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Glycemic Status and Its Impact on Clinical Profile and Outcomes in Tuberculosis Patients: A Hospital-Based Prospective Study in Nepal

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ABSTRACT

Background

Tuberculosis (TB) and diabetes mellitus (DM) are increasing comorbidities in low- and middle-income countries, affecting diagnosis, treatment, and prognosis. This study evaluates glycemic status in newly diagnosed TB patients and its impact on clinical, radiological, and treatment outcomes.

Methods

A hospital-based prospective cohort study was conducted at Tribhuvan University Teaching Hospital, Kathmandu, from July 2023 to August 2024. A total of 140 adult TB patients (≥18 years) were enrolled and followed until the intensive phase of anti-tubercular therapy. DM was diagnosed using American Diabetes Association criteria. Clinical features, laboratory results, and treatment outcomes were compared between TB patients with and without DM.

Results

DM was found in 33 patients (23.6%), most with disease duration <5 years. Diabetic patients were older (mean 56.5 vs. 46.1 years, p-value<0.001) and reported less weight loss (33% vs. 60%, p-value=0.009). Mean adenosine deaminase levels were lower in diabetics (20.9 vs. 37.9 IU/L, p-value=0.043). Hospital stay was longer in diabetics (12.7 vs. 9.3 days, p-value=0.004). Sputum conversion at two months was lower in diabetics but not significant (78.6% vs. 95.9%, p-value=0.068). Peripheral neuropathy was more frequent in diabetics (18% vs. 4%, p-value=0.010). No significant differences were observed in radiological patterns or other adverse drug reactions.

Conclusions

DM is common among TB patients in Nepal and is linked to distinct clinical features, lower ADA levels, prolonged hospitalization, and higher neuropathy risk. Bidirectional screening and optimal glycemic control may improve TB outcomes.

Keywords: diabetes mellitus; Nepal; tuberculosis; treatment outcomes.

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INTRODUCTION

Tuberculosis (TB) remains a leading infectious cause of morbidity and mortality worldwide, with an estimated 10.6 million new cases and 1.4 million deaths in 2019.[1] Despite advances in diagnosis and treatment, TB continues to pose a major challenge in low- and middle-income countries. Nepal, among the 30 high TB burden countries, has a prevalence rate of 245 per 100,000 population.[2] The intersection of TB and non-communicable diseases, particularly diabetes mellitus (DM), has gained attention.[3] DM increases the risk of active TB due to immune dysregulation, and their coexistence is linked to higher bacillary load, delayed sputum conversion, severe radiographic changes, and poorer outcomes.[4] The rising DM prevalence in TB-endemic regions threatens TB control efforts.[5] Globally, DM prevalence among TB patients is 10–30%, with 9.2-12.3% reported in Nepal.[6] This study evaluates glycemic status in newly diagnosed TB patients and its impact on clinical, radiological, and treatment outcomes.

METHODS

This hospital-based prospective cohort study was carried out in the Department of Internal Medicine at the Tribhuvan University Teaching Hospital (TUTH), Kathmandu, Nepal. The study was conducted over a period of 13 months, from July 2023 to August 2024. As a tertiary-level referral center, TUTH receives patients from across the country, providing a diverse clinical population for investigation. The prospective design of this research allowed for real-time data collection and systematic follow-up of participants, thereby enhancing the validity of the findings and reducing recall bias. Prior to initiation, ethical clearance was obtained from the Institutional Review Committee (IRC) of the Institute of Medicine, Maharajgunj Medical Campus, Tribhuvan University (Ref. No. 18(6-11) E2/080/081). All ethical principles outlined in the Declaration of Helsinki were strictly followed. Written informed consent was obtained from every participant before enrollment. For patients who were unable to provide consent themselves due to medical reasons, consent was obtained from their legally authorized representatives. Throughout the study, confidentiality and privacy were maintained by anonymizing patient identifiers and securely storing research records. The study population included adult patients aged 18 years and above with a new diagnosis of tuberculosis (TB), either pulmonary or extrapulmonary. Diagnosis was made in accordance with the National Tuberculosis Diagnosis and Management Guideline, which incorporates clinical, radiological, and laboratory criteria. Only those patients who provided written informed consent were included in the study. Exclusion criteria were carefully defined to reduce confounding factors: patients with HIV infection, type 1 diabetes mellitus, pregnancy, inadequate clinical or laboratory data, or those simultaneously participating in another similar research project were excluded. The rationale for excluding HIV-positive individuals was to avoid the immunosuppressive confounding effects of HIV on TB outcomes, while exclusion of type 1 diabetes focused the study on type 2 diabetes, which has a much higher prevalence in Nepal.

The required sample size was calculated using the standard statistical formula: $n = Z^2*p*q/e^2$, where, Z represents the standard normal deviate at 95% confidence (1.96), p is the estimated prevalence of diabetes among pulmonary TB patients, q=1–p, and e is the acceptable margin of error (5%). Using an estimated prevalence of 9.1% for diabetes in TB patients, the minimum sample size was determined to be 128. To account for a potential non-response or dropout rate of 10%, the final target sample size was increased to 140 patients.

The main exposure variable was the presence of diabetes mellitus (DM), diagnosed according to the criteria of the American Diabetes Association (ADA). This included fasting blood sugar, post-prandial blood sugar, random blood sugar, or glycated hemoglobin (HbA1c) levels, depending on the availability of test results. The primary outcomes assessed were clinical characteristics, radiological features, pleural fluid adenosine deaminase (ADA) levels, duration of hospital stay, sputum conversion at two months, and adverse drug reactions (ADRs).

Secondary variables included demographic and lifestyle parameters such as age, sex, body mass index (BMI), smoking status, and other comorbid conditions. Data were collected by the authors including principal investigator using a structured and pre-tested proforma. The proforma included detailed sections on demographic characteristics, medical history, comorbidities, smoking and alcohol use, clinical symptoms of TB, BMI measurements, laboratory results, and imaging findings. Diabetes-related measurements were recorded systematically to minimize misclassification. Radiological findings were interpreted by qualified physicians with access to digital chest X-rays and other imaging modalities as appropriate. For patients with extrapulmonary TB, pleural fluid was analyzed for ADA, an important diagnostic marker.

Follow-up assessments were carried out at the completion of the intensive phase of anti-tubercular therapy (ATT). Sputum conversion status and the presence of adverse drug reactions were assessed through direct evaluation or telephone interviews. This approach allowed consistent follow-up while minimizing patient inconvenience. To minimize selection bias, all consecutive eligible admissions during the study period were enrolled. Standardized data collection tools ensured uniformity of information across participants. Data were initially entered into Microsoft Excel and later analyzed using Statistical Package for Social Sciences (SPSS) version 16. Descriptive statistics were applied, with continuous variables expressed as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. Inferential statistics were performed to compare groups: independent Student's t-test was used for continuous variables, while Chi-square or Fisher's exact test was used for categorical data, depending on the expected cell counts. A p-value of <0.05 was considered statistically significant throughout the analysis.

RESULTS

A total of 140 newly diagnosed tuberculosis (TB) patients were included in the study. The mean age was 48.6±20.2 years (range 18-95), with 94(67%) male and 46(33%) female patients. The majority were from Bagmati Province (47.9%). Diabetes mellitus (DM) was present in 33 patients (23.6%). Most diabetics (63.6%) had a disease duration of less than 5 years, and peripheral neuropathy was the most frequent DM-related complication (53.1%). Baseline characteristics of TB patients according to diabetes status are shown in Table 1.

Table 1. Baseline characteristics of TB patients according to diabetes status. (n=140)

Variables	Diabetes (n=33)	No Diabetes (n=107)	p-value
Age, Mean ± SD (years)	56.5±17.1	46.1±20.7	<0.001
Sex			
Male, n(%)	24(73%)	72(67%)	0.67
Female, n(%)	9(27%)	35(33%)	
BMI <18.5 kg/m², n(%)	6(18%)	14(13%)	0.389
Smoking, n(%)	12(36%)	48(45%)	0.427
Fever, n(%)	24(73%)	81(75%)	0.819
Cough, n(%)	21(64%)	72(68%)	0.698
Weight loss, n(%)	11(33%)	64(60%)	0.009
Hemoptysis, n(%)	4(12%)	8(7%)	0.477

Pulmonary TB accounted for 57.1% of cases, with 78.8% of these bacteriologically confirmed. Extra-pulmonary TB most commonly involved the pleura (51.7%), followed by abdominal, CNS, and disseminated disease. The distribution of tuberculosis type and site is shown in Table 2.

Table 2. Distribution of tuberculosis type and site. (n=140)

TB Type / Site	Frequency (%)
Pulmonary TB	80(57.1)
Bacteriologically confirmed	63(45.0)
Clinically diagnosed	17(12.1)
Extra-pulmonary TB	60(42.9)
Pleural TB	31(22.1)
Abdominal TB	11(7.9)
CNS TB	12(8.6)
Disseminated TB	4(2.9)

There were no significant differences in hemoglobin, serum albumin, or radiological findings between diabetics and non-diabetics. However, mean Pleural fluid adenosine deaminase (ADA) levels were significantly lower in diabetics. Laboratory and

radiological findings are summarized in Table 3.

Table 3. Laboratory and radiological findings in TB patients with and without diabetes. (n=140)

Parameters	Diabetes (n=33)	No Diabetes (n=107)	p-value
Hemoglobin (g/dL), Mean ± SD	11.4 ± 2.4	11.4 ± 2.3	
Serum albumin (g/dL), Mean ± SD	2.8 ± 0.4	2.8 ± 0.4	
Pleural Fluid ADA (IU/L), Mean	20.9	37.9	0.043
Consolidation on CXR, n (%)	17(100%)	61(97%)	0.456
Cavitation on CXR, n (%)	5(15%)	14(13%)	0.774

Diabetic patients had a significantly longer mean hospital stay. Sputum conversion rates at two months were lower in diabetics, though not statistically significant. Treatment outcomes are presented in Table 4.

Table 4. Treatment outcomes in TB patients with and without diabetes. (n=140)

Outcome	Diabetes	No Diabetes	p-value
Duration of hospital stay (days), mean ± SD	12.7 ± 5.8	9.3 ± 5.8	0.004
Sputum conversion at 2 months*, n(%)	26(78.6%)	26(78.6%)	0.068

**Among bacteriologically confirmed pulmonary TB cases.*

Adverse drug reactions (ADRs) were reported in 38.6% of patients. Peripheral neuropathy was significantly more common in diabetics (Table 5).

Table 5. Adverse drug reaction profile in TB patients with and without diabetes. (n=140)

ADR	Diabetes n(%)	No Diabetes n(%)	p-value
Nausea/vomiting	5(19)	24(23)	0.39
Hepatotoxicity	1(3)	12(11)	0.295
Peripheral neuropathy	6(18)	4(4)	0.01

DISCUSSION

In this hospital-based prospective cohort study from a tertiary care center in Nepal, 23.6% of newly diagnosed tuberculosis (TB) patients were found to have coexisting diabetes mellitus (DM). This prevalence is considerably higher than the estimated DM prevalence in the general adult population of Nepal (8–12%) and is consistent with the global observation that TB patients are disproportionately affected by DM.[1-3] The growing intersection of these two diseases-often referred to as the TB-DM syndemic-poses an increasing threat to TB control programs, particularly in low- and middle-income countries undergoing rapid urbanization and lifestyle changes. Our findings reinforce the urgent need for context-specific strategies to address this dual burden.

The prevalence of DM in TB patients observed in this study aligns with data from other high TB-burden countries, including India (19–25%) and Indonesia (21–30%), and is slightly above the global pooled estimate of 15.3%.[7–8] For example, a large Indian study found a DM prevalence of 23.7% among newly detected TB patients.[9] The relatively high burden observed in Nepal may reflect the dual epidemics of TB and DM in South Asia, coupled with increased detection of hyperglycemia during TB evaluation.[10] These findings strengthen the case for routine DM screening in all newly diagnosed TB patients in Nepal. From a public health perspective, the high prevalence highlights the importance of integrating non-communicable disease (NCD) management within existing TB control programs. We found that diabetic TB patients were significantly older than their non-diabetic counterparts (mean age 56.5 vs. 46.1 years), consistent with findings from other regions.[11–13] This is expected, given the age-related risk for DM and its chronic nature. The association between advancing age and greater TB-DM comorbidity suggests that demographic shifts in Nepal, with increasing life expectancy and rising NCD prevalence, may worsen the syndemic burden in the future.

Interestingly, weight loss was less frequently reported in diabetics (33% vs. 60%, p-value=0.009). This contrasts with some studies that reported equal or higher weight loss among diabetics.[12] Possible explanations include better baseline nutritional reserves in diabetic individuals, earlier healthcare-seeking behavior due to frequent medical interactions,

or differences in metabolic responses to infection. Additionally, while systemic features such as fever and cough were similar between the two groups, diabetic TB patients in other studies often present with more severe respiratory symptoms, higher bacillary loads, and delayed clearance of sputum.[12–13] Although our findings only partially support this, they point to important heterogeneity in symptomatology. Mean adenosine deaminase (ADA) levels in extrapulmonary TB were significantly lower among diabetics (20.9 vs. 37.9 IU/L, p-value=0.043). ADA reflects T-cell-mediated immunity, and its reduction in diabetics may indicate impaired cell-mediated responses caused by chronic hyperglycemia.[14,15] Lower ADA values in diabetics are clinically important, as they may complicate the diagnosis of pleural or other forms of extrapulmonary TB where ADA is commonly used as a biomarker. This suggests that diagnostic thresholds may need adjustment when interpreting ADA levels in TB patients with DM.

Radiologically, our study did not show significant differences in consolidation or cavitation rates between the two groups. This contrasts with several studies reporting a higher proportion of lower lung field involvement and extensive cavitations among diabetics.[14] Differences across studies may reflect variations in TB strain virulence, glycemic control during illness, and methodological differences in imaging interpretation. Our findings suggest that radiological features alone may not be sufficient to identify diabetic TB patients, and clinical and laboratory parameters must be integrated. Diabetic patients had significantly longer hospital stays (12.7 vs. 9.3 days, p-value=0.004), underscoring the additional burden posed by comorbidity. Prolonged hospitalization increases healthcare costs and may expose patients to nosocomial complications. This finding highlights the need for integrated care pathways that manage both TB and DM more efficiently, potentially reducing hospitalization durations. Sputum conversion rates at two months were lower in diabetics (78.6% vs. 95.9%), although not statistically significant (p-value=0.068). Delayed sputum conversion in diabetics has been consistently reported in other studies and is thought to result from impaired host immunity, altered pharmacokinetics of anti-TB drugs, and coexisting complications.[16] Even though our results did not reach statistical significance, the observed trend reinforces concerns about treatment delays and their implications for TB transmission.

Adverse drug reactions (ADRs) were common, and peripheral neuropathy occurred significantly more often in diabetics (18% vs. 4%, p-value=0.010). This is likely due to the synergistic effects of pre-existing diabetic neuropathy and isoniazid-induced neurotoxicity.[17] The finding highlights the importance of proactive pyridoxine supplementation and close neurological monitoring in TB patients with diabetes. Other ADRs, such as hepatotoxicity and gastrointestinal symptoms, did not differ significantly between groups.

The intersection of TB and DM has critical implications for TB control in Nepal. DM is not only associated with altered clinical presentation and diagnostic challenges but also with poorer treatment outcomes, including prolonged hospitalization and higher risk of complications.[18] These findings support the World Health Organization's recommendation for bidirectional screening-testing TB patients for DM and DM patients for TB. Early detection of comorbidity can facilitate timely interventions, improve treatment outcomes, and reduce transmission risks.[19] Our findings also underscore the importance of integrating glycemic control within TB management. Studies suggest that optimizing blood glucose levels improves immune function and accelerates sputum conversion. Although HbA1c was not systematically measured in our study, its incorporation into TB management protocols could help stratify risk and guide individualized treatment. Policymakers in Nepal may also consider routine DM screening at the time of TB diagnosis, particularly in high-risk groups such as older adults and those with extrapulmonary TB.

Limitations

This study has several strengths, including its

prospective design, standardized data collection, and comprehensive inclusion of both pulmonary and extrapulmonary TB cases. The use of ADA criteria for DM diagnosis improves comparability with global studies. However, limitations include its single-center setting, which may limit generalizability; the absence of long-term follow-up to assess relapse or mortality; and the lack of HbA1c testing in all patients, which may have led to misclassification of chronic glycemic status. Additionally, unmeasured confounders such as socioeconomic status, dietary habits, and level of glycemic control during treatment could have influenced the observed associations.

CONCLUSIONS

This study highlights a high burden of DM among newly diagnosed TB patients in Nepal and demonstrates that DM is associated with older age, altered symptom presentation, lower ADA levels, prolonged hospitalization, and increased risk of peripheral neuropathy. These findings underscore the importance of integrating DM management into TB care pathways. National TB programs should implement routine bidirectional screening, optimize glycemic control during TB treatment, and provide targeted patient education. Future multicenter, longitudinal studies are warranted to evaluate long-term treatment outcomes, the cost-effectiveness of integrated care models, and the role of glycemic control in modifying TB prognosis.

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