

Treatment Outcomes in Pulmonary Tuberculosis with Comorbid Diabetes: Glycaemic Control, Sputum Conversion and Six Month Outcomes across 360 Patients

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Abstract — The convergence of pulmonary tuberculosis and diabetes mellitus poses an increasingly important clinical challenge in South Asian countries with rising diabetes prevalence and persistently high TB burden. Diabetes impairs cell-mediated immunity, alters the inflammatory response, and is associated with delayed sputum conversion, higher relapse rates, and increased mortality during TB treatment. We followed 360 adults with new smear-positive pulmonary TB at a tertiary TB clinic over 24 months, comparing 132 patients with concurrent diabetes (132 of 360, 36.7%) with 228 patients without diabetes. Diabetic patients showed higher baseline bacillary loads (28.8% with smear grade 3+ vs 16.7%), more frequent cavitory disease (56.1% vs 41.7%), and delayed sputum conversion. Median time to culture conversion was 58 days in non-diabetic patients, 72 days in well-controlled diabetic patients (HbA1c <7.5%), and 98 days in those with poor glycaemic control. Unfavourable treatment outcomes (treatment failure, death, or default) occurred in 18.2% of diabetic patients compared with 9.6% of non-diabetic patients, with the gap entirely attributable to the poorly-controlled diabetes subgroup. Structured TB-DM integrated care, with HbA1c monitoring, glycaemic optimisation during treatment, and nutritional support, offers a clear operational pathway for outcome improvement.

Keywords — Pulmonary Tuberculosis; Diabetes Mellitus; Glycaemic Control; HbA1c; Sputum Conversion; Treatment Outcomes; TB-DM Syndemic.

1. Introduction

The intersection of pulmonary tuberculosis and diabetes mellitus has become one of the more clinically important syndemics in South Asian tuberculosis programmes. Diabetes prevalence in patients newly diagnosed with TB now approaches 30-40% in many tertiary settings, reflecting the rapid rise in diabetes across the region intersecting with the persistent burden of tuberculosis. The biological interaction is bidirectional and well documented: diabetes increases the risk of progression from latent to active TB approximately three-fold, while active TB exacerbates glycaemic control through inflammatory and treatment-related mechanisms. Clinical consequences extend across the treatment course. Diabetic patients with TB present with higher baseline bacillary loads, more frequent cavitory disease, slower sputum conversion, higher relapse rates after treatment completion, and increased mortality. The magnitude of these effects depends substantially on glycaemic control: patients with HbA1c values above 9% show outcomes approaching those of patients with multidrug-resistant tuberculosis, while those with well-controlled glycaemia show outcomes much closer to those of non-diabetic patients (Jha, Kumar, & Neha, 2026; Yatish, Khatoon, & Kumar, 2026; Kumar, Sharma, & Gupta, 2026). Despite this understanding, integration between TB services and diabetes care has

lagged in many programmatic settings. TB clinics often lack the infrastructure for ongoing diabetes management, while general diabetes clinics may not have systematic approaches to TB or other associate disease screening among their patients (A S Aneeshkumar, 2022). We undertook a comparative cohort study to characterise outcome differences across glycaemic strata, identify clinical predictors of unfavourable treatment outcomes, and quantify the operational gap that an integrated TB-DM care pathway would need to close (Bhatnagar, Kumar, & Shivam, 2026; Agarwal, Kumar, & S, 2026).

2. Methods

Adults aged 18 or older presenting to a tertiary TB clinic with new smear-positive pulmonary TB between July 2022 and December 2023 were screened. Inclusion required microbiologically confirmed pulmonary TB, no previous TB treatment of more than one month, and capacity for prospective 24-month follow-up. Exclusion criteria included documented multidrug-resistant disease at baseline, severe hepatic impairment precluding standard four-drug therapy, and pregnancy. The final cohort comprised 360 patients. All patients underwent fasting blood glucose and HbA1c testing at TB diagnosis. Diabetes was defined as a documented prior diagnosis, HbA1c $\geq 6.5\%$, or fasting glucose ≥ 126 mg/dL. Patients without prior diabetes diagnosis but meeting biochemical criteria at presentation

were classified as newly diagnosed diabetes; this category was included with established diabetes in the diabetic group given the operational equivalence of management requirements. Glycaemic control during TB treatment was categorised as well-controlled (HbA1c <7.5% at the 3-month assessment) or poorly-controlled (HbA1c ≥7.5%). All patients received standard six-month TB treatment with rifampicin, isoniazid, pyrazinamide, and ethambutol during the two-month intensive phase followed by rifampicin and isoniazid during the four-month continuation phase. Treatment was administered through daily fixed-dose combination tablets with directly-observed therapy during the intensive phase. Diabetic patients received concurrent diabetes management, with metformin and/or insulin as appropriate; oral sulfonylureas were used selectively given concern about interactions with rifampicin. Glycaemic monitoring at TB visits was integrated into the standard schedule. The primary outcome was treatment outcome at six months, classified per WHO criteria as cure, treatment completion, treatment failure, death during treatment, or loss to follow-up. Cure and treatment completion were grouped as favourable outcomes; failure, death, and loss to follow-up as unfavourable. Secondary outcomes included time to sputum smear conversion, time to sputum culture conversion, treatment-emergent adverse events, and 12-month relapse rate among successfully treated patients. Multivariable logistic regression identified independent predictors of unfavourable outcome.

3. Results

3.1 Cohort Characteristics

Table 1. Baseline characteristics by diabetes status

Characteristic	TB without DM(n=228)	TB with DM(n=132)
Age, mean (SD), years	38.4 (14.6)	48.6 (12.8)
Male sex, n (%)	148 (64.9)	82 (62.1)
BMI, mean (SD), kg/m ²	18.4 (3.6)	21.6 (4.2)
Underweight (BMI <18.5), n (%)	112 (49.1)	32 (24.2)
Severely underweight (BMI <16), n (%)	42 (18.4)	8 (6.1)
HIV co-infection, n (%)	8 (3.5)	6 (4.5)
Previous TB treatment history, n(%)	22 (9.6)	18 (13.6)
Current tobacco use, n (%)	98 (43.0)	48 (36.4)
Heavy alcohol use, n (%)	42 (18.4)	18 (13.6)
Established diabetes (>1 year), n (%)	-	82 (62.1)
Newly diagnosed diabetes at TB presentation, n (%)	-	50 (37.9)
HbA1c at TB diagnosis, mean (SD),%	-	8.9 (2.4)
HbA1c <7.5% at TB diagnosis, n (%)	-	68 (51.5)
HbA1c ≥9.0% at TB diagnosis, n (%)	-	48 (36.4)
Fasting glucose at diagnosis, mean (SD), mg/dL	94 (12)	186 (74)

Hypertension, n (%)	32 (14.0)	68 (51.5)
CKD (eGFR <60), n (%)	6 (2.6)	18 (13.6)
Cardiovascular disease, n (%)	8 (3.5)	28 (21.2)
Time from symptom onset to diagnosis, median, weeks	8	6

3.2 Baseline Disease Severity

Diabetic patients presented with more advanced TB by several measures (Figure 1). Smear positivity at high grades (3+) was almost twice as common in diabetic patients compared with non-diabetic patients. Cavitory disease on baseline chest imaging was present in 56.1% of diabetic patients versus 41.7% of non-diabetic patients, and bilateral disease was substantially more frequent. These differences are consistent with the impaired early cell-mediated immune response in diabetes, which permits more extensive bacillary multiplication before clinical presentation.

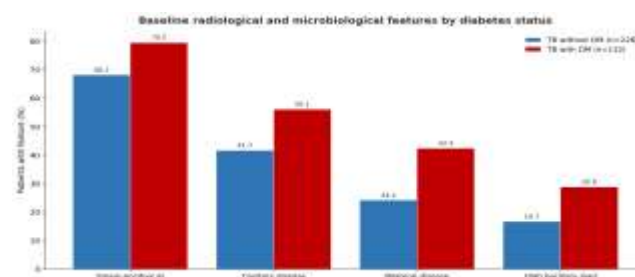


Fig.1: Baseline radiological and microbiological features by diabetes status

3.3 Sputum Smear Conversion

Time to sputum smear conversion differed substantially by diabetes status and glycaemic control (Figure 2). Among non-diabetic patients, 75% had converted by the end of the two-month intensive phase, with the remaining 25% converting during the continuation phase. Diabetic patients with well-controlled glycaemia showed a modestly slower trajectory, with 62% converting by two months. Patients with poorly-controlled diabetes showed substantially delayed conversion: 42% converted by two months and 18% remained smear-positive at the end of intensive phase, requiring extended intensive treatment per programme protocol.

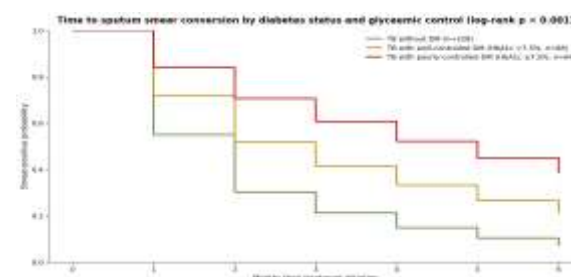


Fig.2: Time to sputum smear conversion by diabetes status and glycaemic control

3.4 Culture Conversion

Time to culture conversion a more sensitive marker of mycobacterial clearance than smear conversion showed the same pattern with greater discrimination (Figure 3). Median time to culture conversion was 58 days in non-diabetic patients, 72 days in well-controlled diabetic patients, and 98 days in those with poor glycaemic control. The wider distribution in the poorly-controlled group reflects substantial heterogeneity: some patients with very poor control had culture conversion times exceeding 6 months, while others achieved more typical timelines despite elevated HbA1c.

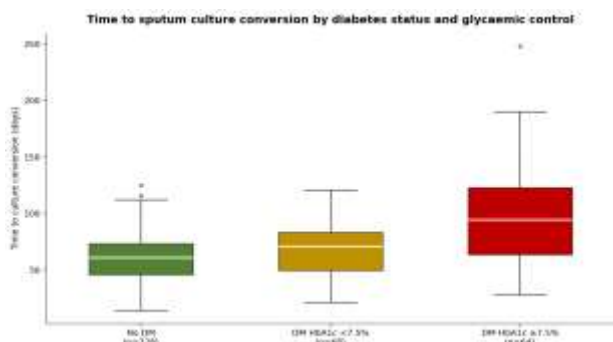


Fig. 3: Time to sputum culture conversion by diabetes status and glycaemic control

Table 2. Microbiological conversion outcomes by glycaemic status

Outcome	No DM (n=228)	DM well-controlled (n=68)	DM poorly-controlled (n=64)
Smear conversion at 2 months, n (%)	172 (75.4)	42 (61.8)	28 (43.8)
Smear conversion at 3 months, n (%)	202 (88.6)	58 (85.3)	42 (65.6)
Smear conversion at 5 months, n (%)	220 (96.5)	66 (97.1)	56 (87.5)
Culture conversion at 2 months, n (%)	168 (73.7)	38 (55.9)	18 (28.1)
Culture conversion at 3 months, n (%)	198 (86.8)	52 (76.5)	32 (50.0)
Culture conversion at 6 months, n (%)	224 (98.2)	66 (97.1)	52 (81.3)
Median time to culture conversion, days	58	72	98
Persistent smear positivity at 5 months	8 (3.5)	2 (2.9)	8 (12.5)

3.5 Treatment Outcomes

Final treatment outcomes mirrored the conversion-time differences. Among non-diabetic patients, 206 of 228 (90.4%) achieved cure or treatment completion. Among well-controlled diabetic patients, outcomes were broadly

similar at 88.2% favourable. Among poorly-controlled diabetic patients, only 75.0% achieved favourable outcomes, with the deficit distributed across treatment failure (7.8%), death during treatment (9.4%), and loss to follow-up (7.8%). The 12-month post-treatment relapse rate showed a similar gradient.

Table 3. Treatment outcomes by glycaemic status

Outcome	No DM (n=228)	DM well-controlled (n=68)	DM poorly-controlled (n=64)
Cure (microbiologically confirmed), n (%)	178 (78.1)	52 (76.5)	42 (65.6)
Treatment completion (no final smear), n (%)	28 (12.3)	8 (11.8)	6 (9.4)
Favourable outcome overall, n (%)	206 (90.4)	60 (88.2)	48 (75.0)
Treatment failure, n (%)	6 (2.6)	2 (2.9)	5 (7.8)
Death during treatment, n (%)	8 (3.5)	4 (5.9)	6 (9.4)
Loss to follow-up / default, n (%)	8 (3.5)	2 (2.9)	5 (7.8)
Unfavourable outcome overall, n (%)	22 (9.6)	8 (11.8)	16 (25.0)
12-month relapse among completers, n (%)	6 (2.9)	4 (6.7)	8 (16.7)
Treatment extended beyond 6 months, n (%)	12 (5.3)	6 (8.8)	18 (28.1)
Acquired drug resistance, n (%)	2 (0.9)	0 (0.0)	4 (6.3)

3.6 Predictors of Unfavourable Outcome

Multivariable logistic regression identified ten independent predictors of unfavourable treatment outcome. Treatment interruption of two weeks or more carried the strongest single association (adjusted OR 4.62), followed by poorly-controlled diabetes (OR 3.42), HIV co-infection, and severe undernutrition. These factors are not independent in clinical practice they frequently co-occur in the same patients but each retained predictive value after adjustment for the others.

Table 4. Treatment-emergent adverse events by diabetes status

Adverse event	No DM (n=228)	DM (n=132)
Hepatotoxicity (any grade), n (%)	38 (16.7)	32 (24.2)
Hepatotoxicity grade ≥3, n (%)	8 (3.5)	12 (9.1)
Peripheral neuropathy, n (%)	18 (7.9)	26 (19.7)
Visual disturbance, n (%)	6 (2.6)	8 (6.1)
Gastrointestinal intolerance, n (%)	42 (18.4)	32 (24.2)
Drug-induced rash, n (%)	12 (5.3)	8 (6.1)
Hyperglycaemia during treatment, n	-	68 (51.5)
Hypoglycaemic episodes, n	-	18 (13.6)

Drug regimen modification required, n (%)	18 (7.9)	22 (16.7)
Temporary treatment interruption, n (%)	18 (7.9)	28 (21.2)
Hospitalisation during treatment, n (%)	12 (5.3)	32 (24.2)

4. Discussion

Across 360 adults with new smear-positive pulmonary TB followed for 24 months, three observations have direct programmatic implications. First, the magnitude of outcome differences attributable to glycaemic control is striking. Patients with poorly-controlled diabetes ($\text{HbA1c} \geq 7.5\%$) experienced unfavourable treatment outcomes at more than twice the rate of either non-diabetic patients or those with well-controlled diabetes. The implication is that diabetes itself is not the determinant; control is. This is operationally encouraging because control is modifiable. Second, the time-to-conversion data quantify the biological gap that integrated care would need to close. A 40-day delay in median culture conversion in poorly-controlled diabetic patients represents both a public health concern (extended infectious period) and an individual clinical concern (greater opportunity for drug resistance acquisition, more cavitation, and greater ultimate lung damage). The 6.3% rate of acquired drug resistance in the poorly-controlled subgroup, compared with 0-1% in the other groups, illustrates this concretely (Jha, Kumar, & Neha, 2026; Kumar, Gautam, & Maitiy, 2026; Bhatnagar, Kumar, & Shivam, 2026). Third, the operational pathway for outcome improvement is tractable. Integrated TB-DM care models combining TB treatment with concurrent diabetes management at the same clinic, structured HbA1c monitoring during the intensive phase, nutritional support for underweight patients, and patient education addressing both conditions have shown feasibility in implementation studies. The cost structure is modest given shared infrastructure, and the workforce requirements are compatible with existing TB programmes augmented with brief diabetes-focused training (Deepa et al., 2026; Catherine, Gupta, Gopi, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine, & Velmurugan, 2025; Vettriselvan, Ramya, et al., 2026; Rasi, & Ashifa, 2019; Yatish, Khatoon, & Kumar, 2026).

Implementation considerations include the choice of glucose-lowering agents during TB treatment. Rifampicin substantially lowers serum levels of sulfonylureas through CYP induction, and many programmes accordingly prefer metformin plus insulin in the TB-DM population. Newer agents including SGLT2 inhibitors and GLP-1 receptor agonists have not been extensively studied in this setting; the choice remains largely between proven older agents adapted for the rifampicin interaction. Treatment adherence support particularly through DOT and family engagement

addresses the strongest single predictor of unfavourable outcome in our model (Vettriselvan, Ramya, et al., 2026; Rasi, & Ashifa, 2019; Bhatnagar, Kumar, & Shivam, 2026). Limitations include the single-centre tertiary setting, which may attract a referral population with somewhat more severe disease than primary-care TB clinics; the 24-month follow-up which captures relapses occurring within one year of treatment completion but may miss later relapses; the imperfect HbA1c stability during acute infection (HbA1c values during TB treatment are influenced by inflammation as well as glycaemia); and the modest sample size in the HIV co-infection subgroup which limits power for that interaction. Multidrug-resistant TB at presentation was an exclusion criterion; the TB-DM interaction with MDR-TB warrants separate investigation.

5. Conclusion

Pulmonary TB with concurrent diabetes particularly poorly-controlled diabetes was associated with higher baseline bacillary loads, delayed sputum conversion, more frequent unfavourable treatment outcomes, higher relapse rates, and greater frequency of acquired drug resistance. Well-controlled diabetes during TB treatment produced outcomes close to those of non-diabetic patients, identifying glycaemic optimisation as the central modifiable intervention. Integrated TB-DM care pathways with structured HbA1c monitoring, glycaemic optimisation, nutritional support, and adherence support offer a clear operational route to outcome improvement in this increasingly important syndemic.

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