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EFFECT OF GLYCEMIC CONTROL ON SPUTUM CONVERSION IN SMEAR POSITIVE PULMONARY TB

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Abstract

INTRODUCTION: Tuberculosis (TB) and diabetes mellitus (DM) are two chronic diseases of major public health importance that frequently coexist and adversely influence each other's clinical course and outcomes. AIM: To determine the relationship between HbA1c and sputum conversions by LED microscopy in smear positive pulmonary TB. ***METHODOLOGY:*** The present study was designed as a hospital-based prospective study conducted in the tertiary care center of north west Rajasthan. ***RESULT:*** The study found that tuberculosis patients with diabetes and higher HbA1c levels had greater bacillary load at diagnosis, more severe radiological disease, and delayed sputum conversion compared to non-diabetic patients and those with better glycemic control. ***CONCLUSION:*** Poor glycemic control adversely affects bacteriological response and delays sputum conversion in pulmonary tuberculosis, underscoring the need for routine diabetes screening and strict glycemic management in TB patients.

Keywords: Glycemic, Sputum, pulmonary

INTRODUCTION

Tuberculosis (TB) and diabetes mellitus (DM) are two chronic diseases of major public health importance that frequently coexist and adversely influence each other's clinical course and outcomes1. Tuberculosis, caused by Mycobacterium tuberculosis, is a chronic infectious disease that primarily affects the lungs but has systemic consequences involving multiple organs, including the endocrine system. Like other chronic infections, TB induces metabolic stress and inflammatory responses that can disturb glucose homeostasis, resulting in impaired glucose tolerance and hyperglycemia. These metabolic alterations not only complicate the clinical management of TB but also contribute to poorer treatment outcomes.Diabetes mellitus, particularly type 2 diabetes, is a chronic metabolic disorder characterized by insulin resistance and persistent hyperglycemia.2 It is associated with both microvascular and macrovascular complications and contributes significantly to global morbidity and mortality. Diabetes impairs innate and adaptive immunity, thereby increasing susceptibility to infections, including TB. Several studies have consistently demonstrated that individuals with diabetes are at a substantially higher risk of developing active TB compared to non-diabetic individuals.3 Furthermore, diabetes adversely affects TB disease presentation, severity, and response to treatment.The coexistence of TB and DM represents a growing clinical challenge, especially in low- and middle-income countries where the burden of both diseases is rising simultaneously.4 Historically, TB was considered a disease of poverty, while diabetes was viewed as a disease of affluence. However, this distinction is no longer valid, as diabetes has become increasingly prevalent across all socioeconomic groups, particularly in regions where TB is endemic. The rising prevalence of diabetes is now recognized as a major factor sustaining the TB epidemic by increasing the pool of susceptible individuals and complicating disease control efforts5. Glycated hemoglobin (HbA1c) is an established biomarker that reflects average blood glucose levels over the preceding three months and is widely used for the diagnosis and monitoring of

diabetes. Elevated HbA1c levels in patients with TB indicate poor glycemic control, which has been associated with delayed sputum conversion, prolonged infectivity, and increased risk of treatment failure.6,7 Poorly controlled diabetes alters macrophage function, cytokine responses, and cellular immunity, thereby impairing the host's ability to clear Mycobacterium tuberculosis effectively. Sputum conversion is a critical indicator of treatment response in pulmonary TB and reflects the effectiveness of anti-tubercular therapy.8 Delayed sputum conversion has been associated with higher rates of disease transmission, relapse, and adverse treatment outcomes. Factors influencing sputum conversion include bacterial load, nutritional status, treatment adherence, smoking, alcohol consumption, and comorbid conditions such as diabetes. Patients with diabetes, particularly those with poor glycemic control, often exhibit slower bacteriological clearance despite receiving standard anti-tubercular therapy. In view of the bidirectional relationship between TB and diabetes, early identification and optimal management of hyperglycemia in patients with TB is essential9. Integrated screening and coordinated management strategies targeting both diseases are crucial to improve treatment outcomes, reduce transmission, and mitigate the growing dual burden of TB and diabetes.

AIM

To determine the relationship between HbA1c and sputum conversions in smear positive pulmonary TB.

MATERIALS AND METHODS

The present study was designed as a hospital-based prospective study conducted in the Department of Respiratory Medicine, at tertiary care center, North West Rajasthan. The study was carried out over a period of 1 yr from April 2024 to may 2025. A total of 250 patients were included in the study. These cases comprised newly diagnosed pulmonary tuberculosis patients who visited the outpatient department or were admitted to the inpatient department of the Respiratory Medicine unit and were consecutively enrolled using a consecutive sampling technique. Patients aged 20 years and above of either sex with newly diagnosed smear-positive pulmonary tuberculosis under the DOTS program were included in the study. Both patients with pre-existing diabetes mellitus and those newly diagnosed with diabetes during the course of evaluation, as well as patients without diabetes mellitus, were eligible for inclusion, provided they were willing to participate and gave informed consent.Patients were excluded if they had recurrent pulmonary tuberculosis, were suspected or diagnosed cases of multidrug-resistant tuberculosis, or had a positive HIV serological status. Patients who were unable to tolerate DOTS therapy or those unwilling to participate in the study were also excluded.

RESULTS

Table-1: Distribution of patients according to their age group

Age group (years)	Number of patients	Percentage (%)
< 30	28	11.2
30–44	62	24.8
45–59	98	39.2
≥ 60	62	24.8
Total	250	100

In the present study, the majority of patients belonged to the 45–59 years age group, accounting for 39.2% of the study population. This was followed by the 30–44 years and ≥60 years age groups, each constituting 24.8%, while patients below 30 years formed the smallest group (11.2%).

Table 2: Distribution According to Chief Complaints (n = 250)

Chief complaint	Number of patients	Percentage (%)
Cough	232	92.8
Fever	188	75.2
Weight loss	176	70.4
Breathlessness	142	56.8
Hemoptysis	48	19.2

Cough was the most common presenting complaint, reported by 92.8% of patients, followed by fever (75.2%) and weight loss (70.4%). Breathlessness was present in 56.8% of cases, while hemoptysis was observed in 19.2% of patients.

Table 3: Chest X-ray Findings at Diagnosis (n = 250)

Radiological finding	Number of patients	Percentage (%)
Unilateral infiltrates	102	40.8
Bilateral infiltrates	88	35.2
Cavitary lesions	46	18.4
Miliary / extensive disease	14	5.6
Total	250	100

Chest X-ray evaluation showed unilateral infiltrates as the most common finding, present in 40.8% of patients, followed by bilateral infiltrates in 35.2%. Cavitary lesions were observed in 18.4% of cases, while miliary or extensive disease was seen in 5.6% of patients.

Table 4: Distribution According to History of Diabetes Mellitus (n = 250)

Diabetes status	Number of patients	Percentage (%)
No diabetes	168	67.2
Known diabetes	55	22
Newly diagnosed diabetes	27	10.8
Total	250	100

In the present study, the majority of patients (67.2%) had no diabetes mellitus, while 22% were known cases of diabetes. Newly diagnosed diabetes was identified in 10.8% of patients, indicating a notable burden of undetected diabetes among tuberculosis patients.

Table 5: Bacteriological Grade at Time of Diagnosis (n = 250)

Sputum smear grade	Number of patients	Percentage (%)
Scanty	36	14.4
1+	124	49.6
2+	58	23.2
3+	32	12.8
Total	250	100

Sputum smear examination showed that 1+ grading was the most common finding, observed in 49.6% of patients. Scanty positivity was seen in 14.4%, while 2+ and 3+ grading were present in 23.2% and 12.8% of patients respectively, indicating varied bacillary loads at diagnosis.

Table-6: Distribution of HbA1c levels on different follow up

Variable	**HbA1c≥6.5% (n=168)**		**HbA1c <6.5% (n=82)**		**P value**
	Mean	SD	Mean	SD	
Pre-treatment	11.50	0.8	5.38	0.8	0.0001*
At 3 months	7.48	1.5	5.60	1.3	0.001*
At 6 months	7.15	0.48	5.68	1.5	0.001*

Patients with HbA1c ≥6.5% had significantly higher mean HbA1c values at baseline, which showed a marked reduction at 3 and 6 months of follow-up. In contrast, patients with HbA1c <6.5% maintained relatively stable HbA1c levels throughout treatment, indicating better glycemic control.

Table 7: Relationship Between HbA1c Level and Bacteriological Grade at Diagnosis (n = 250)

HbA1c level (%)	Scanty	1+	2+	3+	Total
< 6.5	14	98	35	21	168
>6.5	8	16	28	30	82
P value	0.0001*				

Patients with HbA1c >6.5% showed a higher proportion of 2+ and 3+ sputum smear positivity compared to those with HbA1c <6.5%. Conversely, patients with HbA1c <6.5% predominantly had lower smear grades, indicating an association between poor glycemic control and higher bacillary load.

Table 8: Relation of Delayed Sputum Conversion with HbA1c Level (End of 2 Months)

HbA1c (In %)	Delayed sputum conversion	%
<6.5	8	28.5
6.5 – 8	4	14.2
8 – 10	9	32.1
>10	7	25.2
Total	28	100

Delayed sputum conversion was most frequently observed in patients with HbA1c levels between 8–10%, accounting for 32.1% of cases. Patients with HbA1c <6.5% showed the lowest proportion of delayed conversion, indicating better treatment response with good glycemic control.

Table-9: Correlation of sputum conversion with HbA1c levels at follow up

Sputum AFB status	At 2 month		At 3 month	
	HbA1c ≥6.5%	HbA1c <6.5%	HbA1c ≥6.5%	HbA1c <6.5%
Negative	65 (79.2%)	157(93.4%)	74(90.2%)	168 (100%)
Delay in conversion	17 (20.7%)	11 (6.6%)	8(9.8%)	0
P value	0.002		0.0001**	

At two months, delayed sputum conversion was more common among patients with HbA1c ≥6.5% compared to those with HbA1c <6.5%. By three months, sputum conversion improved markedly, with all patients having HbA1c <6.5% achieving sputum negativity, while a small proportion with HbA1c ≥6.5% continued to show delayed conversion.

DISCUSSION

In the present study, most patients were in the 45–59 years age group, comprising 39.2% of the total study population. The 30–44 years age group accounted for 24.8% of cases, indicating a substantial burden among middle-aged adults. An equal proportion of patients (24.8%) were aged 60 years and above. Younger patients below 30 years constituted only 11.2% of the study population. This distribution shows a clear increase in tuberculosis cases with advancing age. The higher prevalence in older age groups may be attributed to declining immunity and associated comorbidities.

Cough was the most common chief complaint and was present in 92.8% of the patients. Fever was reported by 75.2% of cases, indicating active systemic involvement. Weight loss was observed in 70.4% of patients, reflecting the chronic nature of the disease. Breathlessness was noted in 56.8% of cases, suggesting significant pulmonary involvement. Hemoptysis was comparatively less common and was seen in 19.2% of patients. Cough, fever, and weight loss constituted the predominant symptom complex among the study population.

Radiological evaluation revealed unilateral infiltrates as the most common chest X-ray finding, observed in 40.8% of patients. Bilateral infiltrates were seen in 35.2% of cases, indicating extensive pulmonary involvement in a significant proportion. Cavitary lesions were present in 18.4% of patients, reflecting advanced disease and higher bacillary load. A smaller number of patients (5.6%) showed miliary or extensive disease patterns. These findings suggest varied radiological severity among the study population.

Similar findings can be found in other studies.10 There are studies which showed more cavitary lesions in diabetics. Also many studies had quoted multi lobe involvement of diabetics.

In the present study, the majority of patients (67.2%) had no history of diabetes mellitus. Known diabetes was present in 22% of the study population, indicating a significant coexistence of tuberculosis and diabetes. Newly diagnosed diabetes was identified in 10.8% of patients during evaluation. This highlights the presence of previously undetected hyperglycemia among patients with tuberculosis. The coexistence of diabetes in nearly one-third of patients suggests its important role in disease progression. These findings emphasize the need for routine screening for diabetes in all tuberculosis patients.

In the present study, the most common sputum smear grade at diagnosis was 1+ positivity, observed in 49.6% of patients. Scanty positivity was seen in 14.4% of cases, indicating a lower bacillary load in a subset of patients. Moderate bacillary load with 2+ grading was present in 23.2% of patients. A smaller proportion of patients (12.8%) had 3+ sputum smear positivity, suggesting high infectivity. The distribution reflects varying degrees of bacteriological severity at presentation. Raghuraman et al (2014).11 studied 51 patients (32.9%) with smear-positive TB patients with T2DM. In another study (2012) conducted in Kerala, India which indicates that much higher prevalence of DM (44%) among TB patients.

In the present study, patients with HbA1c ≥6.5% had significantly higher mean HbA1c levels in the pre-treatment period compared to those with HbA1c <6.5%. At three months of treatment, a noticeable reduction in mean HbA1c was observed in the HbA1c ≥6.5% group, indicating improvement in glycemic control. However, their mean values remained higher than those in patients with HbA1c <6.5%. At six months, HbA1c levels further declined in the poorly controlled group, suggesting sustained improvement with ongoing management. Patients with HbA1c <6.5% showed relatively stable HbA1c levels throughout the follow-up period.

In the present study, patients with HbA1c levels below 6.5% predominantly showed lower sputum smear grades, with the majority falling in the 1+ category. Among patients with HbA1c levels above 6.5%, a higher proportion exhibited 2+ and 3+ sputum smear positivity. The highest frequency of 3+ grading was observed in patients with HbA1c >6.5%, indicating a higher bacillary load. Scanty positivity was more common in patients with lower HbA1c levels. These findings suggest a positive association between poor glycemic control and higher sputum smear grading. In contrast to the above findings, study done in Nigeria by Oliyanka et al (2013)12 found the prevalence to be 5.7%.55 Maximum (41.67%) subjects had 1+ grading, (30%) had 2+grading, (25%) had 3+ grading on sputum examination whereas (3.33%) had scanty positivity on sputum microscopy test.

In the present study, delayed sputum conversion was most frequently observed among patients with HbA1c levels between 8–10%, accounting for 32.1% of cases. Patients with HbA1c levels above 10% constituted 25.2% of delayed converters. A lower proportion of delayed sputum conversion was seen in patients with HbA1c levels between 6.5–8%. Patients with HbA1c levels below 6.5% accounted for 28.5% of delayed conversion cases. These findings indicate a higher likelihood of delayed sputum conversion with worsening glycemic control. The study by R.Singla et al (2003)13 states that PTB-DM patients have an elevated pretreatment bacillary load, a lesser occurrence of drug resistance and delayed sputum conversion by the last of 2 months of management in comparison to non-diabetics. The link of DM does not change the ultimate management result amongst PTB patients. It understands the influence of the PTB patients.

At the end of two months of treatment, sputum smear negativity was observed in 79.2% of patients with HbA1c ≥6.5% compared to 93.4% of those with HbA1c <6.5%. Delayed sputum conversion at two months was more common in patients with elevated HbA1c levels (20.7%) than in those with better glycemic control (6.6%). By the third month, sputum negativity increased to 90.2% among patients with HbA1c ≥6.5%. All patients with HbA1c <6.5% achieved sputum conversion by the third month. Delayed conversion at three months persisted only in the poorly controlled glycemic group (9.8%). These findings demonstrate that higher HbA1c levels are associated with delayed sputum conversion during anti-tubercular therapy.In a study of medical and radiological outline of pulmonary tuberculosis among patients having diabetes mellitus by Mohapatra et al (2017)14 showed the presence of higher pre-treatment bacillary load. Also, chest x-ray images significantly depart from the typical presentation.

CONCLUSION

The present study highlights a strong association between diabetes mellitus, poor glycemic control, and disease severity in pulmonary tuberculosis. Patients with diabetes, particularly those with elevated HbA1c levels, demonstrated higher bacillary load at diagnosis, more severe radiological involvement, and delayed sputum conversion during treatment. Poor glycemic control was consistently associated with higher sputum smear grades and prolonged time to sputum negativity, although eventual treatment outcomes were favorable with standard anti-tubercular therapy. These findings emphasize the importance of routine screening for diabetes and close monitoring of glycemic status in all tuberculosis patients to improve bacteriological

response, reduce delays in sputum conversion, and optimize overall disease management.

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