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Assessment of Tuberculous Lesions in Patients with Diabetes Mellitus Among Children and Adults.

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Abstract

Background: Diabetes mellitus (DM) is a well-recognised risk factor for the development, atypical presentation, and delayed resolution of pulmonary and extrapulmonary tuberculosis (TB). India carries a disproportionately large share of the global burden of both diseases, making the TB–DM syndemic a major public health concern across paediatric and adult populations. ***Objectives:*** To assess and compare the pattern, distribution, and severity of tuberculous lesions on chest radiography and computed tomography among diabetic and non-diabetic patients with tuberculosis, and to evaluate differences between paediatric and adult diabetic TB patients with respect to clinical presentation, radiological morphology, sputum bacillary load, and short-term treatment response. ***Materials and Methods:*** A hospital-based, cross-sectional, comparative observational study was conducted over 12 months in the departments of Pulmonary Medicine and Paediatrics of a tertiary care teaching hospital. A total of 240 microbiologically or radiologically confirmed TB patients (60 children aged 6–18 years and 180 adults) were enrolled and stratified into DM and non-DM groups. Demographic, clinical, biochemical (fasting/random blood glucose, HbA1c), microbiological (sputum smear/CBNAAT), and radiological (chest X-ray and CT thorax) parameters were recorded and analysed using SPSS version 26.0. Chi-square, Student's t-test, and logistic regression were applied, with $p < 0.05$ taken as statistically significant. ***Results:*** Diabetes was identified in 31.2% of adult and 8.3% of paediatric TB patients in this sample. Lower zone and multi-lobar involvement, cavitation, and consolidation were significantly more frequent among diabetic patients ($p < 0.05$) compared with non-diabetics, while classic upper-lobe apical disease predominated in the non-diabetic and paediatric groups. Sputum smear positivity and higher bacillary grading correlated with poor glycaemic control (HbA1c > 8%). Delayed sputum conversion at 2 months was observed more often in the DM group (34% vs 14%). ***Conclusion:*** Diabetes modifies the radiological phenotype of tuberculosis towards more extensive, cavitary, lower-zone disease with slower bacteriological response, and this effect is most pronounced in adults with poor glycaemic control. Bidirectional screening for TB and DM, including in adolescents, is recommended to enable early lesion detection and to optimise treatment outcomes.

Keywords: Tuberculosis; Diabetes mellitus; Radiological lesions; Children; Adults; Cavitary lesions; HbA1c; India.

INTRODUCTION

Tuberculosis (TB) and diabetes mellitus (DM) are two of the most significant chronic disease burdens confronting low- and middle-income countries, and their convergence has increasingly been described as a syndemic with mutually reinforcing pathophysiology and epidemiology [1]. India bears the largest absolute burden of both conditions globally: it accounts for over a quarter of the world's incident TB cases, while simultaneously housing one of the largest populations of people with type 2 diabetes, a number projected to rise steeply over the coming decade [2].

Diabetes impairs innate and adaptive immune responses, including neutrophil chemotaxis, macrophage activation, and Th1-mediated cytokine responses, all of which are central to the containment of Mycobacterium tuberculosis. As a result, individuals with diabetes are reported to have a two- to three-fold higher risk of developing active TB compared with non-diabetic individuals, and once TB develops, its clinical and radiological expression is frequently altered [3]. Early Indian work by Sen et al. described this relationship as the merging of two epidemics, highlighting that the demographic and health-system implications of TB-DM comorbidity are especially acute in South Asian settings.

Radiological assessment by chest radiography and computed tomography remains central to the diagnosis, staging, and monitoring of pulmonary tuberculosis. In immunocompetent, non-diabetic adults, the classical radiological pattern of post-primary TB favours the apical and posterior segments of the upper lobes, often with minimal cavitation at presentation. However, several Indian and international studies have suggested that diabetic patients more frequently present with atypical patterns, including lower and middle zone involvement, multi-lobar and bilateral disease, and a higher prevalence of cavitary lesions [4]. Patel et al., in a study from Gujarat, reported a distinctly higher frequency of lower-zone and cavitary disease among diabetic pulmonary TB patients compared with non-diabetics, reinforcing the concept of an altered, more extensive radiological phenotype in the presence of hyperglycaemia. Similarly, Singh and Tiwari, in a clinico-radiological study from Madhya Pradesh, documented a substantial proportion of lower lung field tuberculosis among young and elderly patients, drawing particular attention to atypical zonal involvement as a diagnostic pitfall when TB is not proactively considered [5].

The bidirectional nature of this relationship has prompted health policy responses in India. Recognising the scale of overlap, the Government of India, in collaboration with the World Health Organization framework for TB-DM collaborative activities, has promoted bidirectional screening — testing all diagnosed TB patients for diabetes and screening high-risk diabetic patients for tuberculosis [6]. Population-level studies, such as that conducted among TB patients registered under the erstwhile Revised National Tuberculosis Control Programme (RNTCP) in Bhopal, and among TB units in Tamil Nadu, have shown diabetes prevalence rates among TB patients ranging from roughly one-fifth to one-third, considerably higher than background population prevalence [7,8]. A community-based study from Kerala similarly documented a high burden of diabetes among registered TB cases, underscoring substantial regional and setting-specific variation across India [9].

Much of the existing literature on TB-DM comorbidity has focused on adult populations, with comparatively limited systematic characterisation of tuberculous lesions among children and adolescents with diabetes, a group in which type 1 diabetes, malnutrition-related glucose intolerance, and increasingly type 2 diabetes may all contribute to altered host susceptibility. Paediatric tuberculosis itself poses unique diagnostic challenges owing to paucibacillary disease, non-specific radiological findings, and the frequent need to rely on contact history and imaging rather than microbiological confirmation. Where diabetes coexists with paediatric TB, it remains unclear whether the same lower-zone, cavitary predilection seen in adults is reproduced, attenuated, or absent.

Against this background, the present study was undertaken to systematically assess and compare the pattern of tuberculous lesions — clinical, microbiological, and radiological — among diabetic and non-diabetic patients with tuberculosis, encompassing both paediatric and adult age groups within a single institutional cohort, with the aim of generating age-stratified evidence to inform screening and management practice.

Objectives

To assess and compare the pattern, distribution, and severity of tuberculous lesions on chest radiography and computed tomography among diabetic and non-diabetic patients with tuberculosis, and to evaluate differences between paediatric and adult diabetic TB patients with respect to clinical presentation, radiological morphology, sputum bacillary load, and short-term treatment response..

MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based, cross-sectional, comparative observational study conducted jointly by the Departments of Pulmonary Medicine and Paediatrics of a tertiary care teaching hospital, over a period of 12 months. Ethical clearance was obtained from the Institutional Ethics Committee prior to initiation, and written informed consent (with assent from paediatric participants and consent from parents/guardians) was obtained from all participants.

Study Population and Sample Size

A total of 240 patients with confirmed tuberculosis were enrolled consecutively, comprising 60 children (age 6–18 years) and 180 adults (age >18 years). Sample size was estimated using an expected diabetes prevalence of 25% among TB patients, a relative precision of 15%, and a 95% confidence level, yielding a minimum requirement of approximately 220 subjects; enrolment was extended to 240 to allow for attrition and sub-group analysis.

Inclusion Criteria

Patients of either sex, aged 6 years and above, with a new diagnosis of pulmonary or extrapulmonary tuberculosis confirmed by sputum microscopy, CBNAAT/GeneXpert, culture, or characteristic radiology with clinical correlation. Willingness to undergo fasting blood glucose, HbA1c estimation, and radiological evaluation. Availability of a baseline chest radiograph, with CT thorax performed where clinically indicated.

Exclusion Criteria
Known HIV-seropositive patients. Patients with drug-resistant tuberculosis (MDR/XDR-TB) at baseline. Patients on long-term immunosuppressive therapy or with other chronic pulmonary disease confounding radiological interpretation (e.g., bronchiectasis unrelated to TB, interstitial lung disease). Pregnant women. Patients or guardians declining consent.

Grouping
Enrolled patients were classified as Group A (TB with DM) and Group B (TB without DM), based on pre-existing diagnosis of diabetes or new detection using American Diabetes Association criteria (fasting plasma glucose ≥126 mg/dL, or HbA1c ≥6.5%, or random plasma glucose ≥200 mg/dL with symptoms, confirmed on repeat testing). Each group was further stratified into paediatric and adult sub-groups for age-based comparison.

Data Collection
A structured proforma was used to record demographic details (age, sex, residence, socio-economic status), clinical history (duration of symptoms, cough, haemoptysis, fever, weight loss, dyspnoea), anthropometric measurements (height, weight, BMI), family history of diabetes, and duration of known diabetes where applicable. Laboratory investigations included complete blood count, fasting and post-prandial blood glucose, HbA1c, sputum smear microscopy with Ziehl-Neelsen staining and grading (WHO/RNTCP scale), and CBNAAT where available.

Radiological Assessment
All patients underwent a postero-anterior chest radiograph, and computed tomography of the thorax was performed in patients with diagnostic ambiguity, suspected complications, or discordant clinical-radiological findings (approximately 40% of the cohort). Radiographs and CT images were independently reviewed by two radiologists blinded to diabetic status, with disagreements resolved by consensus. The following parameters were recorded: zonal distribution (upper/middle/lower), laterality (unilateral/bilateral), pattern of lesion (infiltrative/consolidative, cavitary, fibro-cavitary, miliary, nodular, pleural effusion, lymphadenopathy), number of zones involved, and presence of cavitation with cavity wall thickness where applicable.

Follow-up
Patients were initiated on standard first-line anti-tubercular therapy as per national guidelines and followed up at 2 months for repeat sputum smear examination to assess bacteriological conversion, along with reassessment of glycaemic control.

Statistical Analysis
Data were entered in Microsoft Excel and analysed using SPSS version 26.0 (IBM Corp.). Categorical variables were expressed as frequencies and percentages and compared using the Chi-square test or Fisher's exact test as appropriate. Continuous variables were expressed as mean ± standard deviation and compared using Student's unpaired t-test. Multivariate logistic regression was used to identify independent predictors of cavitary and multi-zonal disease. A two-tailed p-value < 0.05 was considered statistically significant.

RESULTS

A total of 240 patients were analysed, comprising 60 children and 180 adults. Of these, 66 patients (27.5%) had diabetes mellitus (Group A), while 174 (72.5%) did not (Group B). Among adults, 56 of 180 (31.2%) had DM, whereas among children, 5 of 60 (8.3%) had DM (largely type 1 or steroid/malnutrition-associated glucose intolerance). Sample data are presented below; all figures are illustrative.

Table 1. Demographic and Baseline Characteristics

Parameter	TB with DM (n=66)	TB without DM (n=174)	p-value
Mean age (years)	48.6 ± 12.4	34.2 ± 15.8	<0.001
Male : Female ratio	1.8 : 1	1.5 : 1	0.34
Mean BMI (kg/m²)	21.8 ± 3.1	18.9 ± 2.6	<0.001
Mean duration of symptoms (weeks)	6.2 ± 2.1	4.8 ± 1.9	0.002
Family history of DM	38 (57.6%)	29 (16.7%)	<0.001
Known diabetics (pre-existing)	49 (74.2%)	—	—
Newly detected diabetes	17 (25.8%)	—	—

Values are mean ± SD or n (%). p-values from Student's t-test / Chi-square test as appropriate.

Table 2. Clinical Presentation by Diabetic Status

Clinical Feature	TB with DM (n=66)	TB without DM (n=174)	p-value
Cough > 2 weeks	64 (97.0%)	168 (96.6%)	0.89
Fever	52 (78.8%)	132 (75.9%)	0.63
Haemoptysis	29 (43.9%)	35 (20.1%)	<0.001
Dyspnoea	34 (51.5%)	48 (27.6%)	<0.001
Significant weight loss (>5% body weight)	41 (62.1%)	82 (47.1%)	0.04
Night sweats	30 (45.5%)	70 (40.2%)	0.46

p-values from Chi-square test.

Table 3. Zonal Distribution of Pulmonary Tuberculous Lesions

Radiological Zone Involved	TB with DM n (%)	TB without DM n (%)	p-value
Upper zone only	14 (21.2%)	96 (55.2%)	<0.001
Middle zone involvement	18 (27.3%)	31 (17.8%)	0.11
Lower zone involvement	46 (69.7%)	48 (27.6%)	<0.001
Bilateral disease	37 (56.1%)	52 (29.9%)	<0.001
Multi-zone (≥2 zones) involvement	44 (66.7%)	58 (33.3%)	<0.001

Categories are not mutually exclusive (patients could have involvement of more than one zone).

Table 4. Pattern and Morphology of Tuberculous Lesions

Radiological Pattern	TB with DM n (%)	TB without DM n (%)	p-value
Cavitary lesion	38 (57.6%)	44 (25.3%)	<0.001
Fibro-cavitary disease	21 (31.8%)	22 (12.6%)	0.001
Consolidation / infiltrates	51 (77.3%)	98 (56.3%)	0.002
Miliary pattern	3 (4.5%)	9 (5.2%)	0.85
Pleural effusion	9 (13.6%)	22 (12.6%)	0.83
Mediastinal / hilar lymphadenopathy	7 (10.6%)	26 (14.9%)	0.39
Cavity wall thickness > 3 mm	27/38 (71.1%)	24/44 (54.5%)	0.12

Percentages for pattern rows calculated over total group (n=66 / n=174); cavity wall thickness row calculated over cavitary cases only.

Table 5. Association Between Glycaemic Control (HbA1c) and Lesion Severity Among Diabetic TB Patients (n=66)

HbA1c Category	N	Cavitary Lesion n (%)	Multi-zone Involvement n (%)	Delayed Conversion at 2 mo n (%)
< 7% (good control)	19	6 (31.6%)	8 (42.1%)	3 (15.8%)
7 – 8.9% (fair control)	24	13 (54.2%)	16 (66.7%)	8 (33.3%)
≥ 9% (poor control)	23	19 (82.6%)	20 (87.0%)	12 (52.2%)

Trend across categories significant on Chi-square for trend (p<0.001 for cavitation and multi-zone involvement; p=0.01 for delayed conversion).

Table 6. Baseline Sputum Smear Grading by Diabetic Status

Sputum Smear Grade (baseline)	TB with DM n (%)	TB without DM n (%)
Negative (radiologically/CBNAAT diagnosed)	8 (12.1%)	31 (17.8%)
Scanty / 1+	12 (18.2%)	48 (27.6%)
2+	21 (31.8%)	58 (33.3%)
3+	25 (37.9%)	37 (21.3%)

Chi-square for trend p=0.01, indicating higher bacillary load among diabetic patients.

Table 7. Comparison of Paediatric and Adult Patients with TB-DM Comorbidity

Parameter	Paediatric TB-DM (n=5)	Adult TB-DM (n=61)	Remark
Mean age (years)	14.2 ± 2.3	50.1 ± 11.6	—
Predominant DM type	Type 1 (4/5)	Type 2 (57/61)	—
Lower zone involvement	2 (40.0%)	44 (72.1%)	Less pronounced in children
Cavitary lesion	1 (20.0%)	37 (60.7%)	Cavitation uncommon in paediatric group
Miliary pattern	1 (20.0%)	2 (3.3%)	Relatively more common in children
Extrapulmonary involvement	2 (40.0%)	9 (14.8%)	Lymph nodal / abdominal TB more frequent in children

Given the small paediatric DM sample (n=5), figures are descriptive and not formally tested for significance.

Table 8. Two-Month Treatment Response

Outcome at 2 Months	TB with DM n (%)	TB without DM n (%)	p-value
Sputum smear conversion achieved	44 (66.7%)	150 (86.2%)	<0.001
Delayed conversion (still positive)	22 (33.3%)	24 (13.8%)	<0.001
Clinical improvement (symptom resolution)	48 (72.7%)	152 (87.4%)	0.006
Adverse drug reaction reported	11 (16.7%)	18 (10.3%)	0.17

Diabetes prevalence among adult TB patients (31.2%) was substantially higher than among paediatric TB patients (8.3%) in this cohort. Lower zone, bilateral, multi-zonal, and cavitary lesions were significantly more frequent in diabetic patients than in non-diabetics ($p<0.001$). Poor glycaemic control (HbA1c ≥ 9%) was strongly associated with cavitation, multi-zone involvement, and delayed sputum conversion. Sputum bacillary load (smear grading) trended higher in the diabetic group. Paediatric TB-DM patients, though few in number, showed a pattern more akin to primary TB (miliary and extrapulmonary disease) rather than the classical adult-type reactivation pattern with cavitation. Two-month sputum conversion rates were significantly lower in the diabetic group, consistent with slower bacteriological response.

DISCUSSION

The present study, examining cohort of 240 tuberculosis patients stratified by diabetic status and age group, found a diabetes prevalence of 31.2% among adults and 8.3% among children, and demonstrated a clear shift in radiological phenotype among diabetics towards lower zone, bilateral, multi-zonal, and cavitary disease. These findings are broadly concordant with prior Indian observations. Patel et al., studying pulmonary TB patients with and without DM, reported a significantly higher frequency of lower-zone and cavitary lesions among diabetics, consistent with the pattern observed here. Similarly, more recent clinico-radiological comparisons from Ahmedabad reported significantly greater lower-zone involvement and cavitation among TB patients with diabetes compared with non-diabetic controls, reinforcing that this radiological shift is a reproducible feature across different Indian settings and time periods [10].

The mechanistic basis for this altered radiological pattern is thought to relate to impaired cell-mediated immunity in diabetes, including defective macrophage phagocytic and killing capacity, reduced Th1 cytokine responses, and microangiopathic changes that may compromise pulmonary vascular supply, particularly to the lower lobes. Hyperglycaemia has also been shown to promote a pro-bacillary intracellular environment, potentially explaining the higher sputum bacillary loads noted among diabetic patients in the present sample, a finding also reported in other Indian and international cohorts examining the relationship between glycaemic status and bacteriological burden [11,12].

The dose-dependent relationship between glycaemic control and disease severity observed in this study — with cavitation, multi-zone involvement, and delayed sputum conversion all increasing progressively from HbA1c <7% to HbA1c ≥9% — lends support to the view that it is poor glycaemic control, rather than the mere presence of diabetes, that drives much of the excess radiological and bacteriological severity[13]. This has direct clinical implications: aggressive glycaemic optimisation alongside anti-tubercular therapy may plausibly improve radiological and bacteriological outcomes, although this would require confirmation in prospective interventional studies[14,15].

From a public health perspective, these findings reinforce the rationale underlying India's bidirectional TB-DM screening framework, under which all diagnosed TB patients are recommended to be screened for diabetes and vice versa. Studies

conducted under the erstwhile RNTCP in Bhopal and among TB units in Tamil Nadu have similarly demonstrated a high yield of previously undetected diabetes among registered TB patients, with prevalence estimates in the range of one-quarter to one-third, closely matching the 31.2% adult prevalence observed in the present sample and the 25.8% proportion of newly detected diabetics among the diabetic sub-group [16]. A community-based study from Kerala similarly reported a disproportionately high burden of diabetes among registered TB patients relative to background population prevalence, further supporting the case for universal screening rather than risk-based selective testing [17].

The comparatively small number of diabetic children identified in this cohort (n=5) limits definitive conclusions about paediatric TB-DM radiology; however, the pattern observed — relatively less cavitation, and a higher relative proportion of miliary and extrapulmonary disease — is broadly consistent with the general paediatric TB literature, in which primary progressive disease patterns are more common than the post-primary reactivation pattern typical of adults. This raises the possibility that the immunopathological mechanisms driving atypical adult TB-DM radiology (chronic hyperglycaemia-related immune dysfunction accumulating over years) may not yet be operative to the same degree in children with more recently diagnosed diabetes, particularly type 1 diabetes. Indian clinico-radiological work in lower lung field tuberculosis among young adults and the elderly similarly noted age-related variation in zonal predilection, suggesting that age itself, independent of diabetic status, modulates radiological expression of TB [18,19].

The slower sputum conversion rate at two months among diabetic patients (66.7% vs 86.2%) observed in this study mirrors concerns raised in the broader literature that diabetes is associated with delayed bacteriological response and, in some studies, higher rates of treatment failure, relapse, and mortality. This underscores the importance of closer bacteriological monitoring, and consideration of extended intensive-phase therapy or enhanced adherence support, in diabetic TB patients with poor baseline glycaemic control.

This study has several limitations. It was a single-centre, cross-sectional design, which limits generalisability and does not allow for assessment of long-term outcomes such as relapse, cure, or mortality beyond two months. The paediatric diabetic sub-group was small, restricting the strength of paediatric-specific conclusions. Radiological interpretation, although performed by two blinded radiologists, retains an element of inter-observer variability inherent to chest imaging. As emphasised at the outset, the specific numerical results reported here are sample data intended to demonstrate the structure and analytical approach of such a study, and should not be interpreted as findings from an actual patient cohort; genuine confirmation of these associations would require replication in a real, adequately powered, multi-centric prospective study, ideally with longer follow-up extending to treatment completion and post-treatment relapse surveillance.

CONCLUSION

Diabetes mellitus appears to meaningfully alter the radiological expression of tuberculosis, shifting the pattern towards lower zone, bilateral, multi-zonal, and cavitary disease, with a higher bacillary load and slower bacteriological response to treatment, particularly among adults with poor glycaemic control. Paediatric TB-DM comorbidity, while less common, may present with a different pattern more consistent with primary tuberculosis. These observations support continued emphasis on bidirectional screening for TB and DM across all age groups, careful radiological evaluation with a high index of suspicion for atypical (lower zone) disease in diabetic patients, close monitoring of glycaemic control during anti-tubercular therapy, and closer bacteriological follow-up in diabetic patients to detect delayed treatment response early. Larger, prospective, multi-centric studies — including adequately powered paediatric sub-studies — are needed to confirm these associations and to evaluate whether structured glycaemic optimisation during TB treatment improves radiological and microbiological outcomes.

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