

Trends in Tuberculosis, Treatment Outcomes and Associated Factors at Gambo General Hospital, Ethiopia: A Ten-Year Retrospective Study

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Trends in Tuberculosis, Treatment Outcomes and Associated Factors at Gambo General Hospital, Ethiopia: A Ten-Year Retrospective Study

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Running Title: Trends in Tuberculosis, Treatment Outcomes and Associated Factor

Abstract

Background: Tuberculosis (TB) remains a leading cause of infectious disease mortality worldwide, with sub-Saharan Africa bearing a disproportionate burden. Ethiopia is among the top ten high-burden countries globally. Evaluating trends in TB, treatment outcomes and identifying associated factors is critical for improving TB control, particularly in resource-limited, remote settings.

Objective: To assess trends in TB, treatment outcomes and associated factors among TB patients diagnosed and treated at Gambo General Hospital TB clinic.

Methods: A hospital-based retrospective cross-sectional study was conducted by reviewing medical records of TB patients registered from January 1, 2015 to December 30, 2024 for treatment at GGH. Data were extracted from TB unit registers, laboratory logbooks, and patient files using a standardized electronic data abstraction tool (Kobo Toolbox). A total of 931 patient records were analyzed. Data were analyzed using SPSS version 29.0. Bivariate and multivariable logistic regression models were used to identify factors associated with treatment outcomes, with statistical significance set at $p < 0.05$.

Results: Among the 931 patients, the overall treatment success rate was 86.0% ($n=801$), consisting of 42.3% ($n=394$) cured and 43.7% ($n=407$) treatment completed. Unsuccessful outcomes accounted for 14.0% ($n=130$), including treatment failure 10.8% ($n=101$) and death 3.1% ($n=29$). Annual success rates ranged from 79.2% (2018) to 89.5% (2023). Compared to patients aged ≥ 60 years, younger age groups had significantly lower odds of poor outcomes: ≤ 14 years (AOR=0.36; 95% CI: 0.16–0.82), 15–29 years (AOR=0.35; 95% CI: 0.18–0.66), and 30–44 years (AOR=0.42; 95% CI: 0.23–0.78). Female sex was associated with higher odds of unsuccessful treatment (AOR=1.61; 95% CI: 1.09–2.38), and HIV-positive status was the strongest predictor (AOR=4.39; 95% CI: 2.01–9.59).

Conclusion: GGH has met the WHO success target ($\geq 85\%$), yet significant vulnerabilities remain for patients with HIV co-infection, advanced age, and female gender. These findings highlight that clinical recovery is hindered by a lethal synergy between pathogens and localized socio-economic barriers. Ultimately, improving outcomes in rural settings requires integrating nutritional support and gender-sensitive interventions into standard TB protocols. Future prospective studies should incorporate broader clinical and nutritional variables to better address the complex drivers of TB treatment failure.

Key words: Trend, Tuberculosis, Treatment Outcome, Retrospective Study

1 Introduction

2 Background

3 Tuberculosis (TB) is a chronic airborne infectious disease caused by *Mycobacterium*
4 *tuberculosis* (MTB), and it remains one of the leading causes of death from infectious diseases
5 globally [1–3]. In 2022, the World Health Organization (WHO) reported over 10.6 million new
6 TB cases and 1.3 million deaths, with sub-Saharan Africa accounting for a disproportionate share
7 of the burden [3]. TB is especially severe among HIV-positive individuals, children, and those
8 living in poverty, where diagnostic and treatment services are limited [2,4].

9 Tuberculosis primarily affects the lungs (pulmonary TB), but extrapulmonary
10 manifestations involving the brain, kidneys, spine, and lymph nodes are also common [5].
11 Pulmonary TB is highly contagious, transmitted through coughing, sneezing, and contaminated
12 droplets. The risk of infection depends on exposure intensity and host immunity. Once infected,
13 individuals may carry latent TB for years, with potential progression to active disease under
14 immunosuppression [5].

15 The WHO launched the “End TB Strategy” to address TB burden, which aims for a 95%
16 reduction in TB deaths and a 90% reduction in incidence rate by 2035, compared with 2015 levels.
17 This strategy is built on three pillars: integrated, patient-centered care and prevention; bold policies
18 and supportive systems; and intensified research and innovation [3]. Central to this strategy is the
19 monitoring of TB treatment outcomes, which serve as the primary indicator for evaluating the
20 quality of TB control programs. According to standard definitions, a successful outcome is the
21 sum of cured (a patient who is bacteriologically negative in the last month of treatment) and
22 treatment completed (a patient who finished treatment without evidence of failure but lacks final
23 lab results). Conversely, unsuccessful outcomes include treatment failure, death, loss to follow-
24 up, or being not evaluated [3,6].

25 The current standard of care for drug-susceptible TB follows a standardized, short-course
26 chemotherapy regimen lasting six months. This typically consists of an intensive phase of two
27 months using four first-line drugs—Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), and

Ethambutol (E)—followed by a four-month continuation phase of Isoniazid and Rifampicin (2HREZ/4HR). However, poor adherence, delayed diagnosis, and improper drug use have led to the emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), which require longer, more toxic, and costlier second-line therapies. For drug-resistant cases, regimens are longer and utilize second-line injectable or oral agents, such as Bedaquiline and Linezolid, depending on the resistance profile [7,8]. Globally, 3.6% of new TB cases and 18–20% of previously treated cases are estimated to be MDR-TB, with higher rates in high-burden countries like India, China, and Ethiopia [3].

Globally, treatment outcomes for tuberculosis vary due to differences in health system capacity, patient demographics, and socioeconomic conditions. Studies from India have shown that factors such as gender, poverty, and access to Directly Observed Treatment Short Course (DOTS) centers significantly influence treatment success [9]. In Brazil, urban overcrowding and comorbidities like diabetes and HIV have been linked to poor outcomes [10]. Chinese research has identified alcohol use, delayed diagnosis, and underlying chronic conditions as major contributors to treatment failure [11].

Ethiopia ranks among the top 30 high TB burden countries and is 15th globally for MDR-TB prevalence. Despite implementing the DOTS strategy since 1992 and expanding TB services through public–private mix (PPM) models, treatment success rates remain below the WHO target of 90% [1,6]. The national average was 86% in 2021, with regional disparities and facility-level gaps contributing to suboptimal outcomes [5].

In Oromia Region, GGH serves as a referral center for TB care. However, there is limited evidence on long-term burden of TB, treatment outcomes, and associated factors in this facility. A study in Southwestern Oromia revealed that HIV co-infection, previous TB treatment, and low baseline BMI were strong predictors of unfavorable outcomes among MDR-TB patients [7]. These findings underscore the need for localized data to guide interventions and improve treatment success.

Methods

Study design, area and period

A ten-year retrospective cross-sectional study was conducted from January 5 to March 31, 2026, at GGH, situated in Lepis Kebele, Kore District, West Arsi Zone, Oromia Regional State, Ethiopia. Established in 1929, the facility provides a comprehensive range of medical services, including outpatient and inpatient care, maternal and child health, surgical procedures, specialized TB treatment clinics, and programs for HIV/AIDS and malaria control.

Eligibility Criteria

Inclusion Criteria

The study included:

- All tuberculosis cases—including pulmonary TB (smear-positive and smear-negative) and extrapulmonary TB (EPTB) across all age groups (adult and pediatric) diagnosed and registered for treatment at GGH between January 1, 2015 and December 31, 2024.
- Patients with complete and legible medical records containing essential variables for analysis.

Exclusion Criteria

The study excluded:

- Patients transferred into or out of GGH during the course of treatment, due to incomplete outcome data.
- Records with missing or incomplete documentation of key variables that could compromise the validity of analysis.

Sample Size

A total of 931 TB patient records, documented between 1st January 2015 and 31st December 2024, was included. These cases represent all available and eligible records with completed treatment documentation in the GGH TB registry.

Sampling technique and procedure

A consecutive sampling technique was employed, whereby all eligible tuberculosis patient records available in the hospital's treatment logbooks were included in the study without random selection. The selection process involved a systematic review of 1,645 initial entries. Following the exclusion of 92 records due to critically missing socio-demographic or temporal data, the remaining 1,553 TB patient records were assessed. To ensure the integrity of the treatment outcome analysis, a further 622 records were excluded because their outcomes were undocumented, primarily due to patients being transferred out to other facilities like Shashemene Referral Hospital. This consecutive inclusion process resulted in a final analytical sample of 931 records, consisting of 829 (89.1%) Pulmonary TB (PTB) cases and 102 (10.9%) Extra-Pulmonary TB (EPTB) cases (Figure 2).

Selection of study participant

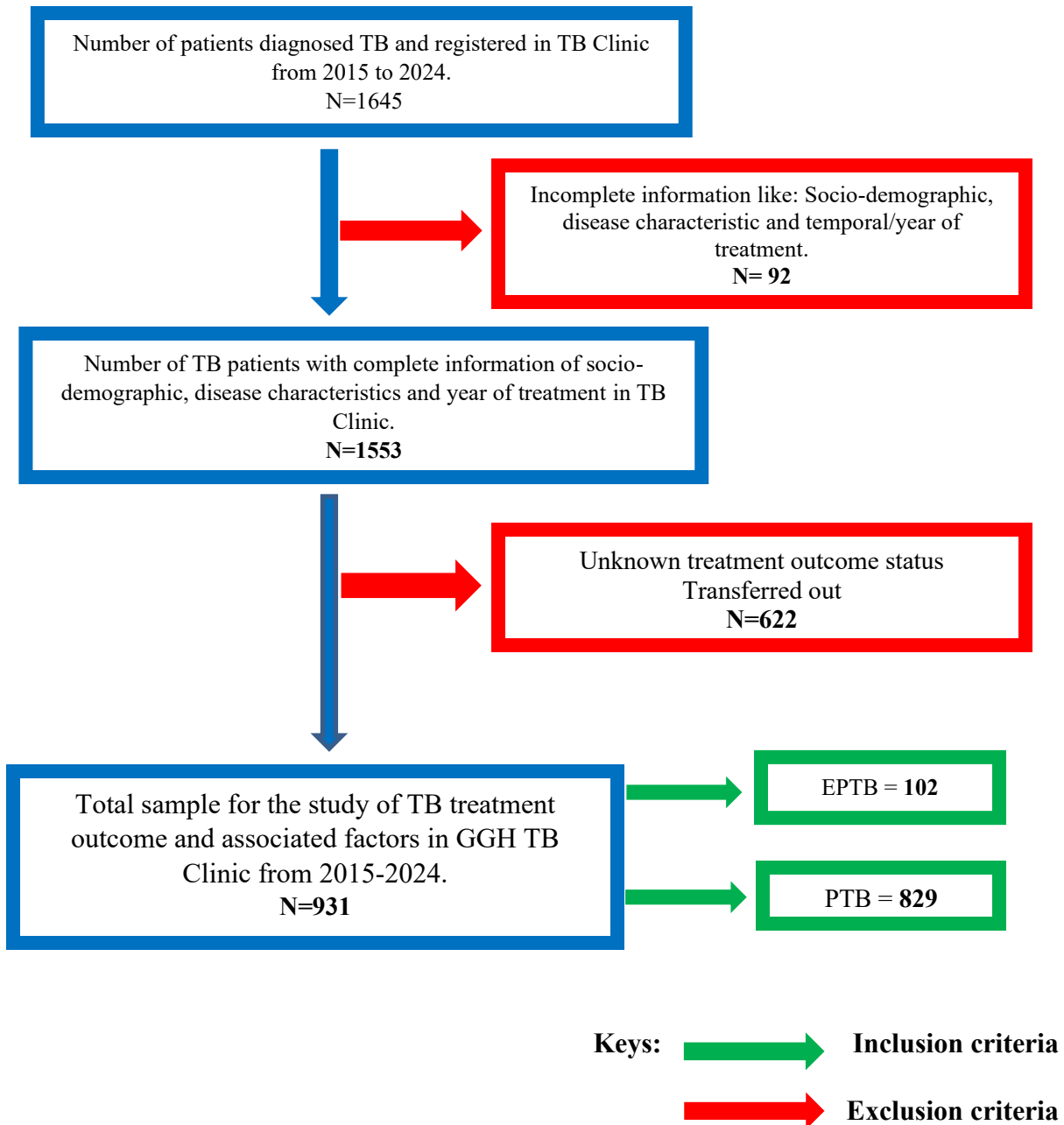


Figure 1. Schematic presentation of participant selection among TB patient in GGH.

Data Collection Techniques

This study utilized a retrospective record review approach. Secondary data was extracted from tuberculosis treatment registration books maintained at the TB clinic of GGH. The data source was included all TB patient records registered between January 1, 2015 and December 30, 2024. Data abstraction was conducted using a structured electronic data collection form developed

in Kobo Toolbox, a digital platform designed for secure and efficient field data capture. The tool was customized to include all relevant variables aligned with the study objectives and inclusion criteria.

A structured data abstraction checklist (Supplementary File 1) was developed based on the national TB recording and reporting formats. The checklist was used to collect the following variables: Patient identification number (anonymous coding), age, sex, residence, type of TB (smear-positive PTB, smear-negative PTB, extrapulmonary TB), TB category (new case, retreatment case), HIV status, date treatment started and completed and treatment outcome.

The data collection period was from January to March 2026. Data collection was conducted by two trained TB clinic nurses assisted by the principal investigator. All collected data was reviewed for completeness and consistency before entry. Incomplete or illegible records was excluded based on predefined criteria.

Data processing and analysis

After data collection using Kobo Toolbox, all entries were reviewed for completeness, consistency, and coding accuracy. The cleaned dataset was exported to SPSS version 29.0 for statistical analysis. To assess annual case counts was compiled and plotted across the ten-year study period, allowing for visual inspection of fluctuations over time. Line graphs and bar chart plots were used to illustrate trends in TB burden, stratified by sex, age group, TB type, Nutritional status and HIV status.

Descriptive statistics was computed to summarize patient characteristics and treatment outcomes. Frequencies and percentages were used for categorical variables, while means and standard deviations was used to describe continuous variables. Treatment outcomes were classified as treatment success (the sum of patients who were declared cured and those who had completed treatment) or unsuccessful treatment (the sum of patients who experienced treatment failure or death). The treatment success rate was calculated as the proportion of patients who were cured or completed treatment and the unsuccessful treatment rate was calculated as the proportion of patients who experienced treatment failure or death.

To identify factors associated with treatment outcomes, bivariate analysis was performed using chi-square tests for categorical variables. Crude odds ratios (COR) with 95% confidence intervals were calculated to estimate the strength of association between independent variables and treatment outcomes. Variables with a p-value less than 0.25 in bivariate analysis was included in a multivariable logistic regression model to control for potential confounders and identify independent predictors of unsuccessful treatment outcomes. Adjusted odds ratios (AOR) with corresponding 95% confidence intervals was reported to quantify the magnitude and direction of associations.

Operational Definitions

Definitions of TB treatment outcome and case based on WHO tuberculosis treatment guidelines and the Ethiopian national TB guidelines [8,14].

- **TB treatment outcome:** The final known status of a TB patient who was started on anti-TB treatment, categorized as either a successful outcome or an unsuccessful outcome.
- **Cured:** An initially sputum smear-positive patient who is sputum smear negative at or one month prior to, the completion of TB treatment and on at least one previous occasion (usually at the end of the second or fifth month).
- **Treatment completed:** A patient who completed anti-TB treatment without evidence of failure but for whom sputum smear or culture results are not available in the last month of treatment and on at least one previous occasion.
- **Treatment failure:** A patient whose sputum smear is positive at the fifth month of treatment or later during the course of treatment.
- **Died:** A patient who died for any reason during the course of treatment.
- **Treatment success:** The sum of patients who were declared cured and those who had completed treatment.
- **Treatment Unsuccess:** A composite outcome defined as the sum of patients who experienced treatment failure or death from any cause during the course of treatment.

Results

Socio-Demographic and Clinical Characteristics of the Study Participants

A total of 931 patient records were collected and included in the final analysis. The study population had a mean age of 34.4 years with standard deviation of 15.9. Regarding gender distribution, more than half of the participants were male 526 (56.5%) (Table 1).

Table 1. Socio-Demographic and Clinical Characteristics of TB patients at GGH (2015–2024).

Variable	Category	Frequency
Age (Years)	≤14	92 (9.9)
	15-29	243 (26.1)
	30-44	347 (37.3)
	45-59	161 (17.3)
	≥60	88 (9.5)
Sex	Male	526 (56.5)
	Female	405 (43.5)
TB Type	P/Neg	380 (40.8)
	P/Pos	449 (48.2)
	EPTB	102 (11.0)
Nutritional Assessment	SAM	215 (23.1)
	MAM	617 (66.3)
	Normal	99 (10.6)
HIV Status	Negative	760 (81.6)
	Positive	31 (3.3)
	Not Tested	140 (15.0)

Ten-Year Trends in Patient Enrollment and Clinical Characteristics (2015–2024)

The ten-year retrospective analysis revealed notable temporal trends in annual patient enrollment, varying from 86 cases in 2015, reaching a minimum of 45 in 2020, and showing a peak of 205 cases in 2021 (Figure 2). The annual distribution by gender showed that males represented the majority of cases across nearly all years, peaking at 126 in 2021, while female cases peaked at 79 in the same year (Figure 3). The distribution across age groups consistently peaked within the 30–44-year category, accounting for 99 cases during the 2021 surge period (Figure 4).

Regarding clinical profile trends, Smear-Negative PTB reached its highest frequency of 147 in 2021, whereas Smear-Positive PTB peaked at 105 in 2022. The frequency of EPTB remained low but stable, ranging from 3 to 14 cases per year (Figure 5). Nutritional status trends revealed a persistent high burden of malnutrition over the decade, with MAM frequencies reaching 180 in 2021, while SAM was most frequent in 2015 with 53 cases (Figure 6). Finally, the annual trend of HIV status showed that HIV-negative results were most frequent, peaking at 177 in 2021, while the highest annual count of HIV-positive cases was 7 in the same year (Figure 7).

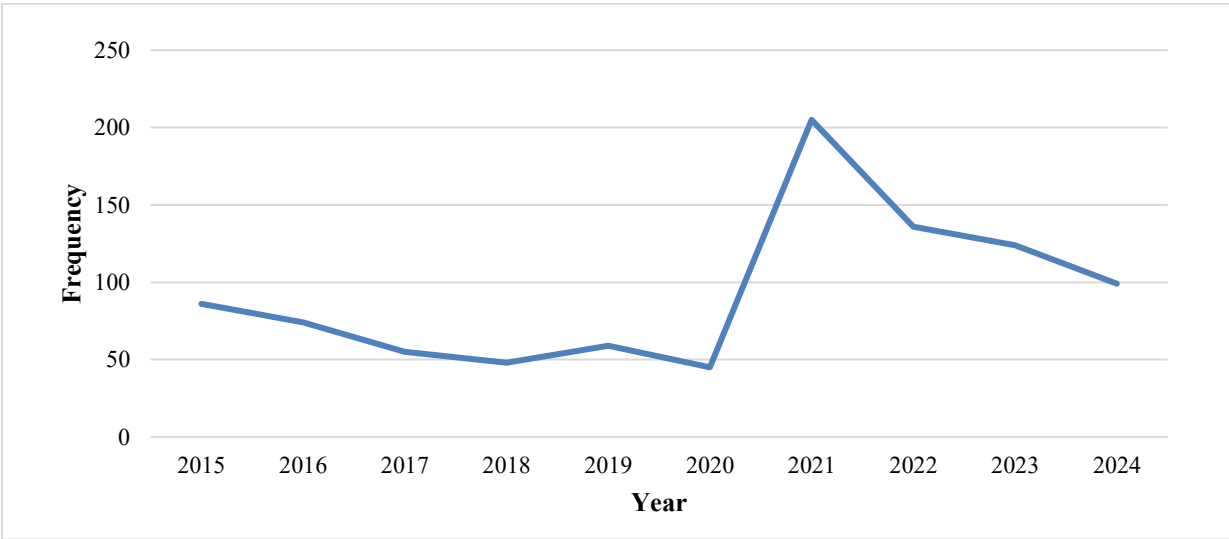


Figure 2. Ten-year trend in total TB patient enrollment at GGH (2015–2024).

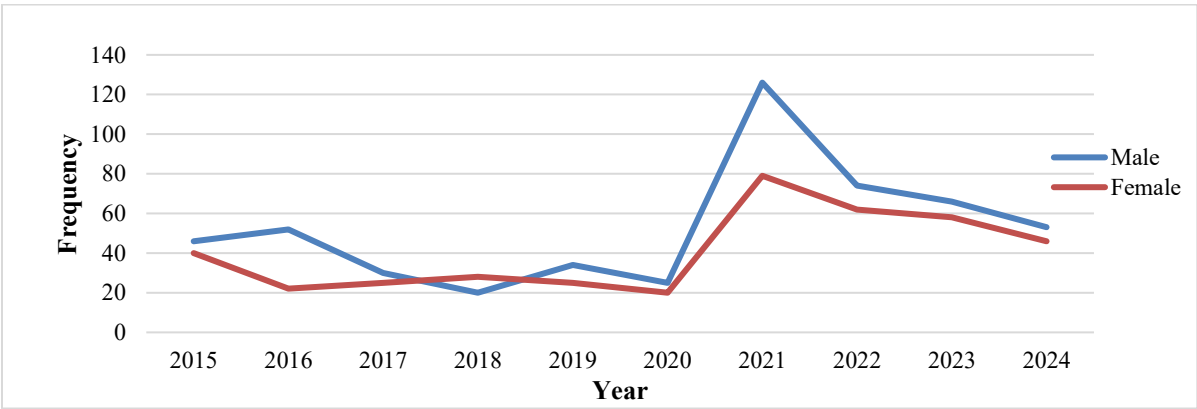


Figure 3. Ten-year trend of TB patients at GGH (2015–2024) stratified by sex.

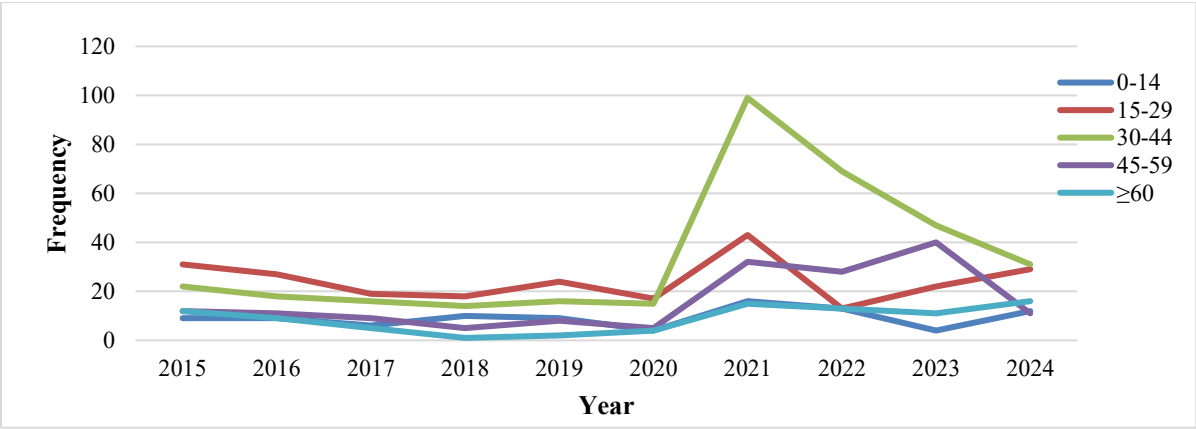


Figure 4. Ten-year trend of TB patients at GGH (2015–2024) stratified by age category.

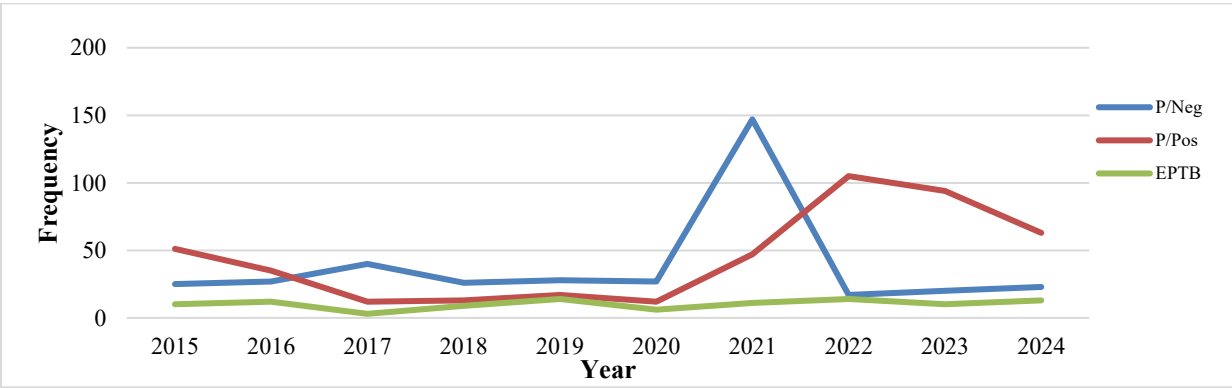


Figure 5. Ten-year trend of TB patients at GGH (2015–2024) stratified by TB type

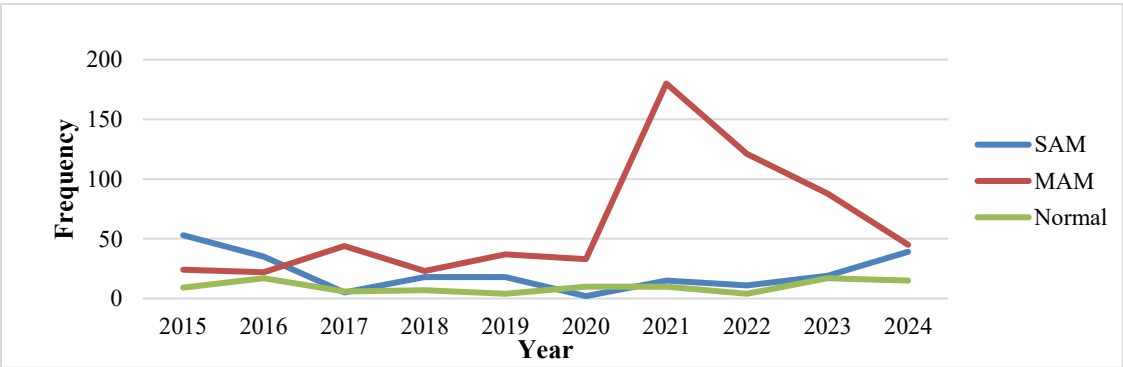


Figure 6. Ten-year trend of TB patients at GGH (2015–2024) stratified by nutritional status
Footnotes: SAM: Severe Acute Malnutrition; MAM: Moderate Acute Malnutrition

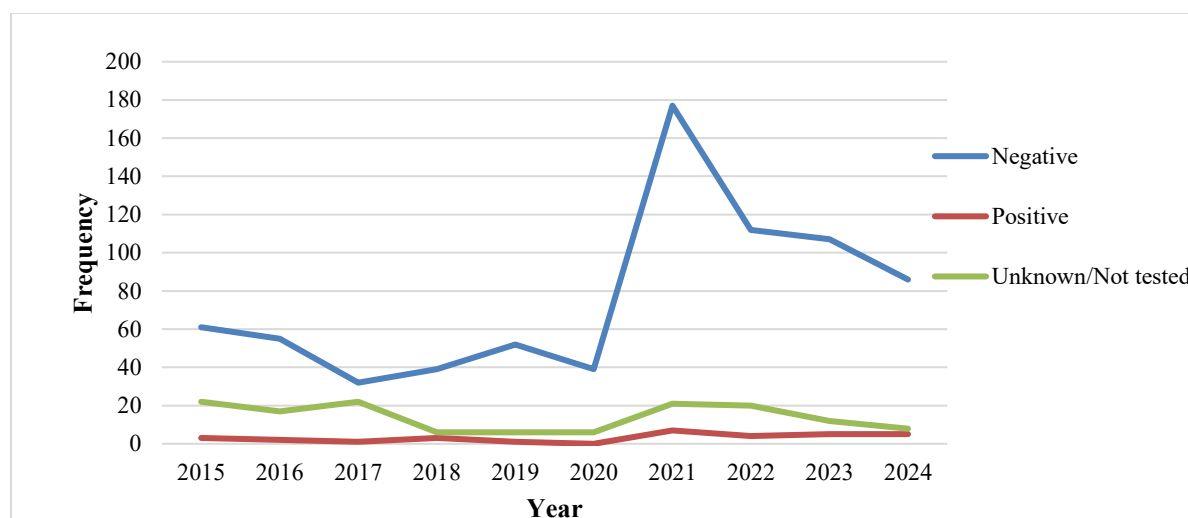


Figure 7. Ten-year trend of TB patients at GGH (2015–2024) stratified by HIV status.

Treatment outcome of TB patients

Based on the final study population of 931 patients, the distribution of treatment outcomes and their relative proportions are as follows:

Regarding treatment success, 394 (42.3%) patients were Cured and 407 (43.7%) reached Treatment Completed. This results in an overall treatment success rate of 86.0%. Conversely, the proportion of unsuccessful treatment outcomes was 14.0%, consisting of 101 (10.8%) cases of Treatment Failure and 29 (3.1%) cases where the patient Died (figure 8).

The ten-year trend of treatment success rates across the study period demonstrated high performance, ranging from a minimum of 79.2% in 2018 to a maximum of 89.5% in 2023. Despite the significant surge in patient volume during 2021, the success rate remained robust at 86.8%. Conversely, the proportion of unsuccessful treatment outcomes fluctuated within a range of 10.5% at its lowest in 2023 to a peak of 20.8% in 2018. For the most recent study year, 2024, the success rate was recorded at 85.9%, with unsuccessful outcomes accounting for 14.1% (figure 9).

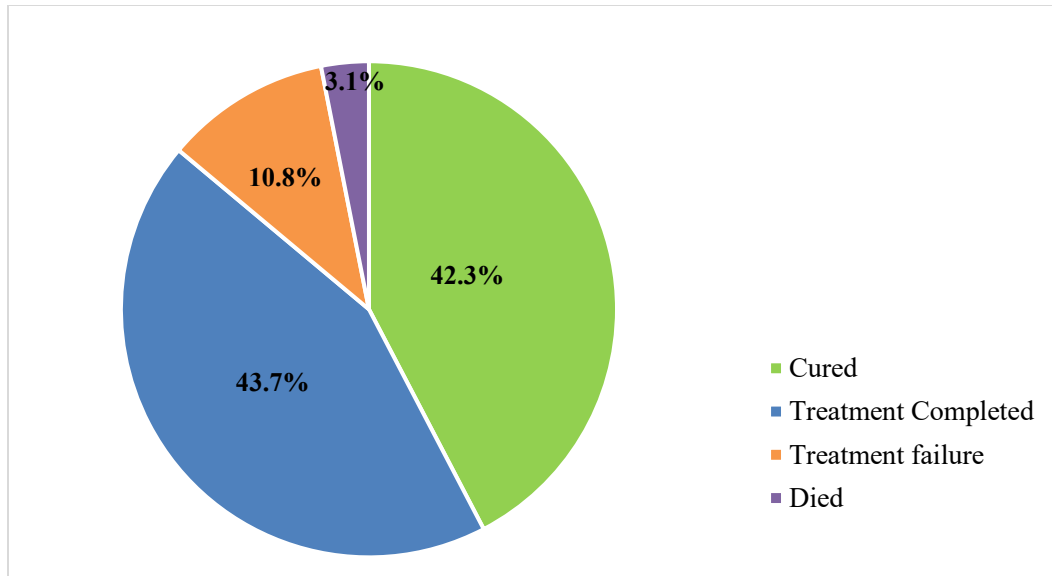


Figure 8. Final outcome proportions of TB patients at GGH (2015–2024)

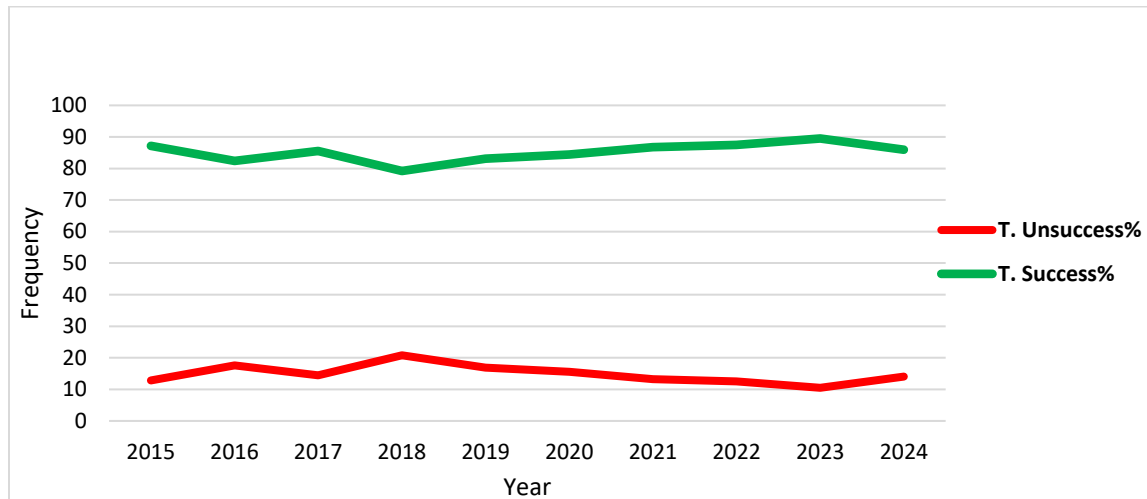


Figure 9. Ten-year trend of Treatment Unsuccess and Treatment Success of TB patient at GGH (2015–2024)

Factors Associated with Unsuccessful Outcomes among TB patients

In the bivariate logistic regression analysis, all independent variables—including age, sex, TB type, nutritional status, and HIV status—demonstrated a p-value of less than 0.25 and were consequently included in the final multivariable logistic regression model.

The multivariable logistic regression analysis identified several significant independent predictors of tuberculosis treatment outcomes. Younger age groups were significantly less likely to experience unsuccessful treatment outcomes compared to those aged 60 years or older. Specifically, children aged 14 years or younger (AOR = 0.36; 95% CI: 0.16–0.82; p = 0.015),

individuals aged 15–29 years (AOR = 0.35; 95% CI: 0.18–0.66; $p = 0.001$), and those aged 30–44 years (AOR = 0.42; 95% CI: 0.23–0.78; $p = 0.006$) all showed significantly lower odds of poor outcomes. Regarding gender, being female was associated with significantly higher odds of unsuccessful treatment compared to being male (AOR = 1.61; 95% CI: 1.09–2.38; $p = 0.017$). Additionally, HIV status proved to be a critical predictor, as HIV-positive patients had over four times higher odds of an unsuccessful treatment outcome compared to their HIV-negative counterparts (AOR = 4.39; 95% CI: 2.01–9.59; $p = 0.001$) (Table 2).

Table 2. Bivariate and multivariable analysis factors associated with treatment outcomes of TB patients at GGH (2015-2024).

Variable	Category	TB Treatment Outcomes		COR	AOR	p-value
		T. Unsuccess	T. Success			
Age (Years)	≤14	11 (12.0)	81 (88.0)	0.43 (0.20-0.96)	0.36 (0.16-0.82)	0.015*
	15-29	30 (12.3)	213 (87.7)	0.45 (0.24-0.84)	0.35 (0.18-0.66)	0.001*
	30-44	41 (11.8)	306 (88.2)	0.43 (0.24-0.77)	0.42 (0.23-0.78)	0.006*
	45-59	27 (16.8)	134 (83.2)	0.64 (0.34-1.22)	0.63 (0.32-1.24)	0.180
	≥60	21 (23.9)	67 (76.1)	<i>Ref</i>	<i>Ref</i>	
Sex	Female	66 (16.3)	339 (83.7)	1.41 (0.97-2.04)	1.61 (1.09-2.38)	0.017*
	Male	64 (12.2)	462 (87.8)	<i>Ref</i>	<i>Ref</i>	
TB Type	EPTB	18 (17.6)	84 (82.4)	1.19 (0.67-2.13)	1.13 (0.61-2.11)	0.698
	P/Pos	54 (12.0)	395 (88.0)	0.76 (0.51-1.13)	0.71 (0.47-1.08)	0.112
	P/Neg	58 (15.3)	322 (84.7)	<i>Ref</i>	<i>Ref</i>	
Nutritional Assessment	SAM	46 (21.4)	169 (78.6)	1.41 (0.76-2.64)	1.32 (0.69-2.55)	0.404
	MAM	68 (11.0)	549 (89.0)	0.64 (0.36-1.16)	0.67 (0.36-1.25)	0.207
	Normal	16 (16.2)	83 (83.8)	<i>Ref</i>	<i>Ref</i>	
HIV Status	Not Tested	16 (11.4)	124 (88.6)	0.84 (0.48-1.48)	0.87 (0.49-1.55)	0.633
	Positive	13 (41.9)	18 (58.1)	4.71 (2.24-9.91)	4.39 (2.01-9.59)	0.001*
	Negative	101 (13.3)	659 (86.7)	<i>Ref</i>	<i>Ref</i>	

Footnotes: *Significant; SAM: Severe Acute Malnutrition; MAM: Moderate Acute Malnutrition; EPTB: Extra-Pulmonary Tuberculosis.

VIF ranged from 1.04 to 1.42, indicating no significant multicollinearity. The final multivariable logistic regression model was statistically significant ($\chi^2 = 44.604$, $p < 0.001$), indicating that the model effectively distinguished between successful and unsuccessful treatment outcomes. The goodness-of-fit was confirmed by Pearson ($\chi^2 = 132.667$, $p = 0.635$) and Deviance ($\chi^2 = 152.330$, $p = 0.208$) tests, both of which indicated a well-fitting model. Furthermore, the model correctly classified 85.8% of the cases.

Discussions

The study identified a total magnitude of 931 tuberculosis cases over the ten-year period, with annual case counts exhibiting significant fluctuation from a low of 45 in 2020 to a pronounced peak of 205 cases in 2021. This dramatic surge in 2021, representing a more than fourfold increase in patient volume compared to the previous year, aligns with regional observations of a "rebound effect" in TB notifications following the initial service disruptions caused by the COVID-19 pandemic [15].

The 2022 WHO global TB report provides a critical framework for understanding this temporal trend. The COVID-19 pandemic caused a massive global diagnostic gap, with an 18% decline in new TB notifications in 2020 due to restricted access to healthcare and overwhelmed diagnostic systems. At GGH, the sharp decline in 2020 reflects these barriers to care, while the 2021 peak demonstrates the local system's effort to close the diagnostic gap. This mirrors the WHO's observation that 2021 served as a critical recovery year for identifying cases that were missed or "hidden" during the initial phases of the pandemic [16].

While urban centers often report more stable notification trends due to consistent active case-finding, the variations seen at GGH—particularly the sharp decline in 2020 followed by the 2021 peak—likely reflect the impact of external factors such as fluctuating healthcare accessibility and community awareness [8].

The study achieved an overall treatment success rate of 86.0% among 931 patients, with unsuccessful outcomes accounting for 14.0%. This success rate indicates that the hospital has consistently met the WHO target of at least 85% [3], demonstrating resilient local TB control over the last decade even during the 2021 volume surge. However, given that the study population consisted of new cases with a low HIV-positive prevalence, the proportion of unsuccessful outcomes remains a point of concern [8].

When compared to international benchmarks, the success rate at GGH stands above the 2023 global average of 83% [14] and is markedly higher than findings from Zimbabwe (57%) [17] and Nigeria (76.6%) [13]. These disparities likely stem from the high proportion of new cases in the Gambo cohort, whereas studies in Nigeria and Zimbabwe often reflect higher burdens of retreatment and drug-resistant cases which typically yield lower success rates.

277 Within Ethiopia, the 86.0% success rate aligns with regional trends but sits slightly below
278 the highest performing areas. For instance, this study findings are comparable to Zewditu
279 Memorial Hospital (83.1%) [18] and Wolayta Sodo (82.5%) [19], yet lower than the rates reported
280 in South Gondar (89.0%) [20], Motta Town (88.4%) [21], and Wollo (88.1%) [22]. The variation
281 between these local studies can be justified by differences in geographical accessibility and patient-
282 specific factors. In this study high percentage of patients were diagnosed with SAM or MAM.
283 Malnutrition is a well-documented driver of delayed recovery and increased vulnerability to
284 complications, which explains why unsuccessful outcomes persist even in a predominantly new-
285 case population.

286 The 14.0% unsuccessful outcome rate remains a point of concern. This suggests that the
287 underlying biological and social challenge continue to impede total success. Compared to Jimma,
288 where unsuccessful outcomes were approximately 11.8% [23], the higher rate at GGH may reflect
289 the rural nature of the catchment area where malnutrition and long travel distances create barriers
290 to treatment adherence.

291 The unsuccessful outcome rate of this study is notably higher than the 2–5% range typically
292 expected for similar low-risk, predominantly drug-susceptible groups [3]. While some regional
293 studies report higher failure rates of 19.3% [24], others achieve rates as low as 7.5% [25]. This
294 study findings more closely resemble study populations burdened by high HIV co-infection or
295 retreatment cases, despite our population being predominantly new cases with low HIV
296 prevalence. Several factors may explain this persistence: unrecognized isoniazid mono-resistance
297 affects 5–10% of new cases in Ethiopia and goes undetected by standard protocols [26].
298 Additionally, the high prevalence of malnutrition in this group may lead to poor drug absorption
299 or impaired immunity [27,28], while laboratory-related misclassification could falsely elevate
300 unsuccessful figures.

301 The analysis demonstrated that younger age is a highly significant protective factor against
302 unsuccessful treatment outcomes at GGH. Children aged 14 years or younger showed 64% lower
303 odds of unsuccessful treatment. Similarly, young adults aged 15–29 and those aged 30–44
304 exhibited 65% and 58% lower odds, respectively, compared to patients aged 60 years or older.
305 This indicates that the elderly are the most vulnerable group in this population, likely due to age-

related physiological decline, higher rates of comorbidities like diabetes, and increased susceptibility to drug-induced toxicity.

These findings are corroborated by Ethiopian studies which identified advanced age as a primary driver of unsuccessful treatment outcomes across diverse regions [1,24–26]. Older patients in these settings often present with advanced disease due to diagnostic delays commonly encountered in rural environments [26]. Furthermore, research highlighted that in Ethiopia, older patients were significantly more likely to experience unsuccessful treatment due to lower medication tolerance and physiological vulnerabilities [24,25]. Globally, the WHO emphasizes that the "graying" of the TB epidemic poses a unique challenge, as elderly patients often suffer from atypical symptoms that overlap with chronic obstructive pulmonary disease (COPD) or malignancy, further complicating the clinical course [3].

In this study, gender was identified as a significant independent predictor of treatment success. Female patients had 1.61 times higher odds of experiencing an unsuccessful treatment outcome compared to males. This finding is particularly striking as it diverges from the global trend reported by the WHO and other studies, which typically identify males as being at higher risk due to substance use and poor healthcare-seeking behavior [14,29].

The "opposite" trend observed at GGH requires specific local justification. Consultations with local TB experts and a closer examination of the study's demographic context suggest that socio-cultural and economic barriers play a more dominant role than biological ones. In rural communities surrounding GGH, women often face significant restricted healthcare decision-making power and financial dependency on male heads of households, which can delay both the initiation of treatment and adherence to long-term therapy [30]. Furthermore, the heavy burden of unpaid domestic labor and childcare often forces women to prioritize household responsibilities over regular clinic visits, especially when travel distances are long. These factors combined suggest that at GGH, the "gender gap" in TB outcomes is driven more by socio-economic vulnerability and nutritional neglect than by the behavioral risks typically associated with male patients in global literature.

In this study, HIV status emerged as the most powerful predictor of unsuccessful treatment outcomes. HIV-positive patients had over four times higher odds of experiencing treatment failure compared to their HIV-negative counterparts. Although the HIV prevalence in this study population was relatively low at 3.3%, the intensity of this association underscores the devastating biological synergy between the two pathogens, where HIV accelerates TB progression and TB simultaneously increases HIV viral replication. These findings are consistent with broader regional data across Ethiopia. For instance, in the South Gondar Zone, patients living with HIV were approximately three times more likely to experience unsuccessful outcomes (AOR=3.07) [20]. Similarly, studies in Motta Town and Southwest Ethiopia reported comparable risks, with AORs of 3.35 [21] and 2.14 [5], respectively. In more extreme cases, such as in Harar, the odds of unsuccessful treatment for co-infected patients reached as high as 6.5 [25].

The persistence of poor outcomes among co-infected patients at GGH can be attributed to several critical factors. First, the low immunity associated with HIV infection reduces the host's ability to respond to anti-TB chemotherapy, leading to higher mortality rates compared to TB infection alone [20]. Second, patients often face a high "pill burden" and the fear of drug-drug interactions between ART and TB medications, which frequently leads to sub-optimal adherence or treatment interruption [24,25].

Furthermore, the WHO global TB report and the Ethiopian national guidelines confirms that despite the expansion of antiretroviral therapy (ART), mortality remains unacceptably high in the co-infected population. These biological and behavioral challenges are further exacerbated by the high rates of adverse drug reactions common in the Ethiopian context [3,8].

Strengths

A primary strength of this study is the ten-year longitudinal design, which allowed for the observation of long-term trends in tuberculosis treatment outcomes and the identification of significant fluctuations, such as the 2021 case surge. Furthermore, the study utilized a total population (census) approach, including every eligible record from the GGH TB clinic rather than a sampled subset. By capturing the entire patient population over a decade, the study eliminates

sampling bias and provides a high level of statistical power and representativeness for the local catchment area.

Limitations

Despite its strengths, several limitations must be acknowledged. First, the study was constrained by the retrospective nature of hospital records; due to incomplete or inconsistent registration entries, the multivariable analysis was restricted to five consistently available variables. This narrowed focus may have overlooked broader clinical complexities—such as specific comorbidities beyond HIV, smoking status, or detailed socioeconomic indicators—potentially introducing measurement bias and limiting the depth of the predictive model.

Second, the retrospective design means certain clinical subgroups, such as diagnosed drug-resistant TB cases that were transferred out to specialized treatment centers, could not be fully captured in the final outcome analysis, which may influence the broader picture of unsuccessful treatment rates. Finally, the retrospective design prevents the establishment of direct causality between the identified predictors and treatment outcomes.

Conclusion

The findings of this study offer a significant scientific insight: achieving the WHO success threshold does not necessarily imply the absence of deep-seated clinical and social vulnerabilities within a TB program. While the 86.0% success rate confirms the operational efficacy of the DOTS framework at GGH, the 14.0% unsuccessful rate reveals a "hidden" burden of failure that is biologically and sociologically driven.

Scientifically, this study shifts the focus toward the synergy of multiple vulnerabilities. The extreme fourfold risk associated with HIV-positive status, even in a low-prevalence setting, confirms that the biological interplay between TB and HIV remains the most aggressive driver of treatment failure, likely exacerbated by the high prevalence of SAM. Furthermore, the finding that women face significantly higher odds of poor outcomes—contradicting many global male-centric risk models—suggests that in rural Ethiopia, social determinants of health act as biological barriers. When gender inequality restricts a patient's nutritional priority and healthcare-seeking

autonomy, it manifests clinically as treatment failure. Ultimately, the science of this study concludes that TB recovery is a multi-dimensional process; diagnostic tools are necessary, but they cannot overcome the physiological and systemic "drag" caused by malnutrition, advanced age, and gender-based socio-economic fragility.

Recommendations

To improve clinical outcomes, GGH should transition toward a patient-centered, risk-stratified model of care. This involves integrating nutritional rehabilitation directly into the pharmacological regimen to address the physiological barriers to recovery. Rather than a universal follow-up model, a risk-based triage system should be implemented, providing prioritized community-based DOTS and frequent clinical reviews for vulnerable groups—specifically HIV-positive patients, women, and the elderly—to mitigate the high risk of treatment interruption.

Addressing social and systemic determinants is equally critical to reducing identified gender and age-related disparities. Targeted outreach, such as decentralized drug distribution or community-led adherence groups, should be developed to accommodate the domestic labor burdens and travel constraints faced by women in rural areas. At the policy level, the FMOH should prioritize the transition from paper-based registries to standardized electronic health records. This is a prerequisite for ensuring data integrity, enabling real-time patient tracking, and expanding diagnostic protocols to capture unrecognized drug resistance.

Finally, future research must investigate the underlying mechanisms of these identified risks. Qualitative studies should explore the intra-household dynamics, such as food security and decision-making autonomy, that contribute to higher failure rates among women. Simultaneously, prospective clinical research into non-communicable comorbidities in the elderly is necessary. This will determine if age-related failure is purely physiological or driven by undetected chronic conditions, allowing for a more integrated and effective approach to geriatric TB care.

411 **Abbreviations**

412	AOR	Adjusted Odds Ratio
413	CI	Confidence Interval
414	COR	Crude Odds Ratio
415	DOT'S	Directly Observed Therapies short-course
416	EPTB	Extra Pulmonary Tuberculosis
417	FMOH	Federal Ministry Of Health
418	GGH	Gambo General Hospital
419	HIV	Human Immunodeficiency Virus
420	MAM	Moderate Acute Malnutrition
421	MDR-TB	Multi Drug Resistant Tuberculosis
422	MTB	Mycobacterium Tuberculosis
423	PTB	Pulmonary Tuberculosis
424	SAM	Severe Acute Malnutrition
425	WHO	World Health Organization
426	XDR-TB	Extensive Drug Resistant Tuberculosis

427 **Ethical approval**

428 Ethical approval for this study was obtained from the Institutional Review Board (IRB) of
429 the School of Postgraduate Studies at Madda Walabu University, Shashemene Campus (Reference
430 No. መወደሻ/3912/18; Shashemene) ((Supplementary File 2). As the study involves retrospective
431 review of medical records, individual informed consent was not needed. Personal identifiers such
432 as names was kept confidential. All information obtained was used solely for the purpose of

achieving the stated research objectives, and data were stored securely to prevent unauthorized access. The recruitment period for this study began on **05/01/2026** and ended on **31/03/2026**. All methods were performed following the relevant guidelines and regulations.

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Availability of data and materials

The data set used can be obtained from the corresponding author.

Clinical trial number

Not applicable.

Authors' contributions

GWA: Proposal development, laboratory work, data analysis and review of the manuscript

DSA: Supervision of the study, data analysis and preparation of the manuscript.

KUB: Supervision of the study, data analysis and review of the manuscript.

TDW: Data collection, supervision of laboratory work and review of the manuscript.

JGD: Data collection, supervision of laboratory work and review of the manuscript.

BL: Proposed the study, supervised the study, data analysis and review of the manuscript.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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