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Pre-Diagnosis and Pre-Treatment Loss to Follow-Up Among Individuals with Presumptive Tuberculosis and Diabetes Mellitus: A Retrospective Study Using Routine Surveillance Data in Minahasa, North Sulawesi

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Abstract

Tuberculosis (TB) remains a foremost infectious cause of death worldwide and stands as a major public health concern, particularly in high-burden countries such as Indonesia. Loss to follow-up (LTFU) during the early stages of the TB care cascade, including diagnostic evaluation and treatment initiation, contributes to under-detection and ongoing transmission. Patients with diabetes mellitus (DM) are at increased risk of TB and poor outcomes, with evidence on early-stage LTFU in this population remaining limited in specific settings such as district-level health systems. The objective of this study is to assess the proportion of pre-diagnosis and pre-treatment LTFU and to explore associated factors among presumptive TB individuals with DM. A retrospective cross-sectional study was performed using secondary data from *Sistem Informasi Tuberkulosis* (SITB). The study population comprised presumptive TB individuals with DM aged ≥18 years recorded between January 1 and November 30, 2025. Total sampling was applied. The chi-square or Fisher's exact test was employed for bivariate statistical analysis. A p-value <0.05 was considered statistically significant. A total of 289 presumptive TB individuals with DM were included. Pre-diagnosis LTFU was 4.8 %, while pre-treatment LTFU was 6.4 %. Pre-diagnosis LTFU was significantly associated with area of residence (p=0.021), mode of entry into the TB program (p<0.001), and HIV status (p=0.037), suggesting that disparities in healthcare access and clinical characteristics may influence completion of the diagnostic process. No significant associations were observed for pre-

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treatment LTFU, likely due to the very limited number of events. Early-stage attrition in the TB-DM care cascade remains low but critical (4.8% pre-diagnosis and 6.4% pre-treatment LTFU). Geographical factors, entry points, and HIV comorbidity significantly influence diagnostic continuity. Minimizing patient loss requires strengthening localized tracking, enhancing referral coordination, and optimizing TB-HIV integration within routine health systems.

Keywords: pre-diagnosis LTFU, pre-treatment LTFU, SITB, tuberculosis

Introduction

Tuberculosis (TB) persists as a critical public health challenge globally, ranking among the primary contributors to mortality, especially within developing and resource-limited nations.[1,2] Indonesia remains one of the high TB burden countries, ranking second globally after India and contributing 10% of the global TB incidence. Furthermore, a substantial gap exists between estimated and diagnosed TB cases, indicating potential losses along the diagnostic cascade.[2] This gap reflects ongoing challenges in early case detection, access to diagnostic services, and continuity of care, which may ultimately affect treatment outcomes and hinder TB control efforts.[3,4]

The TB care cascade describes the continuum of care, from case detection and diagnostic evaluation to confirmation of diagnosis, initiation of treatment, and ultimately treatment outcomes such as cure or treatment completion. At each stage of this cascade, patients may be lost to follow-up (LTFU), either before diagnosis or before treatment initiation.[5,6] Early-stage LTFU contributes to the under-detection of TB cases and may facilitate ongoing transmission within the community.[7]

Patients with diabetes mellitus (DM) are at an increased risk of developing TB and experiencing poor treatment outcomes.[8] TB-DM comorbidity presents additional challenges, including delayed diagnosis and difficulties in maintaining continuity of care.[9] According to the Indonesian National TB Report 2023, the proportion of notified TB patients with confirmed DM comorbidity reached 9.0%.[10] Therefore, understanding the patterns of LTFU among presumptive TB individuals with DM is essential for improving program performance.

Evidence from high TB burden countries indicates that LTFU across the TB care cascade remains considerable. In Uganda, pre-diagnosis LTFU was reported at 28.3% and pre-treatment LTFU at 13.7%. Pre-treatment LTFU was also reported at 21.98% in China and 22.1% in India.[6,7,11] Within the Indonesian context, domestic evidence underscores even more critical gaps during the early operational stages; a prospective evaluation in Jogjakarta revealed that up to 43.5% of presumptive TB individuals were LTFU during the diagnostic work-up phase in primary health care.[12] Concurrently, examining post-diagnostic links in routine programmatic data, a retrospective cascade evaluation of drug-resistant TB patients at a tertiary referral hospital in West Java reported that 14.2% of confirmed individuals experienced pre-treatment LTFU before treatment initiation.[13]

Despite the documented 9.0% dual burden of TB-DM in Indonesia, existing domestic studies have fragmented the care cascade by evaluating either pre-diagnosis or pre-treatment attrition in isolation, rather than tracing both early stages consecutively. Furthermore, these available data were strictly confined to general or specialized TB

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populations in highly centralized, urban tertiary facilities, leaving a distinct empirical gap regarding the comprehensive, multi-stage patient loss among individuals presenting with comorbid metabolic conditions. Across these diverse global and domestic contexts, patient attrition is driven by multiple determinants, including sociodemographic characteristics, health system factors, and clinical conditions. Barriers such as limited access to healthcare services, weak referral systems, and fragmented care pathways can significantly increase patient attrition across the TB care cascade.[7,14,15] Nevertheless, documentation of the specific operational and clinical factors associated with pre-diagnosis and pre-treatment LTFU, particularly among individuals with DM, remains critically limited in decentralized settings.

In the Minahasa regency, DM remains a major public health concern, ranking as the third most common disease in 2024 with 5,982 reported cases, while TB accounted for 899 reported cases.[16] To monitor this substantial dual disease burden, Indonesia has implemented an integrated TB recording and reporting system through *Sistem Informasi Tuberkulosis* (SITB), enabling more systematic patient tracking across the health system.[17,18] Within this district-wide programmatic framework, the SITB captures data from a multi-tiered healthcare network comprising primary health care and regional hospitals across expansive suburban and rural landscapes. While this multi-tiered structure is a standard national feature, prior domestic research has evaluated care cascades only within single, isolated facilities.

In contrast, this study leverages the comprehensive district-wide SITB data in Minahasa to capture the fluid movement and subsequent attrition of patients across the entire local health system. Despite this integration, ensuring continuity of care across the TB care cascade remains challenging, particularly during the diagnostic and pre-treatment stages.[6,7] Addressing this issue requires identifying points of patient loss across the TB care cascade to inform targeted interventions that improve early detection and treatment outcomes.[19] To bridge these gaps, this study provides the first comprehensive evaluation of a consecutive, multi-stage care cascade tailored to individuals with presumptive TB and DM in a decentralized setting. Therefore, the objective of this study is to assess the proportion of pre-diagnosis and pre-treatment LTFU and to explore associated factors among individuals with presumptive TB and DM in Minahasa, North Sulawesi.

Method

Study Design and Data Source

This analytical observational study employed a retrospective cross-sectional approach using secondary data from the *Sistem Informasi Tuberkulosis* (SITB), managed by *Dinas Kesehatan Kabupaten* Minahasa. SITB is an electronic recording and reporting system used in the TB control program in Indonesia, which enables integrated management of TB case data by healthcare facilities and health authorities across various administrative levels.[18] Before analysis, the dataset was cleaned and verified for completeness and consistency.

Population and Sample

The study enrolled all registered presumptive TB individuals with comorbid DM registered in SITB during the study period. A total sampling approach was employed, in which all records meeting the predefined inclusion and exclusion criteria were included in the analysis. Inclusion criteria included all presumptive TB individuals with comorbid DM aged ≥18 years recorded between January 1, 2025, and November 30, 2025. Individuals who were undergoing TB treatment at the time of registration were excluded.

Data Collection and Procedures

Data were extracted from the SITB within the specified study period. A data cleaning process was performed to eliminate duplicate entries and resolve case misclassifications. The remaining records were then selected based on the predefined eligibility criteria, establishing a validated baseline dataset. This dataset was subsequently evaluated through the early stages of the TB care cascade. Individuals were categorized as pre-diagnosis LTFU if they did not undergo any form of diagnostic examination. Meanwhile, those with a confirmed positive TB diagnosis who failed to initiate therapy, demonstrated by the absence of both treatment initiation follow-ups and a recorded treatment start date, were classified as pre-treatment LTFU.

Variables and Operational Definitions

The dependent variables evaluated in this study were pre-diagnosis LTFU and pre-treatment LTFU. Meanwhile, the independent variables consisted of demographic characteristics (age and sex), a geographical factor (area of residence), health system characteristics (mode of entry, level of healthcare facility, and facility ownership), and clinical factors (HIV status and TB treatment history).

Mode of entry was classified into self-presented, facility-based screening, and active case finding. Self-presented referred to individuals who came to healthcare facilities on their own for TB examination. Facility-based screening included TB-DM screening, inter-facility referrals, and TB screening through the free health check-up program (*Program Cek Kesehatan Gratis/ CKG*). Active case finding included individuals identified through community health workers and contact investigation.

Area of residence was categorized as residing within or outside Minahasa Regency, based on the residential address recorded in SITB. Individuals residing outside Minahasa were included because they accessed TB services at healthcare facilities located within Minahasa Regency.

A presumptive TB individual is defined as an individual presenting with signs or clinical symptoms suggestive of TB, including persistent cough for two weeks or more, night sweats, fever lasting more than two weeks, weight loss, or a history of contact with a TB patient.[20] TB examination refers to investigations performed to establish a TB diagnosis, including bacteriological examinations (X-pert MTB/RIF and AFB smear microscopy) as well as radiological examination (chest radiography).[21]

Data Analysis

Descriptive and bivariate statistical analyses were performed to evaluate the data. Descriptive statistics summarized the baseline and demographic characteristics of the study participants, with categorical variables presented as frequencies and percentages. Bivariate analyses assessed the associations between the independent variables and the primary outcomes (pre-diagnosis LTFU and pre-treatment LTFU). The chi-square test was employed as the primary inferential method. Exact testing was performed for sparse data, employing Fisher's exact test for 2×2 dimensions and the Fisher–Freeman–Halton test for larger contingency tables, with significance determined at $p < 0.05$.[22] All statistical analyses were performed using IBM SPSS Statistics version 27.

Ethics

This study used secondary data without personal identifiers. All data were anonymized and kept confidential. Ethical approval was obtained from the Ethics Committee of Universitas Padjadjaran (No. 944/UN6.KEP/EC/2025), and research permission was granted by Badan Kesatuan Bangsa dan Politik Kabupaten Minahasa (No. 070/BKPP-421/XI/2025).

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Result

During the study period from January 1 to November 30, 2025, a total of 292 presumptive TB individuals with DM were initially identified within the SITB database in Minahasa Regency. Based on the predefined eligibility criteria, three records were excluded from the analysis (two individuals were aged < 18 years, and one individual was already undergoing anti-TB therapy at the time of registration). This initial screening process yielded a final analytical sample of 289 eligible participants (Figure).

To trace pre-diagnosis LTFU, the diagnostic examinations of these 289 eligible individuals were tracked within the surveillance system. In this sample, 4.8% (14/289) of participants were classified as pre-diagnosis LTFU because they did not undergo any diagnostic evaluations after being registered as presumptive cases. Conversely, the remaining 95.2% (275/289) participants successfully proceeded to TB diagnostic investigations.

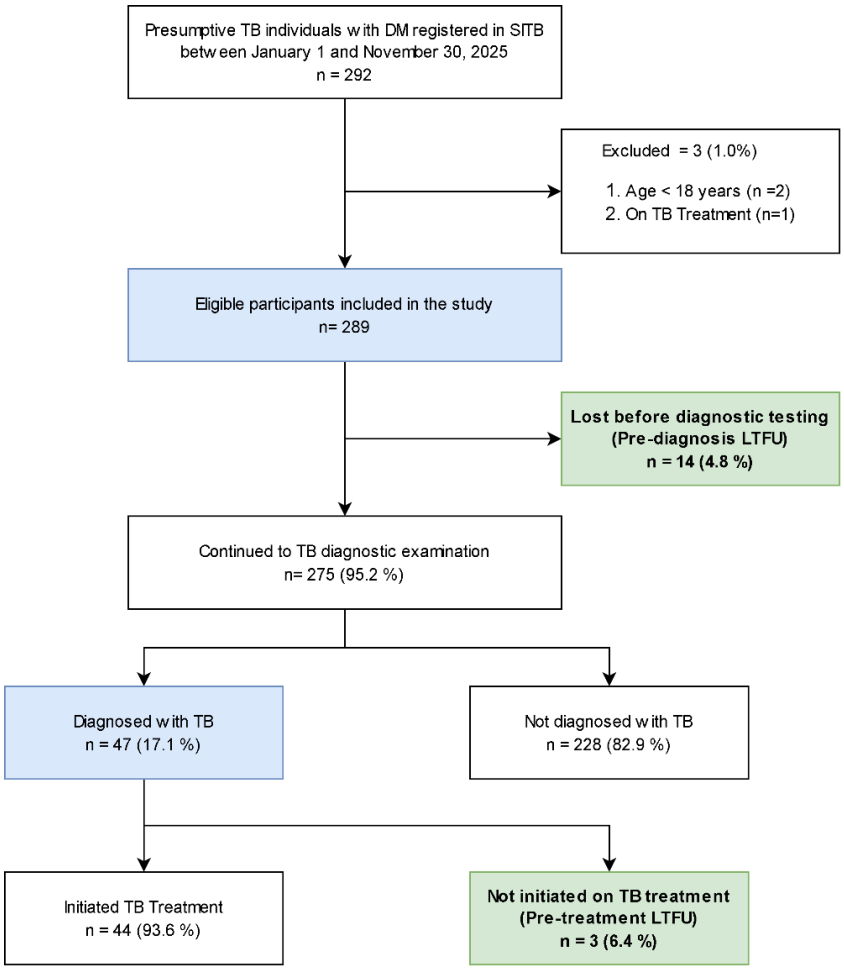

Figure 1. Flow chart of study participant selection

Among the 275 individuals who underwent diagnostic testing, 82.9% (228/275) of participants were confirmed negative or not diagnosed with active TB. Meanwhile, active TB infection was successfully established in 17.1% (47/275) of participants through positive bacteriological or radiological findings. To determine the occurrence of pre-treatment LTFU, the treatment initiation dates for these 47 diagnosed patients were further verified. The tracking results revealed that 6.4% participants (3/47) experienced pre-treatment LTFU due to their failure to initiate anti-TB therapy. The complete

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schematic flow of participant selection, tracking, and outcome categorization is illustrated in Figure.

Characteristics of Participants and Factors Associated with Pre-diagnosis LTFU

Among the study participants (Table 1), the highest proportion was observed in the 45–64-year age group (51.2%), with a range of 20–88 years. Females accounted for the highest proportion (61.2%). The majority of participants resided in the Minahasa regency (91.7%). Most participants were identified through self-presentation (77.9%). In addition, the majority of individuals were registered at primary healthcare facilities (76.1%), and (86.9%) received care at government-owned facilities. Among the study participants, 1.0% were people living with HIV (PLHIV) and had a history of previous tuberculosis treatment.

The bivariate analysis demonstrated that area of residence, mode of entry, and HIV status were significantly associated with pre-diagnosis LTFU. Regarding area of residence, individuals living outside the Minahasa regency experienced a significantly higher rate of pre-diagnosis LTFU than those living within Minahasa (16.7% vs 3.8%; p=0.021). In terms of mode of entry, the proportion of pre-diagnosis LTFU was highest among individuals identified through active case finding (35.7%), followed by facility-based screening (4.0%) and self-presenters (3.1%) (p<0.001). Significant variations in pre-diagnosis LTFU were also observed according to HIV status (p=0.037), with the highest rate of discontinuation found among people living with HIV (PLHIV) (33.3%), followed by individuals with unknown HIV status (6.6%) and HIV-negative individuals (2.7%).

Table 1. Characteristics of Participants and Factors Associated with Pre-diagnosis LTFU

Characteristics	Participants (n=289)		Non LTFU (n=275)		LTFU (n=14)		*p-value*
	N	%[d]	N	%[e]	N	%[e]	
Age (years)							0.688[c]
18-44	39	13.5	38	87.4	1	2.6	
45-64	148	51.2	139	93.9	9	6.1	
≥ 65	102	35.3	98	96.1	4	3.9	
Sex							0.811[a]
Male	112	38.8	107	95.5	5	4.5	
Female	117	61.2	168	94.9	9	5.1	
Area of residence							**0.021[b]***
Minahasa	265	91.7	255	96.2	10	3.8	
Outside Minahasa	24	8.3	20	83.3	4	16.7	
Mode of Entry							**<0.001[c]***
Self-presented	225	77.9	218	96.6	7	3.1	
Facility-based	50	17.3	48	96.0	2	4.0	
Active case finding	14	4.8	9	64.3	5	35.7	
Level of Healthcare Facility							0.530[b]
Primary	220	76.1	208	75.6	12	85.7	
Advanced	69	23.9	36	24.4	2	14.3	
Facility Ownership							1.000[b]

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Table 1. (Extension)

Characteristics	Participants (n=289)		Non LTFU (n=275)		LTFU (n=14)		*p-value*
	N	%[d]	N	%[e]	N	%[e]	
Government	251	86.9	239	95.2	21	4.8	
Private	38	13.1	36	94.7	2	5.3	
HIV Status							**0.037[c*]**
Negative	149	51.6	145	97.3	4	2.7	
PLHIV	3	1.0	2	66.7	1	33.3	
Unknown	137	47.4	128	93.4	9	6.6	
TB Treatment History							0.581[c]
New	272	94.1	259	95.2	13	4.8	
Previous Treated	3	1.0	3	100.0	0	0	
Unknown	14	4.8	13	92.9	1	7.1	

** = significant at p < 0.05; a =chi square test; b = Fisher exact test; c = Fisher-freeman-Halton exact test; d = Column Percentage; e = Row Percentage*

Factors Associated with Pre-treatment LTFU

Associations between the studied variables and pre-treatment LTFU are presented in Table 2. No statistically significant associations were identified. Due to the very limited number of pre-treatment LTFU events (n = 3), sparse cell counts were observed across several variables.

Table 2. Factors Associated with Pre-treatment LTFU (n=47)

Characteristics	Non LTFU (n=44)		LTFU (n=3)		*p-value*
	n	%[d]	N	%[d]	
Age					0.085[c]
18-44 years	9	100.0	0	0	
45-64 years	21	95.5	1	4.5	
≥ 65 years	14	87.5	2	12.5	
Sex					1.000[b]
Male	26	92.9	2	7.1	
Female	18	94.7	1	5.3	
Area of residence					0.343[b]
Minahasa	39	95.1	2	4.9	
Outside Minahasa	5	83.3	1	16.7	
Mode of Entry					1.000[c]
Self-presented	39	92.9	3	7.1	
Facility-based	4	100.0	0	0	
Active case finding	1	100.0	0	0	
Level of Healthcare Facility					1.000[b]
Primary	18	94.7	1	5.3	
Advanced	43	92.9	2	7.1	
Facility Ownership					0.557[b]
Government	27	96.4	1	3.6	
Private	17	89.5	2	10.5	
HIV Status					
Negative	26	92.9	2	7.1	1.000[b]
PLHIV	0	0	0	0	
Unknown	18	94.7	1	5.3	

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Table 2. (Extension)

Characteristics	Non LTFU (n=44)		LTFU (n=3)		*p-value*
	n	%[d]	N	%[d]	
TB Treatment History					1.000[c]
New	36	92.3	3	7.7	
Previous Treated	2	100.0	0	0	
Unknown	6	100.0	0	0	
Diagnostic Type					1.000[b]
Bacteriologically	25	92.6	2	7.4	
Clinically	19	95.0	1	5.0	

** =significant at p < 0.05; a =chi square test; b = Fisher exact test; c = Fisher-freeman-Halton exact test; d=row percentage*

Discussion

Discontinuities in the TB care cascade were identified among presumptive TB individuals with DM. The pre-diagnosis LTFU rate of 4.8% in Minahasa was notably lower than the 43.5% reported in previous domestic research in Jogjakarta.[12] Similarly, the proportion of pre-treatment LTFU observed in this study 6.4% was lower than the 14.2% estimate reported in West Java.[13] However, these comparisons should be interpreted cautiously, as previous studies generally included the overall presumptive TB population rather than presumptive TB individuals with DM. The relatively lower proportion observed in this study may be related to the implementation of collaborative TB-DM activities within the district health system in Minahasa. In line with the national TB-DM collaborative framework, individuals with DM are routinely screened for TB symptoms. In contrast, patients diagnosed with TB are screened for DM through bi-directional screening.[20,23] This integration may facilitate earlier identification of presumptive TB cases among individuals with DM and facilitate referral for diagnostic evaluation. Although the proportion of pre-diagnosis and pre-treatment LTFU in this study was relatively low, missed linkage to diagnostic and treatment services remains important from a public health perspective, as individuals who are lost before diagnosis or treatment initiation may continue to experience delayed care and ongoing transmission.[24–26] Strengthening these integrated services may help reduce losses during the early stages of the TB care cascade.

The association between area of residence and pre-diagnosis LTFU may reflect disparities in access to TB diagnostic services. Minahasa shares administrative borders with several neighboring districts and municipalities.[27] In this study, 8.3% of participants resided outside Minahasa. This cross-border healthcare utilization reflects a complex interplay of geographic proximity and infrastructure. For residents living on the fringes of neighboring districts, traveling to a healthcare facility within Minahasa's administrative boundaries is often shorter and less economically burdensome than traveling to the central facilities of their own districts. Consequently, this cross-border movement directly affects the care cascade, as the association between area of residence and pre-diagnosis LTFU reflects disparities in regional access and limitations in patient tracking. Primary healthcare centers (PHC) in Indonesia generally operate under strict decentralized mandates within designated geographic service areas, meaning that electronic and active patient tracing systems (community health workers or *Kader*) are legally and operationally confined to residents. When a patient from outside the regency fails to return for diagnostic results, local health workers lack the administrative authority and logistical mechanisms to conduct home visits or trace contacts across district lines.[28] This structural barrier significantly exacerbates pre-diagnosis LTFU among non-residents.

Mode of entry was significantly associated with pre-diagnosis LTFU. Most presumptive TB individuals with DM entered the diagnostic pathway through self-

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presentation (77.9%), followed by facility-based screening and active case finding (17.3% and 4.8%). This finding may reflect differences in healthcare-seeking behavior and patient engagement across screening approaches.[29] Individuals identified through active screening may have weaker links to healthcare services, increasing the likelihood of discontinuation during the diagnostic process.[30,31] In addition, delays in diagnostic procedures or the absence of same-day results may further contribute to pre-diagnosis LTFU.[32,33]

HIV status was significantly associated with pre-diagnosis LTFU. This finding may reflect limited engagement with healthcare services, including low uptake of HIV testing, as well as potential stigma that hinders individuals from knowing or disclosing their HIV status.[7,14] Previous studies have reported that the integration of TB and HIV services can improve patient retention and reduce LTFU through more coordinated monitoring and regular contact with healthcare providers.[34] In contrast, individuals with unknown HIV status are less likely to be engaged with the healthcare system, thereby increasing their risk of being lost along the care cascade.[35,36]

In this study, no significant factors associated with pre-treatment LTFU were identified. This finding should be interpreted cautiously because the number of pre-treatment LTFU cases was very limited (n = 3), which may have reduced the statistical power to detect meaningful associations. Although bivariate analysis was performed using the Fisher-Freeman-Halton test, which is appropriate for sparse data and small cell frequencies, the results should be considered exploratory rather than confirmatory.[37] Previous studies have reported that factors such as non-availability of patient tracking information, poor patient-provider communication, older age, history of TB disease, distance of residence from the health facility, complexity of navigating the system, and health care worker attitude.[7,11] The discrepancy between the present findings and previous evidence may be related to the small number of outcome events in this study.

These findings hold direct practical implications for reinforcing the integrated TB-DM care cascade within the district health system. To minimize attrition during the critical pre-diagnosis and pre-treatment phases, health authorities must prioritize strengthening early patient tracking and enhancing referral coordination across all levels of care. Specifically, this requires streamlining the programmatic linkage between screening and diagnostic verification to ensure that individuals identified through active finding or cross-border visits are not lost in transition. Furthermore, optimizing TB-HIV integration within the existing routine screening architecture is essential to overcome barriers to healthcare engagement and reduce LTFU among vulnerable subgroups. By focusing on these localized operational improvements, the district health system can effectively secure a continuous care continuum, ensuring that individuals under dual-disease evaluation are promptly diagnosed and immediately enrolled in treatment.

This study used routinely collected program data from the SITB, allowing analysis of real-world conditions. However, several limitations should be considered. The analysis was limited to variables available in the SITB database, and several potentially relevant factors, such as socioeconomic status, patient knowledge, and quality of patient-provider communication, could not be assessed. The very limited number of pre-treatment LTFU events may also have reduced the statistical power to detect meaningful associations. Furthermore, as this study was conducted in a single regency, the findings may not be generalizable to other settings with different health system characteristics and TB program implementation.

Conclusion

Proportions of pre-diagnosis LTFU (4.8%) and pre-treatment LTFU (6.4%) among presumptive TB individuals with DM were identified in this study. Geographical factors, health system entry points, and clinical comorbidities were significantly associated with pre-diagnosis LTFU, suggesting that multiple determinants influence continuity of care within the TB diagnostic pathway. In contrast, no significant factors were identified for

pre-treatment LTFU. However, this latter finding should be interpreted with caution, as the very limited number of outcome events limited the statistical power to detect meaningful associations, leaving these observations exploratory rather than confirmatory. These findings highlight the critical importance of strengthening early patient tracking, referral coordination, and optimizing TB-HIV integration to minimize attrition before TB diagnosis and treatment initiation among presumptive TB individuals with DM.

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