

A Comparative Study of Cure and Relapse in Diabetic and Non-Diabetic Pulmonary TB Patients

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Abstract: Background: Diabetes Mellitus is now among the most common causes of compromised immunity that favour Tuberculosis development in present time. Methods: This study was a prospective cross-sectional study with the objective to observe the effect of Type II Diabetes Mellitus on cure rates and relapse rates in Pulmonary TB patients. Our study included 75 participants of whom 27 were diabetic and 48 non-diabetic TB patients recruited at M. L. B. Medical College Jhansi from June 2021 to October 2022 for the study. All routine laboratory investigations were done based on standard clinical procedures and protocols and patient related clinical information were recorded after obtaining written consent from the participants on the prepared proforma. Results: In our study 27 out of 75 patients of TB in our study were diabetic. It was observed that diabetic patients relapsed more frequently than non-diabetic patients within 12 months of ATT completion. Relapse was seen more in >60 years age group (31.25%), males (87.50%), rural background (75%) and TB patients with relatively higher HbA1c levels (57%). Cure rate in TBDM was lower (33%) than in non-diabetic TB patients. (77%). Conclusion: To conclude we can say that cure rates in TBDM patients were lesser and relapse rate was higher than in non-diabetic TB patients.

Keywords: tuberculosis, diabetes mellitus, HbA1c, relapse

1. Introduction

Mycobacterium tuberculosis, a bacterium, is the source of the infectious disease known as tuberculosis (TB). A person with tuberculosis spreads it through the air. In a single year, a patient may infect ten or more individuals.¹The WHO estimates that there were 10 million new (incident) cases of TB worldwide in 2019 (range: 9-11 million; rate: 130 per 100, 000 people). In India, tuberculosis is a serious health issue that results in 220, 000 annual deaths.² Diabetes affected 9.3% of people aged 20 to 79 worldwide in 2019, with a range of 4.7 to 12.2%. China has 116.4 million people with diabetes in 2019, followed by India with 77 million, the United States with 31 million, Pakistan with 19.4 million, Brazil with 16.8 million, and Mexico with 16.8 million (12.8 million).

Immunological impairment has played a major role in TB susceptibility throughout history, and with the DM pandemic, DM is now among the most common causes of compromised immunity that favour TB development.³The present investigation was conducted with the aim of investigating deeper into the impact of DM on TB, specifically in terms of relapse and cure rates.

2. Material and Methods

Study Design: Our study was a comparative Hospital based observational study to observe the effect of TIIDM on cure rates and relapse rates in Pulmonary TB patients.

Study Setting: The study included all PTB patients coming to Department of General Medicine and Department of TB & Chest, of our tertiary care institute during the period from June 2021 to October 2022 and who fulfilled the inclusion criteria.

Ethical guidelines: Ethical clearance for the study was taken from Institution Ethics Committee and the study adhered to the principles enumerated in Declaration of Helsinki.

Sample size: Taking reference of a meta-analysis of 65 studies using the random-effect model which showed that the overall pooled prevalence of diabetes among TB patients in South Asian countries was 21%.⁴ It came out to be 64 by applying the formula below.

Estimate a proportion with absolute precision

$$N \geq Z^2_{1-\alpha/2} X p (1-p) / d^2$$

Where Alpha (α) = 0.05 and estimated proportion (p) = 0.21 and d is estimated error taken as 0.1. After factoring in a 10% loss to the follow-up rate and rounding the result, the figure obtained was 75 for the study.

Selection Of Participants: Adult patients who visited the Chest and TB Outpatient Department of our tertiary care institute during the study period (June 2021 to October 2022) were considered for inclusion in the study if they fulfilled the inclusion criteria for the study and satisfied the case definition of pulmonary TB according to NTEP and DM Type II according to ADA.

Inclusion criteria:

All PTB patients on DOTS – ATT. Exclusion criteria: EPTB patients with/without PTB, Age less than 18years and above 75 years, Patients with comorbidities like –HIV, Cancer, COVID-19, Severe Anemia, Diabetes Mellitus Type 1/other types, HTN, Viral hepatitis, Severe burns, Chemo/radiation, Malnutrition, Post splenectomy, CLD, Patient taking drugs causing immunocompromised state, CKD, Neuropathies, Sepsis, Chronic smoker (>20 years), Chronic alcoholic (>10

years)

Methods of measurement:

The patients were recruited in the study consecutively till the required sample size was reached. Informed written consent was obtained from patients. Patient's demographic data and detailed history was recorded. Following the recording of a detailed patient history, a comprehensive clinical examination was conducted for each patient. All patients underwent a comprehensive evaluation, including a hemogram, metabolic profile with HbA1c, electrocardiogram, and X-ray chest P/A view. Sputum smear for AFB was examined in all the patients. All patients are screened for HIV, HBsAg, HCV and COVID-19. CBNAAT was done in sputum smear positive patients to look for Rifampicin and Isoniazid resistance. The pertinent patient information and corresponding outcomes were meticulously recorded on a preconceived, structured proforma that was designed specifically for the objectives of the investigation.

The primary outcome of the study was to compare the cure and relapse rates between diabetic and non-diabetic TB groups. This was determined by analyzing the sputum smear reports of patients after 12 months of ATT treatment completion. The secondary objective of the investigation was to evaluate whether there existed any statistically noteworthy differences between the two groups with regard to their demographic characteristics.

Statistical analysis:

The collected data was organized in the forms of tables. The continuous variables were analyzed in terms of means and interpreted by student independent "t" test. In respect of categorical variables was expressed in terms of percentages and they were interpreted by Chi-square or fisher's exact test wherever applicable. The statistical analyses outlined above were conducted utilizing the IBM SPSS (Statistical Package for Social Sciences) software package version 23. The p values less than 0.05 ($p < 0.05$) was considered statistically significant at 95% confidence interval.

3. Results

The mean age in the TBDM group was 52.50 ± 11.117 years and 37.11 ± 13.871 years in non-diabetic TB patients, the difference was statistically significant too ($p < 0.0001$). Majority (33%) of the TB patients were in the age group of 41-50. Relapse was seen in 94% of the diabetic patients who were above the age of 40 years while 58% of the non-diabetic patients who got cured, were younger than 40 years of age. Male contributed 49 (65%) of the TB patients in our study. In TBDM patients, cure rates were found lesser in males (39% i.e., 9 out of 23 male TBDM) than in females (60% i.e., 3 out of 5 female TBDM). Among non-diabetics, cure rates in males (77% i.e., 20 out of 26 non diabetic male TB patients) and females (76% i.e., 16 out of 26 non diabetic female TB patients) were found to be almost equal. Majority (80%) of the TB patients in our study were inhabitants from rural areas while only 20% belonged to the urban areas. Relapse rate of 85% was seen among the patients from rural background. Higher number of patients of TB i.e., 55 (73%) of 75 in our study were belonging to joint family while rest were members of nuclear family. Mean HbA1C level was

8.53 in cured Diabetic TB patients and 9.03 in relapsed cases. From the sputum reports of the TB patients in our study revealed that 16 (57%) patients of TB in diabetic group relapsed after 12 months of ATT treatment while only 12 (43%) got cured in TBDM group.

Table 1: Demographic characteristics of TB patients

Age Group (in years)	Diabetic (n=28)		Non-Diabetic (n=47)	
	Cured n (%)	Relapsed n (%)	Cured n (%)	Relapsed n (%)
18-30	0 (0)	0 (0)	14 (38.89)	4 (36.36)
31-40	1 (8.33)	6 (37.50)	7 (19.94)	3 (27.27)
41-50	8 (66.67)	6 (37.50)	8 (22.22)	3 (27.27)
51-60	2 (16.67)	4 (25)	6 (16.67)	0 (0)
>60	1 (8.33)	5 (31.25)	1 (2.78)	1 (9.09)
Mean±SD	52.50±11.117		37.11±13.871	
p* Value	<.00001			
Sex				
Female	3 (25)	2 (14.28)	16 (44.44)	5 (45.45)
Male	9 (75)	14 (85.72)	20 (55.56)	6 (54.54)
Fisher's Extract	0.724		0.003	
p* value	0.624		1	
Region				
Rural	8 (66.67)	12 (75.00)	29 (80.56)	11 (100)
Urban	4 (33.33)	4 (25.00)	7 (19.44)	0
Fisher's Extract	0.233		2.513	
p* value	0.691		0.133	
Type Of Family				
Joint	8 (66.67)	11 (68.75)	25 (69.44)	11 (100)
Nuclear	4 (33.33)	5 (31.25)	11 (30.56)	0
Fisher's Extract	0.014		0.732	
p* value	1		0.682	

Data presented as mean±standard deviation or Numbers; * $p < 0.05$ was considered significant.

Table 2: Mean HbA1c Level in TB patients

Mean HbA1c	Cured	Relapsed	P*-value
Diabetic Patient	8.53±0.609	9.03±0.099	0.003 (S)
Non-diabetic Patient	5.54±0.570	5.86±0.317	0.06 (NS)

Data presented as mean±standard deviation. * $P < 0.05$ was considered significant.

Table 3: Sputum Report at 12 months after ATT completion

Sputum Report after 6 months of ATT	Diabetic Patient (n=28)	Non-diabetic Patient (n=47)	P*-value
Positive (Relapsed)	8	5	0.04 (S)
Negative (Cured)	20	42	
Total	28	47	
Sputum Report after 12 months of ATT			
Positive (Relapsed)	16	11	0.03 (S)
Negative (Cured)	12	36	
Total	28	47	

Data presented as Number. * $P < 0.05$ was considered significant.

4. Discussion

Prevalence of diabetes in our study group was found to be 37.3% which is higher as compared to the studies conducted by Pin-Hui Lee et al⁵ and Vinay Mahishale et al⁶. Most of the TB patients having diabetes in our study belonged to a higher age group. The prevalence of diabetes is seen to increase as the age progresses. This finding is similar to

studies conducted by John Titus George et al (2022)⁷ and V Nissapatorn et⁸ al in which it was seen that that patients in the TBDM group were significant older than in the non-diabetics TB group. In our study, the male: female ratio of PTB patients in diabetics and non-diabetics was found to be 4.6: 1 and 1.2: 1 respectively, this is in line with the studies conducted by John Titus George et al⁷ and V Nissapatorn et al⁸ (2005). Factors like increased access to healthcare by male counterparts and better family support for male patients, more community exposure by male patients, can result in increased prevalence of TB in diabetic male patients. Among TBDM patients, cure rates were found lesser in males (39%) than in females (60%). Diabetic males are at an increased risk of poorer treatment outcomes as compared to non-diabetic males. Most of the relapsed TB patients belonged to a rural background. This can be attributed to a poorer access to healthcare and free medical facilities, lack of resources etc. The study did not find any significant contribution of the community/ neighborhood in which the patient resides. The mean HbA1c of TBDM patients who relapsed was more than in those who were declared cured, and the result was statistically significant. This is consistent with studies done by John Titus George et al⁷ and Vinay Mahishale et al⁸. Our study found higher relapse rates of TB in diabetic patients (57.1%) as compared to non-diabetic patients (23.4%) within 12 months of treatment completion. While the cure rates were lower in diabetic patients (42.9%) as compared to non-diabetic patients (76.6%). The relapse of TB on the basis of Sputum microscopy revealed statistically significant results after 12 months of ATT completion. The results are statistically significant at the interval of 6 months and 12 months. Among the TB patients who had relapsed, ~50% of them had sputum confirmation by the end of initial 6 months from ATT course completion. TB relapse can be due to the same strain or a different strain in susceptible individuals.

5. Conclusion

From our study we conclude that relapse was seen more in higher age groups, males, rural background and relatively higher HbA1c levels. Cure rates in TBDM patients were lesser than in non-diabetic TB patients.

References

- [1] WHO. Global tuberculosis control. WHO report. WHO/HTM/TB/2006.362. Geneva: World Health Organization, 2006. [cited 2023 Feb 15].
- [2] Uttar Pradesh National Health Mission [Internet]. [cited 2023 Feb 15]. Available from: <https://upnrhm.gov.in/Home/NTEP>.
- [3] Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, Shaw JE, Bright D, Williams R; IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019 Nov; 157: 107843. doi: 10.1016/j.diabres.2019.107843. Epub 2019 Sep 10. PMID: 31518657.
- [4] Gautam S, Shrestha N, Mahato S, Nguyen TPA, Mishra SR, Berg-Beckhoff G. Diabetes among tuberculosis patients and its impact on tuberculosis treatment in South Asia: a systematic review and meta-analysis. *Sci Rep.* 2021 Jan 22; 11 (1): 2113.
- [5] Lee PH, Lin HC, Huang AS, Wei SH, Lai MS, Lin HH. Diabetes and risk of tuberculosis relapse: nationwide nested case-control study. *PLoS One.* 2014 Mar 24; 9 (3): e92623. doi: 10.1371/journal.pone.0092623. PMID: 24663327; PMCID: PMC3963913
- [6] Mahishale V, Avuthu S, Patil B, Lolly M, Eti A, Khan S. Effect of Poor Glycemic Control in Newly Diagnosed Patients with Smear-Positive Pulmonary Tuberculosis and Type-2 Diabetes Mellitus. *Iran J Med Sci.* 2017 Mar; 42 (2): 144-151. PMID: 28360440; PMCID: PMC5366362.
- [7] George JT, Miraclin AT, Sathyendra S, Michael JS, Prasad J, Rebekah G. Pulmonary tuberculosis and diabetes mellitus: Clinical profile and outcomes. *Int J Mycobacteriol* 2022; 11: 400-6
- [8] Nissapatorn V, Kuppasamy I, Jamaiah I, Fong MY, Rohela M, Anuar AK. Tuberculosis in diabetic patients: a clinical perspective. *Southeast Asian J Trop Med Public Health.* 2005; 36 Suppl 4: 213-20. PMID: 16438212.