among diabetics was 2.456 (95% CI = 1.31-4.61) which similar to that reported by Jeon and Murray.[11] They also concluded that the risks of tuberculosis were increased in diabetics irrelevant of population and study design. They stated that the odds ratio from the case control studies was in the range of 1.16 to 7.83. The odds ratio in the present study was 2.456.

The BMI found lower among the cases may be because of the weight loss that is commonly associated with Tuberculosis. Since the cases were chosen upto three months after diagnosis, the initial few weeks can be associated with weight loss giving the current findings

Another case control study[12] conducted from Tanzania in 2011 found that the risk of tuberculosis among diabetics was 2.2 times more among diabetics compared to non-diabetics which was dependent on the HIV status. They also reported that the prevalence of diabetes among cases was 16.7% compared to 9.4%. However, we found a greater prevalence in cases (67%) compared to controls (33%).

One more systematic review and meta-analysis was conducted by Foe-Essomba *et al.*[13] in 2021. They included 10 cohort studies, 14 cross sectional studies and 23 case control studies. In all, it had 5,03,760 cases and 35, 96, 845 controls. From case control studies, the odds of getting tuberculosis for diabetics was 2.4 (95% CI = 2.0 to 2.9) compared to non-diabetics. We

Table 2: Comparison of mean SBP, DBP, BMI and FBG in cases and controls

Characteristics	Mean±2 SD		*P*
	Cases	Controls	
Body mass index (kg/m^2)	20.82±5.01	25.63±4.84	<0.001
Systolic blood pressure (mmHg)	117.59±19.59	125.15±17.89	<0.001
Diastolic blood pressure (mmHg)	79.01±12.96	81.93±10.74	0.011
Fasting blood glucose (mg/dl)	120.07±55.19	109.48±41.97	0.026
Age	47.94±12.07	48.63±11.78	0.553
Per capita income (INR)	4533.70±2199.39	4791.45±2805.75	0.290

t-test was used to calculate the *P*

Table 3: Logistic regression model for risk factors of tuberculosis

	B	*P*	Odds ratio	95% C.I. for odds ratio	
				Lower	Upper
Residence (Urban)	-1.562	0.072	0.210	0.038	1.147
Education (Illiterate)		-	1		
Education (primary or secondary)	-0.597	0.065	0.551	0.292	1.038
Education (higher)	0.072	0.834	1.074	0.551	2.096
Family history of TB	2.911	<0.001	18.372	4.053	83.280
Smoking (yes)	0.496	0.115	1.642	0.886	3.043
Tobacco chewing (yes)	1.092	0.017	2.980	1.218	7.292
Known case of DM (yes)	0.899	0.005	2.456	1.310	4.606
BMI (kg/m^2)	-0.177	<0.001	0.838	0.794	0.884
SBP (mmHg)	-0.026	0.010	0.974	0.955	0.994
DBP (mmHg)	0.025	0.114	1.025	0.994	1.058
FBG (mg/dl)	0.002	0.371	1.002	0.997	1.008
Constant	6.150	<0.001	468.798		

also found exactly similar odds of 2.456 (95% CI = 1.31-4.61) for diabetics compared to non-diabetics.

Al-Rifai *et al*.[14] also conducted one systemic review and meta-analysis in 2017. Overall they included 44 studies as per their eligibility criteria. These were from 16 countries and the total number of participants were 58,468,404. They found that the odds of tuberculosis among the diabetics was 2.09 (95% CI 1.71–2.55) from the case control studies. This odds ratio is slightly lower compared to the present study odds ratio of 2.456.

It has been projected that the number of diabetics will increase to 642 million by the year 2040.[15] Considering the relative risk of 3.59 from the available research, the tuberculosis-diabetes co-morbidity is going to pose a public health challenge in the near future.[16] Tuberculosis usually occurs among the poor population and now-a-days the diabetes is also becoming more common in them. Thus, diabetes may pose a challenge to the control of tuberculosis. Hence, lifestyle modifications for prevention of diabetes to effectively fight the tuberculosis are the need of the hour.

The present study was carried out on a limited sample size from one randomly selected area. The findings may not be generalizable, but given that the results are very close to the findings of the systematic review and meta-analysis, the issue of generalizability may not be affecting the present study results. All care was taken to avoid any biases due to measurement. Most of the data was direct observation or direct measurements on the individuals except education, occupation and income. Here for these particular variables, the data was dependent on the participants only. Hence, chances of bias for these data cannot be ruled out. Confounding bias was taken care by matching and also during analysis by applying the binary logistic regression analysis. But, we did not take into account the effect of HIV positive in this study. As per one study[12] HIV had a significant interaction effect with diabetes.

Actual biases possible were selection bias which was removed by simple random sampling of cases and proper selection of controls. Those who were on treatment were only taken as cases to avoid the selection bias in cases. For controls, presumptive check list was used to rule out TB. Interviewer bias and recall bias were possible which was removed by actual observation and direct measurements. Confounding bias which is common has been taken care by matching during data collection and by applying logistic regression during analysis. It was a community based case control study, hence hospital related biases have been removed.

Present study findings that diabetes is a strong risk factor for TB is of immense primary health care importance. As we know, the rural societies are the present day transition societies. Their income is increasing and naturally they are more inclined towards less physical activity, sedentary lifestyle and high fat diet. These factors increase the risk of diabetes and the prevalence of diabetes is also increasing in the rural parts of India. Given this backdrop along with lack of secondary and tertiary care facilities in rural India, primary health care has to take up this challenge. In addition to the proper implementation of diabetes component of the National Program for prevention and control of non-communicable diseases, the primary health care workers also need to be trained in the active case finding of TB among known diabetics.

Conclusion

Diabetes was a significant risk factor for tuberculosis after adjusting for age, BMI, tobacco chewing and family history of tuberculosis and other variables. Hence, all diabetics should be regularly screened for symptoms of tuberculosis. At the same time, efforts made towards prevention of diabetes in the community can reduce burden of tuberculosis in the community.

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Conflicts of interest

There are no conflicts of interest.

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