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Original Research Article

COMPARISON OF CLINICAL, RADIOLOGICAL PATTERN AND OUTCOME OF NEW SPUTUM POSITIVE PULMONARY TUBERCULOSIS WITH TYPE 2 DIABETES WITH THEIR DIABETIC CONTROL STATUS

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Abstract

Background: Tuberculosis and Diabetes mellitus have a bidirectional relationship. Diabetes is the most important risk factor for developing tuberculosis and may affect its presentation, while TB may worsen glycaemic control in patients with DM. This study aimed to compare the clinical and radiological patterns and outcomes of new sputum-positive patients with diabetes mellitus to their diabetic control status.**Materials and Methods:** This prospective study was conducted on 80 outpatients and inpatients with new sputum-positive pulmonary tuberculosis with known or newly diagnosed type 2 diabetes mellitus attending the Department of Respiratory Medicine, Tirunelveli Medical College Hospital, Tirunelveli, for 18 months. Diabetic patients were divided into optimally controlled and poorly controlled groups depending on HbA1C status [HbA1C < 7%-optimal glycaemic control (OGC) and HbA1C ≥ 7%-poor glycaemic control (PGC)]. Symptom scores were calculated based on cough, dyspnoea, fever, chest pain, and weight loss. **Results:** The cough was the predominant symptom (99%). Patients with PGC presented with higher sputum AFB smear positivity rates than those with OGC (81% vs. 19%). There were no significant differences in age, sex, symptom score, symptom duration, Sputum AFB grading, or number of cavities between the groups. There was a significant difference in BMI, sputum AFB at presentation, side of the lesion, involvement of lung zones, type of lesion, and extent and distribution of CXR lesions between the groups. Compared with the OGC group, the PGC group had a less favourable outcome (100% vs. 80%). **Conclusion:** Poor glycaemic control in patients with tuberculosis and diabetes mellitus leads to advanced disease and unfavourable treatment outcomes, thus requiring early diagnosis and treatment to improve the outcomes of both the diseases.

INTRODUCTION

Tuberculosis and diabetes mellitus have a bidirectional relationship. Diabetes is the most important risk factor for developing tuberculosis and may affect its presentation, whereas TB may worsen glycaemic control in patients with DM.[1] Most of the diabetics remain undiagnosed or poorly controlled. Based on the rising trend of the global burden of DM, the prevalence will reach 438 million by 2030.[2] Low and middle-income countries have a higher prevalence of diabetes and tuberculosis than high-income countries.[3,4] The prevalence of DM in TB is 2–4.6 times higher than that in the general population. In diabetic patients with TB, approximately 64% are new cases of DM, which emphasises the importance of screening for DM in tuberculosis patients.[5] The ninth most common complication of DM is Tuberculosis, with a risk of 4.8% compared to 0.8% in non-diabetics.[6,7] The incidence of extrapulmonary tuberculosis is less common in patients with diabetes.

Diabetes is associated with adverse TB treatment outcomes, including treatment failure, death, and relapse. The risk of developing TB relapse is 2-3-fold higher in diabetics.[8] A higher susceptibility to TB in diabetes is related to a longer duration of diabetes and poor glycaemic control. Thus, it is important to assess the association between TB and glycaemic control for early screening and treatment for better outcomes of tuberculosis.[9,10] Most previous studies have compared clinico-radiological profiles and outcomes of tuberculosis in DM and non-DM patients, but studies comparing tuberculosis profiles between diabetic patients based on their glycaemic control are limited. Thus, our study focused on comparing clinical and radiological patterns and outcomes of new sputum-positive tuberculosis patients with diabetes mellitus based on their glycaemic control.

Aim

This study aimed to compare the clinical and radiological patterns and outcomes of new sputum-positive patients with diabetes mellitus to their diabetic control status.

MATERIALS AND METHODS

This prospective study was conducted on 80 outpatients and inpatients with sputum-positive pulmonary tuberculosis with known or newly diagnosed type 2 diabetes mellitus attending the Department of Respiratory Medicine, Tirunelveli Medical College Hospital, Tirunelveli, for 18 months. The study was approved by the institutional ethics committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

Patients aged > 18 years who were willing to provide informed consent for new sputum-positive pulmonary tuberculosis with known or newly diagnosed type 2 diabetes mellitus were included.

Exclusion Criteria

Patients aged < 18 years who were unwilling to provide informed consent for the study, who were previously treated for tuberculosis with extrapulmonary tuberculosis, patients with drug-resistant tuberculosis, patients with HIV infection, malignancy, chronic kidney disease, chronic liver disease, pregnancy, long-term steroid therapy, or immunosuppressant use were excluded.

After obtaining written informed consent, the patients were selected according to the inclusion criteria. Pulmonary tuberculosis was diagnosed according to the Revised TB Control Program (RNTCP) technical and operational guidelines. Diabetes mellitus was diagnosed using the WHO Health Organization diagnostic criteria: fasting plasma glucose >126 mg/dl, 2 h plasma glucose >200 mg/dl, and glycosylated haemoglobin >6.5%. Diabetic patients were divided into optimally controlled and poorly controlled groups depending on HbA1C status [HbA1C < 7%-optimal glycaemic control (OGC) and HbA1C ≥ 7%-poor glycaemic control (PGC)]

A symptom score (0–7) was calculated based on the presence of cough, dyspnoea, fever, chest pain, haemoptysis, loss of appetite, and weight loss (one point for each symptom was assigned). Patients with a symptom score >4 were classified as having highly symptomatic disease. Body Mass Index (BMI) was calculated as weight in m2 and BMI classification was performed according to WHO Asia Pacific guidelines.

Chest radiographs were divided into three zones on each side of the upper, middle, and lower zones. The upper zone extends up to the level of the lower margin of the anterior 2nd rib, the mid-zone extends from the level of the lower border of the 2nd rib to the level of the lower border of the 4th rib, and the lower zone extends from the level of the lower border of the 4th rib to the diaphragm.

The CXR reading focused on lung parenchymal opacity and cavitation. Radiological lesions on CXR were classified as minimal, moderately advanced, and far advanced according to the American Thoracic Society (ATS) criteria.

RESULTS

Most of the patients (71%) were in the age group above 50 years in both groups. The youngest patient was 26 years old, and the oldest was 84 years old ($p = 0.16$); there was no statistical significance. Most patients were males (64%) in both the poor and optimal control groups. This difference was not statistically significant ($p = 0.69$). The majority of PGC patients were Underweight and the Majority of OGC patients were of normal weight. The correlation between BMI and glycaemic control was statistically significant ($p = 0.04$).

Cough (99%) was the predominant symptom in the study population, followed by fever, in both groups. There was no statistically significant difference between the glycaemic control and symptom scores ($p = 0.90$). Most patients in both groups presented with a duration of symptoms of < 2 months, but the difference was not statistically significant. PGC patients presented with higher sputum AFB smear positivity rates than those with OGC (81% vs. 19%) and a significant correlation between sputum AFB at the time of presentation and glycaemic control ($p = 0.03$).

Patients had a high bacillary load, and a statistically insignificant difference was observed between sputum AFB grading and glycaemic control ($p > 0.05$). Bilateral lesions were mostly observed in the PGC group and unilateral lesions were mostly observed in the OGC group. This difference was statistically significant ($p = 0.006$). Multiple zone involvement was commonly observed in the PGC group, whereas single zone involvement was commonly observed in the OGC group ($p = 0.01$).

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Cavitary lesions were more commonly observed in PGC patients (75%) than in OGC patients, with a statistically significant correlation between cavitary lesions and glycaemic control (p = 0.001). In both groups, single cavitary lesions were noted in most patients, and there was no statistically significant difference between glycaemic control and number of cavities (p = 0.31).

Moderately advanced and far-advanced lesions were more commonly observed in the PGC group (63% and 25% vs. 45% and 5%, respectively) than in the OGC group. Minimal lesions (50%) were also common in the OGC group. Lower lung field involvement was more commonly observed in the PGC group than in the OGC group (80% vs. 55%), and a statistically significant difference was observed between glycaemic control and the Distribution of CXR lesions (p = 0.03). [Table 1]

Most of the patients in both groups showed sputum conversion at the end of IP (93% in the PGC group vs. 95% in the OGC group), sputum AFB positivity at the end of IP was noted in three patients and two patients belonging to the PGC group, HbA1C of 9.7% and 12% with moderately advanced lesion in the PGC group, and one patient (HbA1C, 6.6%) in the OGC group was sputum AFB-positive at the end of IP. Two patients died within 2-4 weeks of diagnosis, and they had HbA1C levels were 7% and 10.2%, respectively.

Sputum conversion was observed in most patients (93% in the PGC group vs. 100% in the OGC group), and sputum-positive sputum was observed at the end of the continuation phase. Most of the patients had successful outcomes (95%). However, compared with the OGC group, the PGC group had a less favourable outcome (100% vs. 80%). [Table 2]

Table 1: Comparison of patient characteristics between groups

		Poor glycaemic control	Optimal glycaemic control	P value
Age	<50 years	19	4	0.16
	>50 years	41	16	
Sex	Male	39	12	0.69
	Female	21	8	
Body mass index	Underweight	39	8	0.04
	Normal weight	21	12	
Symptom score	>4	29	10	0.9
	<4	31	10	
Symptom's duration	<2 months	49	15	0.59
	>2 months	11	5	
Sputum AFB at presentation	Positive	52	13	0.03
	Negative	8	7	
Sputum AFB grading	>2+	35	5	0.055
	<1+	17	8	
Side of the lesion	Bilateral	33	4	0.006
	Unilateral	27	16	
Involvement of lung zones	Multiple zones	43	8	0.01
	Single zones	17	12	
Type of lesion	Cavitary	45	7	0.001
	Non- cavitary	15	13	
Number of cavities	Multiple	15	1	0.31
	Single	30	6	
The extent of CXR lesion	Minimal	7	10	<0.001
	Moderate	38	9	
	Advanced	15	1	
Distribution of CXR lesion	Lower lung field (LLF)	48	11	0.03
	Other than LLF	12	9	

Table 2: Relation of sputum conversion at end IP, sputum conversion at end of CP, and outcome between groups

		Poor glycaemic control	Optimal glycaemic control
Sputum conversion at the end of IP	Negative	56	19
	Positive	2	1
	Died	2	0
Sputum conversion at the end of CP	Negative	56	20
	Positive	2	0
	Died	2	0
Outcome	Cured	56	20
	Treatment failure	2	0
	Drug-resistant TB	0	0
	Died	2	0

DISCUSSION

Among the total study population of 80 patients with TB and DM, 20 (25%) had optimal glycaemic control (OGC), whereas 60 (75%) had poor glycaemic control (PGC). The majority of patients were in the PGC group. Similarly, a higher proportion of patients in the PGC group was

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observed in a study by Chiang et al. (88.8% vs. 11.2%). This indicates that most patients with TB and diabetes usually have poor glycaemic control.[11] This may be related to illiteracy, unawareness, and low socioeconomic status. In contrast to our study, Tabarsi et al. reported 40% of patients with optimal glycaemic control.[12]

In the present study, 71 number of the patients were aged > 50 years. This is consistent with the findings of Patel et al. (>50 years, 60%).7 We observed a male predominance (64%) in our study. Deshmukh et al. and Tripathy et al. among many studies also found male predominance. This may be due to smoking habits, occupational exposure, or genetic and sociocultural differences. Although the cause of this discrepancy is not clear.[13,14] The majority of the PGC (65%) were Underweight with a statistical significance which contrasts with a study done by Amare et al. who observed 62.7% had normal weight.[15]

Cough (99%) was the predominant symptom in the present study, followed by fever, as reported by Nielsen et al. and many studies, but there is no relationship observed between HbA1C and clinical symptoms and symptom scores.[16] This is consistent with the study conducted by Park et al. who reported no differences in clinical symptoms regardless of HbA1C.[17] Alisjahbana et al. reported that TB patients with DM had more symptoms but not a more severe form of TB.[18] Higher symptom scores were not observed in the PGC group in our study which is consistent with the findings of previous studies.

In our study, higher sputum AFB positivity rates were observed in the PGC group, and they had a higher bacillary load at the time of presentation (86% vs. 65%). This observation correlated with the study conducted by Vulli et al. and many other studies. Vulli et al. observed that 73.2% of patients with PGC had a higher bacillary load.[19] Bilateral lesions (55%) were most frequently observed in the PGC group, whereas unilateral lesions (80%) were most frequently observed in the OGC group.

In our study, multiple zone involvement was more common in the PGC group than in the OGC group (72% vs. 40%, respectively). Multilobar involvement in the PGC group has been observed in many previous studies. In our study, cavitary lesions were more common in the PGC group than in the OGC group (75% vs 35%). Similar observations made by Avuthu et al., Cavities and isolated lower field involvement were more common in uncontrolled diabetics than well-controlled diabetics and observed in studies done by Chiang et al., Park et al. and Perez-Guzman et al.[20,21,17,22] The increased frequency of cavitary lesions in diabetics with poor glycemic control is due to reduced expression of Th1-related cytokines observed by Yamashiro et al.[23]

Most of the study population (86%) had a single or multiple cavitary lesions. In both groups, a single cavitary lesion was observed which is in contrast to many previous studies. Moderately advanced and far-advanced lesions were more commonly observed in the PGC group (63% and 25% vs. 45% and 5%, respectively) than in the OGC group. Minimal lesions (50%) were common in the OGC group, as observed in Manishale et al. and Avuthu et al.[24,20]

In the present study, most patients in the PGC group had isolated lower lung field involvement than those in the OGC group (80% vs. 55%, respectively). This phenomenon has been observed in several studies. This may be related to greater perfusion (glucose-rich blood) in the middle and lower lobes; thus, TB bacilli find a more favourable environment for growth. Atypical radiological findings of lower lung field lesions, cavitary lesions, and multilobar involvement with moderate and advanced tuberculosis were noted in our PGC patients. These atypical radiological manifestations may lead to a significant delay in TB diagnosis; thus, clinicians should have a high degree of suspicion to screen all tuberculosis patients for DM.

In the PGC group, 93.3% had successful outcomes, 3.3% had treatment failure, and 3.3% died. A study conducted by Singla et al. observed successful outcomes in 97.1%, treatment failure in 0%, and death in 0.7%.[25] In the study Leung et al. observed successful outcomes in 73%, treatment failure in 0%, and death in 9.9%.26 Vishwanathan and Gawde observed successful outcomes in 87%, treatment failure in 7.9%, and death in 1.1%. In the present study, 100% successful outcomes were observed in the OGC group.[27]

We observed a mortality rate of 3.3% in our study, which may be related to the increased TB severity. Recent studies showed that the association of diabetes mellitus did not alter the response of pulmonary tuberculosis to treatment by Singla et al. and it was also observed that in well-controlled diabetes the course of tuberculosis is not different from the patients without diabetes.[25]

CONCLUSION

In patients with Tuberculosis and diabetes mellitus, poor glycaemic control is associated with advanced tuberculous disease, higher bacillary load, higher lower lung field involvement, higher cavitary lesions, delayed sputum conversion, and unfavourable TB treatment outcomes, whereas optimal glycaemic control is associated with less severe tuberculosis disease and satisfactory TB treatment outcomes. Tight glycaemic control makes anti-tuberculosis treatment more effective. Thus, all patients with tuberculosis should be screened for diabetes mellitus at the initiation of anti-tuberculosis treatment to improve the outcomes of both diseases.

Considering the rising burden of DM, it is necessary to expand TB control programs to focus on the early diagnosis of DM in patients with TB and vice versa. Randomised Controlled trials are needed to assess the extent to which Unsatisfactory TB treatment

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outcomes can be prevented by optimal glycaemic control.

Limitations

The present study was a single-centre study, and the results cannot be generalised. The relationship between drug-resistant Tuberculosis and Diabetes mellitus was not assessed. post-TB treatment HbA1C levels were not assessed. Patients with extrapulmonary TB were not included in the present study.

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