Original Research Article

Collision of two epidemics: prevalence of diabetes in tuberculosis patients in urban Ludhiana

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ABSTRACT

Background: Co-association between tuberculosis (TB) and diabetes has been observed for more than 2000 years. The burden of the both diabetes and tuberculosis is very high in India. Diabetes in TB patient decreases the success of anti-tubercular therapy and overall cure rates, which causes social and economic burden to country. The objective of the study was to find out the prevalence of diabetes mellitus in patients with tuberculosis under RNTCP treatment.

Methods: This cross-sectional study was conducted in DOTS centers under Civil Hospital TU of Ludhiana, Punjab. 300 TB cases, above 18 years of age were included and screened for diabetes. Patients were interviewed regarding demographic profile and family history of diabetes. Height, weight, blood pressure, BMI and waist hip ratio were recorded.

Results: The prevalence of diabetes in tuberculosis patients was found to be 21.3% (known diabetics- 6.3%, new diabetes cases- 15%). There was a statistically significant association of diabetes with older age and high BMI.

Conclusions: Specific guidelines for management of the dual disease may help in improving the overall success of treatment.

Keywords: Tuberculosis, Diabetes mellitus, Epidemics, Fasting blood sugar

INTRODUCTION

The co-association between tuberculosis (TB) and diabetes has been observed for more than 2000 years by Avicenna (780-1027AD).¹ Before the discovery of insulin the diagnosis of diabetes was a death sentence within five years and the usual cause of death was tuberculosis.²

A probable cause of increased incidence of pulmonary TB in diabetics could be due to the defective host defences and immune cell functions, with predominantly an impairment of the cell mediated immune response. Previous studies have shown that diabetic patients are three times more prone to develop tuberculosis; diabetes mellitus (DM) is also recognized as an independent risk factor for lower respiratory tract infection.³⁴ Treatment response to anti-tubercular treatment (ATT) is also varied in diabetic patients in the form of delayed treatment response, and treatment failure, relapses, drug resistance and more numbers of deaths.⁵

ATT drugs also decrease the effectiveness and concentration of anti-diabetic drugs and make blood sugar control difficult. On the other hand, there is reported reduction of 53% in rifampicin concentration with co-administration of oral hypoglycaemic drugs, raising concern for treatment failure and development of drug resistance.⁶

Approximately 95% of tubercular patients and 70% of diabetic patients are living in low and middle income
countries.\textsuperscript{7,8} India has high burden of both TB and DM. In India, 2.2 million people are diagnosed to have tuberculosis annually with mortality rate of 0.24 million per year. India contributes 20-25\% cases of all tuberculosis patients globally.\textsuperscript{9} India has the second largest population of diabetics in the world.\textsuperscript{10} So there is an expected increase in patients with both TB and DM.

In recent times, a significant thrust has been placed on the burgeoning dual epidemic of TB and diabetes both globally and in India because of the huge social and economic burden on individuals and countries. In 2011 the World Health Organization (WHO) and the international union against tuberculosis and lung disease (IUATLDS) have developed a collaborative framework and guidelines for joint management of TB and DM, recommends bidirectional screening for both diseases.\textsuperscript{11} Studies that screened for DM among TB patients reported a wide range of DM prevalence among TB patients, ranging from 6.5 to 44\%.\textsuperscript{12-20} There is a paucity of data regarding the prevalence of diabetes among tuberculosis patients in Punjab and this study hopes to bridge that gap.

**METHODS**

This facility-based cross-sectional study was conducted under department of community medicine of Christian Medical College, Ludhiana, Punjab in DOTS center providing ATT therapy for TB patients under civil hospital tuberculosis unit (TU) urban of Ludhiana. The TU is a sub district supervisory unit established for 5 lakh population under RNTCP. The reference population is all TB patients taking directly observed treatment short course (DOTS) under RNTCP. The sample size was estimated based on previous studies with an assumed prevalence of 25\% and a precision of 20\% using the formula n=4pq/d\textsuperscript{2} the sample size was calculated as 300. All TB cases more than 18 years of age, including new and re-treatment cases, sputum positive, sputum negative and extra-pulmonary cases registered with the revised national tuberculosis control programme (RNTCP) and currently on treatment were included in the study during the period 1\textsuperscript{st} January to 31\textsuperscript{st} December 2015. The study was approved by the ethics committee of CMC, Ludhiana.

A list of all TB patients currently on DOTS was made from all the DOTS centers. The days of DOTS therapy ascertained for all patients were listed. On the first visit, the purpose of the study was explained to the participant in the local language and participant information sheet written in Hindi/Punjabi (local language) was provided. All the consenting participants were interviewed using the pretested questionnaire, based on the WHO- STEPS questionnaire along with capturing demographic data.

Family history of diabetes and family history of TB was noted. Information regarding category of DOTS treatment, type of TB (pulmonary, extra pulmonary), sputum status, weight of patient at the initiation of treatment and current phase of treatment (IP, CP) were entered from the TB treatment card. For the patients who have already been diagnosed for diabetes, details regarding the time of diagnosis and treatment were collected.

The height, weight, body mass index (BMI), blood pressure (BP), waist circumference (WC) and hip circumference (HC) was measured by using portable electronic scales or monitors, as per WHO- STEPS methodology.\textsuperscript{21} The participants were asked to come the next day after overnight fasting and the fasting capillary blood glucose levels of the patient were measured using a standardized glucometer. Diabetes was classified as per WHO criteria. If FBS was less than 110 mg\%, we consider them as non-diabetic patients. If fasting blood glucose was more than or equal to 126 mg\% we considered them as diabetic patients and included in study. Patients whose FBS was between 110 and 125 mg\%, they were considered as having impaired glucose tolerance and was not considered as diabetic. Patients with abnormal fasting blood were referred to the nearby government dispensary.\textsuperscript{22} Tuberculosis patients were categorised in to sputum smear positive pulmonary tuberculosis, sputum negative pulmonary tuberculosis and extra pulmonary tuberculosis according to revised national tuberculosis control programme (RNTCP) diagnostic criteria new and re-treatment cases are noted separately.\textsuperscript{23}

The data was entered in microsoft excel sheet and analysed using SPSS software. The results were expressed in frequencies and proportions. The significance of association of different factors with diabetes was tested using chi-square test. A p value of <0.05 was taken as statistically significant.

**RESULTS**

Among the total 300 tuberculosis patients included in the study, prevalence of diabetes was found to be 21.3\% and prevalence of pre-diabetes found to be 16.7\% by using the diagnostic criteria as mentioned in the methodology. Out of the 64 diabetic patients 45 patients were newly detected diabetics (70.3\%) and the remaining 19 (29.6\%) were already known patients of diabetes.

The characteristics of the study participants are shown in (Table 1). The mean age of the tuberculosis patients was 34.96 years with a standard deviation of 14.88. More than 60\% of the TB patients were aged less than 40 years. Majority were males and constituted 61\% of the study participants. Occupation-wise, the largest proportion consisted of unskilled workers.

The proportion of the tuberculosis patients with BMI <18.5 was 37.3\%. The mean BMI of the whole study population was 19.29 kg/m\textsuperscript{2} (SD=3.44). Abdominal obesity as indicated by high waist circumference and high waist hip ratio was seen in 27.4\% of females and 8.7\% of
males. Nearly two thirds (70.3%) of the participants had pulmonary TB and the remaining 29.7% had extra-pulmonary TB. Among the cases of extra-pulmonary TB, maximum 49.4% had pleural effusion.

Table 1: Characteristics of study participants.

| Categories          | Frequency (N) | Percentage (%) |
|---------------------|---------------|----------------|
| **Age groups (in years)** |               |                |
| ≤20                 | 57            | 19             |
| 21–30               | 100           | 33.3           |
| 31–40               | 54            | 18             |
| 41–50               | 37            | 12.3           |
| 51–60               | 30            | 10             |
| >60                 | 22            | 7.3            |
| **Sex**             |               |                |
| Male                | 183           | 61             |
| Female              | 117           | 39             |
| **Occupation**      |               |                |
| Factory workers     | 111           | 37             |
| Others              | 189           | 63             |
| **State of origin** |               |                |
| Punjab              | 165           | 55             |
| Others              | 135           | 45             |
| **BMI (kg/m²)**     |               |                |
| <18.0 (underweight) | 112           | 37.3           |
| 18.0-22.9 (normal)  | 147           | 49             |
| 23.0-24.9 (overweight) | 20         | 6.7           |
| >25 (obesity)       | 21            | 7              |
| **Type of TB**      |               |                |
| Sputum positive pulmonary | 140         | 66.3          |
| Sputum negative pulmonary | 71          | 33.6          |
| Extra pulmonary     | 89            | 29.7           |
| **Treatment category** |             |                |
| CAT I               | 209           | 69.7           |
| CAT II              | 77            | 25.7           |
| CAT IV MDR          | 14            | 4.7            |

Table 2: Prevalence of diabetes mellitus in TB patients across different groups.

| Variables               | Non-diabetic (<110) N (%) | Pre-diabetic (110-125) N (%) | Diabetic (≥126) N (%) | P value |
|-------------------------|---------------------------|-----------------------------|-----------------------|---------|
| **Sex**                 |                           |                             |                       |         |
| Male                    | 112 (61.2)                | 29 (15.8)                   | 42 (23)               | 0.666   |
| Female                  | 74 (63.2)                 | 21 (17.9)                   | 22 (18.8)             |         |
| **Treatment category**  |                           |                             |                       |         |
| CAT I                   | 132 (63.2)                | 29 (13.9)                   | 48 (23.0)             | 0.328   |
| CAT II                  | 46 (59.7)                 | 17 (22.1)                   | 14 (18.2)             |         |
| MDR                     | 8 (57.1)                  | 4 (28.6)                    | 2 (14.3)              |         |
| **BMI**                 |                           |                             |                       |         |
| <18.0 (underweight)     | 75 (67.0)                 | 20 (17.9)                   | 17 (15.2)             | 0.001   |
| 18.0-22.9 (normal weight) | 96 (65.3)                | 23 (15.6)                   | 28 (19.0)             |         |
| 23.0-24.9 (overweight)  | 10 (50.0)                 | 2 (10.0)                    | 8 (40.0)              |         |
| >25 (obesity)           | 5 (23.8)                  | 5 (23.8)                    | 11 (52.4)             |         |
| **Sputum status**       |                           |                             |                       |         |
| Sputum positive pulmonary TB | 83 (59.2)             | 23 (16.4)                   | 34 (24.2)             | 0.409   |
| Sputum negative pulmonary TB | 45 (63.3)           | 11 (15.4)                   | 15 (21.1)             |         |
| Extra pulmonary TB      | 58 (65.2)                 | 16 (18.0)                   | 15 (16.8)             |         |

The comparison of diabetes mellitus prevalence among tuberculosis patients across different groups is shown in (Table 2). Among the variables there was a statistically significant association with older age, higher BMI in diabetic individuals. There were no statistically significant association with sex distribution, sputum positivity and category of tuberculosis treatment in diabetics. The mean age of patients with diabetes was 48.56 years with a standard deviation of 14.23. There was a higher prevalence for diabetes in older population above the age of 40 years more than half of TB cases were found to be diabetic, comparing with all tuberculosis
patients which was statistically significant (p<0.001). The mean BMI of diabetic patients was 20.74 kg/m² (SD=4.20). The higher BMI in diabetic individuals was found to be statistically significant (p<0.001). There was no statistically significant relation in the treatment category with diabetics.

DISCUSSION

The prevalence of diabetes mellitus in India reported by Anjana et al ranges from 5.3% to 13.6% in different regions and pre-diabetes from 8.1% to 14.6%. The prevalence of DM in Punjab is around 13.6% and pre-diabetes is 14.6%. In this study we found overall prevalence of diabetes in TB patients was 21.3% including both previously known 6.3% and newly diagnosed cases 15%, which was high comparing with general population. The similar high prevalence of diabetes in tuberculosis patient was also reported in studies from other regions of India, and abroad.

A study from Kerala by Balakrishnan et al reported diabetes prevalence of 44% in tuberculosis patients. In this study they had used HbA1c >6.5% as diagnostic criteria. A study from Tamil Nadu by Viswanathan et al reported diabetes prevalence of 25.3% in TB patients. Study from Pondicherry study by Raghuraman et al also showed higher diabetic prevalence of 29% in tubercular patients. Study from south Mexico reported prevalence of diabetes of 29.63% in tubercular patients.

In our study we found that 16.7% of tubercular patients were having impaired glucose tolerance. Similar high prevalence of impaired glucose tolerance of 16.98% was also reported by Jain et al. But they have used oral glucose tolerance test for diagnosis.

Our study has shown a significantly higher prevalence of diabetes in older population. Mean age of diabetic patients was 48.56±14.238 years, mean age of pre diabetic patients was 33.28±10.868 years, and mean age of non-diabetic patients was 30.74±13.238 years with p value 0.000. Similar study reports are there from India.

The mean BMI of diabetic patients was 20.745±4.207 kg/m², the higher BMI in diabetic individuals was found to be statistically significant (p=0.001). This finding was consistent with other study reports by Balakrishnan et al, and Manoj et al from Kerala and the finding was differed with the finding of study by Raghuraman et al from Puducherry.

In our study proportion of diabetics was more 24.3% in pulmonary TB as compared to 18% extra pulmonary TB, but the association was not statistically significant (p=0.466). The study done by Viswanathan et al from Tamil Nadu reported that pulmonary TB compared to extra pulmonary TB was associated with a higher risk of diabetes with an odds ratio of 3.06 (95% CI 1.69–5.52, p<0.001).

There was no significant association between RNTCP category of treatment and diabetes in our study with p value 0.328. Similar findings were reported by other studies from south India.

CONCLUSION

The study shows high burden of diabetes in tubercular patients. It is recommended that the bi-directional screening for DM and TB is very important. There is need to formulate standard guidelines for management of both diseases together. Before that, there is a need for future research to answer many questions about the co-management of diabetes and tuberculosis and better understanding the epidemiology of theco-epidemics, to find biological basis of the association between tuberculosis and diabetes. We also recommend further multi-centric studies with large sample size to know the overall prevalence of diabetes in tubercular patients in India.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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