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Research article

Trends of unsuccessful treatment outcomes and associated factors among tuberculosis patients in public hospitals of Bale Zone, Southeast Ethiopia: A 5-year retrospective study

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ABSTRACT

Introduction: Tuberculosis (TB) is a curable disease caused by the tubercle bacillus and its treatment is designed to cure, interrupt transmission, and prevent drug resistance. These aims have not yet been achieved in many regions of the world, particularly in developing countries like Ethiopia. Thus, this study was designed to assess the trends of unsuccessful treatment outcomes and associated factors among patients with TB in two public hospitals in the Bale zone, southeast Ethiopia.

Methods: A 5-year retrospective data among 1281 patients with TB who registered and started treatment (from July 2013 to June 2018/19) in two selected Bale zone hospitals was retrieved. Together with descriptive statistics, binomial and multinomial logistic regression modeling were carried out using STATA version 14 to estimate the odds ratio.

Results: The overall unsuccessful TB treatment outcomes in this study was 10.4% and moderately decreased over the year of treatment (from 14.1% to 8.4%, x2 = 7.35, and p = 0.011). Approximately 34 (7.6%) of pulmonary positive and 34 (7.4%) of pulmonary negative TB patients had experienced treatment failure and death, respectively. The level of the hospital, patients with smear-negative and extrapulmonary, transferred in, aged, and human immunodeficiency virus status were found to have a statistically significant association with unsuccessful treatment outcomes of patients with TB.

Conclusion: In this study, approximately one-tenth of patients with TB had unsuccessful treatment outcomes that moderately declined over the year of treatment. Strengthening control efforts like counseling during the intensive and continual phases of treatment and scheduling home visits is recommended.

1. Introduction

Tuberculosis (TB) is a curable disease caused by the microorganism tubercle bacillus. It primarily affects the lungs, giving rise to pulmonary TB, which is often highly communicable. The TB bacilli may affect other parts of the body, such as lymph nodes, the spine, the brain, kidneys, and joints, which are called extrapulmonary TB [1, 2].

Internationally, TB treatment saved about 54 million lives between 2000 and 2017; conversely, the diagnostic and treatment gaps persist. The perfect treatment of TB was designed to cure the patient, interrupt transmission of TB to other people, and prevent drug resistance. These aims have not yet been achieved in many regions of the world, particularly in developing countries like Ethiopia [1]. The main problems that arise during treatment are the death of the patients, default, treatment failure, and resistance to the drugs [3]. Regardless of the comprehensive struggles to fight TB, the low treatment success rate in Africa, particularly in Sub-Saharan countries like Ethiopia, is intrinsically related to the non-completion of treatment due to deaths and loss to follow up [4, 5].

Irrespective of the struggles made under the global End TB strategy, a significant number of people are unknown to the health system or do not receive proper treatment, particularly in low-and middle-income countries [6, 7]. In these settings, delayed appearance for treatment and loss to follow up from treatment are the two major challenges that TB programs face [2]. One in five patients with TB continues to loss to follow up from treatment. As untreated TB intimidates the well-being of an individual and society, loss to follow up from treatment may increase the risk of prolonging infectiousness, drug resistance, and relapse [1].

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The treatment success rates formerly reported from the different parts of Ethiopia ranged from 29.5% to 89.2%. Similarly, access to treatment, poor socioeconomic status, health service utilization, treatment-seeking behavior, and poor knowledge of the disease were found to have a significant association with treatment outcomes. Moreover, family size, sex, age, educational status, hospitalization, comorbidity (human immunodeficiency virus, HIV), and having a positive smear at the second month of follow-up were identified as significant factors of unsuccessful TB treatment outcomes [1, 8, 9, 10, 11, 12].

In Ethiopia, the National Tuberculosis and Leprosy Control Program introduced the short course directly observed treatment strategy in 1994, which is available in 90% of geographic locations whereas the treatment success is between 75% and 87% within the international arrangement [13, 14]. Even though the Ethiopian National TB program functions under the worldwide TB control strategy, there are challenges in its delivery [5, 15].

Determining TB treatment outcomes is important to evaluate the quality of the local health care system and to amend systemic failures before the incidence and prevalence of multidrug-resistant TB rises [10, 16, 17, 18]. In Ethiopia, a considerable number of studies have been conducted, showing different TB treatment outcomes [19, 20]. Yet, more evidence is essential about TB treatment outcomes for all forms of TB, all age groups, and about the trend of the outcomes. Trends of unsuccessful treatment outcomes among patients with TB have not been assessed recently in southeast Ethiopia (specifically in Bale Zone Hospitals). Thus, this study aimed to assess trends and factors associated to unsuccessful treatment outcomes among patients with TB in two Bale Zone hospitals in Southeast Ethiopia.

2. Methods

2.1. Study setting

This study was carried out in two public hospitals in the Bale Zone. The Bale zone encompasses 21 districts, 20 urban, and 351 rural kebeles, with a total population of 1,402,492. There are 90 health centers and five hospitals in the Bale Zone (one Primary and Referral Hospital, three General Hospitals). Two hospitals were chosen at purposively from a total of five for their substantial number of tuberculosis patients. The number of patients with tuberculosis in selected hospitals has fluctuated from 41 to 187 every year over the last 5 years [21].

2.2. Study design and population

A 5-year retrospective cohort study using the registration book that contains information about patients with TB was conducted at the DOTS clinic of two Bale Zone hospitals. Patients with TB from all diagnostic categories were registered from July 2013/14 to June 2018 and who had a follow-up in two hospital TB clinics with complete socio-demographic and treatment outcome data were eligible for the study. Those with incomplete data were excluded from the study. Patients were registered, tested for active pulmonary TB, diagnosed, treated, and referred to other DOTS clinics following the National Tuberculosis, Leprosy, and TB/HIV Prevention and Control Program Guideline [13].

2.3. Data collection procedures and quality assurance

Data were extracted from the registers of the selected hospitals using a structured data extraction checklist adapted from previous studies [22, 23]. Before data collection, one-day training was provided on data collection tools for data collectors by the principal investigator. Data extraction was conducted by two nurses working at the TB clinic of the selected hospitals.

2.4. Study variables

Dependent variable is a treatment outcome that categorize into cure/complete, treatment failure/loss to follow up and deaths in which cure/complete treatment considered as successful treatment outcome while treatment failure/loss to follow up and deaths considered as unsuccessful treatment outcome as indicated under operational definition.

Independent variables include demographic and clinical characteristics such as sex, Age, place of residence, level of hospitals, types of TB, categories of patient with TB, HIV test status, and year of treatment.

2.5. Data processing and analysis

These data were checked for completeness and then coded and entered into a database using Epi Data version 3.1. Descriptive statistics were used to generate frequency tables, graphs, and multinomial logistic regression modeling for outcome variable was carried out using STATA Version 14 to estimate crude and adjusted odds ratios. The variables with a p-value < 0.20 in the bivariable multinomial logistic regression analysis can be candidate for the multivariable multinomial logistic regression. A P-value < 0.05 and an adjusted odds ratio with 95% confidence intervals were considered to declare statistical significance.

2.6. Operational definition

Successful outcome: includes cured patients with pulmonary TB (i.e., negative smear microscopy at the end of treatment and at least one previous follow-up test) and treatment completed with a resolution of symptoms [13].

Unsuccessful outcome: Includes patients with pulmonary TB with treatment failure, lost to follow-up, not evaluated, or death [13].

3. Results

3.1. Demographic and clinical characteristics of patients

Of the 1281 patients with TB who registered for treatment, 1257 were included with full information with regard to treatment outcome and date, whereas 24 patients with incomplete data were excluded. Of the patients with TB included for further analysis, 726 (57.8%) were male patients and 911 (72.5%) were urban residents. The median age of participants was 26 years, and the majority of participants were in the 15–24 age categories. Approximately 446 (35.5%) and 246 (19.6%) of patients were pulmonary TB and HIV positive, respectively (Table 1).

3.2. Trends of treatment outcomes

Of the patients with TB following treatment in the past 5 years, approximately 10.4% had unsuccessful treatment outcomes. The unsuccessful treatment outcomes (treatment failure, loss to follow up, not evaluated, MDR TB, and death) were decreased slightly over the year of treatment from 14.1% in 2013 to 8.4% in 2018 ($x^2 = 7.35$ and $p = 0.011$). Relatively high proportions of treatment failure/loss to follow were reported among previously treated (8.5%) and transferred in (17.7%) TB patients' category, respectively (Table 1, Figures 1 and 2).

3.3. Factors associated with unsuccessful treatment outcomes

Sociodemographic and other clinical-related factors in relation to TB treatment outcome were analyzed by binomial and multinomial logistic regression. Patients who were being treated in the general hospital were nearly four times more likely to have treatment failure/loss to follow up than those treated in the referral hospital (AOR = 4.21 and 95% CI: 1.82,

Table 1. Demographic and clinical characteristics with treatment outcomes of TB patients in two public hospitals of Bale Zone from July 2013 to June 2018, Ethiopia, (n = 1257).

Variables	n_T (%)	Treatment outcomes		
		Cure + complete	Failure + loss to follow up + not evaluated n (%)	Death n (%)
Level of hospital				
Referral hospital	414 (32.9)	387 (93.5)	7 (1.7)	20 (4.8)
General hospital	843 (67.1)	739 (87.7)	58 (6.9)	46 (5.5)
Patient place of residence				
Urban	911 (72.5)	814 (89.4)	49 (5.4)	48 (5.3)
Rural	299 (23.8)	273 (91.3)	13 (4.3)	13 (4.3)
Prison	47 (3.7)	39 (83.0)	3 (6.4)	5 (10.6)
Sex				
Male	726 (57.8)	651 (89.7)	40 (5.5)	35 (4.8)
Female	531 (42.2)	475 (89.5)	25 (4.7)	31 (5.8)
Age				
≤14	100 (8.0)	93 (93.0)	4 (4.0)	3 (3.0)
15–24	418 (33.3)	382 (91.4)	27 (6.5)	9 (2.2)
25–34	329 (26.2)	297 (90.3)	18 (5.5)	14 (4.3)
35–44	166 (13.2)	145 (87.3)	8 (4.8)	13 (7.8)
45–54	119 (9.5)	101 (84.9)	3 (2.5)	15 (12.6)
55–64	62 (4.9)	55 (88.7)	4 (6.5)	3 (4.8)
>65	63 (5.0)	53 (84.1)	1 (1.6)	9 (14.3)
Type of TB				
Pulmonary TB positive	446 (35.5)	392 (87.9)	34 (7.6)	20 (4.5)
Pulmonary TB negative	462 (36.8)	411 (89.0)	17 (3.7)	34 (7.4)
Extrapulmonary TB	349 (27.8)	323 (92.6)	14 (4.0)	12 (3.4)
TB patients category				
New	1131 (90.0)	1026 (90.7)	47 (4.2)	58 (5.1)
Retreated	47 (3.7)	38 (80.9)	4 (8.5)	5 (10.6)
Transferred in	79 (6.3)	62 (78.5)	14 (17.7)	3 (3.8)
HIV status				
Positive	246 (19.6)	211 (85.8)	6 (2.4)	29 (11.8)
Negative	1011 (80.4)	915 (90.5)	59 (5.8)	37 (3.7)
Year of treatment				
2013–2014	396 (31.6)	342 (86.4)	22 (5.6)	32 (8.1)
2015–2016	476 (37.8)	430 (90.3)	28 (5.9)	18 (3.8)
2017–2018	225 (30.6)	354 (91.9)	15 (3.9)	16 (4.2)
The phase of treatment in months				
0–2 months	41 (3.3)	0	9 (22.0)	32 (78.0)
3–5 months	62 (4.9)	0	30 (48.4)	32 (51.6)
6–12 months	1154 (91.8)	1126 (97.6)	26 (2.3)	2 (0.2)

n_T – Total frequency, n-frequency of independent variables with outcome variable.

9.75) and had no relation with other treatment outcomes. Patients with extrapulmonary TB were 52% less likely to have failure/loss to follow-up treatment outcomes in relation to patients with pulmonary TB (AOR = 0.48 and 95% CI: 0.25, 0.92) and had no relation to the death of patients with TB. Patients who were transferred in from other health facilities had an almost four times higher risk of treatment failure/loss to follow up than newly registered patients with TB (AOR = 3.62 and 95% CI: 1.83, 7.16) but no association with death. Patients with TB aged 45 years and above were four times at a higher risk of death than patients under 24 years of age (AOR = 4.20 and 95% CI: 2.03, 8.70). There were 68% lower odds of death among TB patients who had negative HIV test status compared to their counterparts (AOR = 0.32 and 95% CI: 0.19, 0.56) and no association with the TB patients treatment failure (Table 2).

4. Discussion

To determine TB treatment outcomes, it is important to evaluate the quality of the local health care system and to amend systemic failures before the incidence and prevalence of MDR TB rises [10]. This study aimed to assess trends and factors associated to unsuccessful treatment outcomes among patients with TB in two Bale Zone hospitals in Southeast Ethiopia.

In this study, the overall unsuccessful treatment outcome was 10.4%, which indicated that it was slightly reduced over the year of treatment (from 14.1% to 8.4%). The lower unsuccessful treatment outcomes in this study might be due to the improvement of program managers and treatment providers' commitment. Strict and continuous defaulters tracing practice was followed in the community by the health extension workers at each kebele. This study finding was somewhat higher than the study finding in the Arsi Zone, Ethiopia of 8.6% [24] and lower than the study finding in Gondar, Ethiopia of 18.3% [25]. This dissimilarity may be due to different study periods, economic conditions, and the efforts of health facilities as well as healthcare providers at all levels.

Treatment failure is the main danger to the control of TB as these patients are at a greater risk of developing drug-resistant TB and are often associated with uncomplimentary retreatment outcomes [26]. In this study, treatment failure merged with loss to follow up was 5.2%; this finding is higher than the study finding in Asella Hospital, Ethiopia of 0.2% [18]. This discrepancy might be due to a different study period. The lower treatment failure in this study might be due to the deployment of health extension workers in the community that aimed to deliver selected major impact packages of curative and preventive measures in Ethiopia [27]. Patients who have followed treatment in a general hospital have higher risk of treatment failure/loss to follow up than patients with treated TB in a referral hospital and had no relation to the death of patients with TB. This discrepancy might be related to the characteristics of health service providers and reform implementation. The odds of having treatment failure/loss to follow up were 52% less likely to occur in patients with extrapulmonary TB than in patients with smear-positive pulmonary TB. This study finding was inconsistent with the study of Felege Hiwot referral hospital, Ethiopia [28].

Patients who were transferred in from other healthcare facilities had almost a 3.62 times higher risk of treatment failure/loss to follow up than new registered patients with TB. This is consistent with a study conducted in the Arsi Zone of Ethiopia [24], the Northern part of Ethiopia [12]. The possible justification for this finding might be due to the change in the environment (health facility) and health service providers of transferred patients. Death due to TB is one of the major serious treatment outcomes and that could be related to different comorbidities [29]. In this study, the proportion of deaths was 5.3%, which is comparable with the study findings in Assela Hospital, 6% [18], in the Arsi zone, 7.4% [24], and a lower study finding from Gondar Hospital, 10% [25] and 13.6% in South Africa [30]. The discrepancy in this finding might be due to the duration of the study and, currently, more attention is given to TB prevention and control. Older age has been reported to be a risk factor for death due to dropped immunity and comorbidities [29]. In

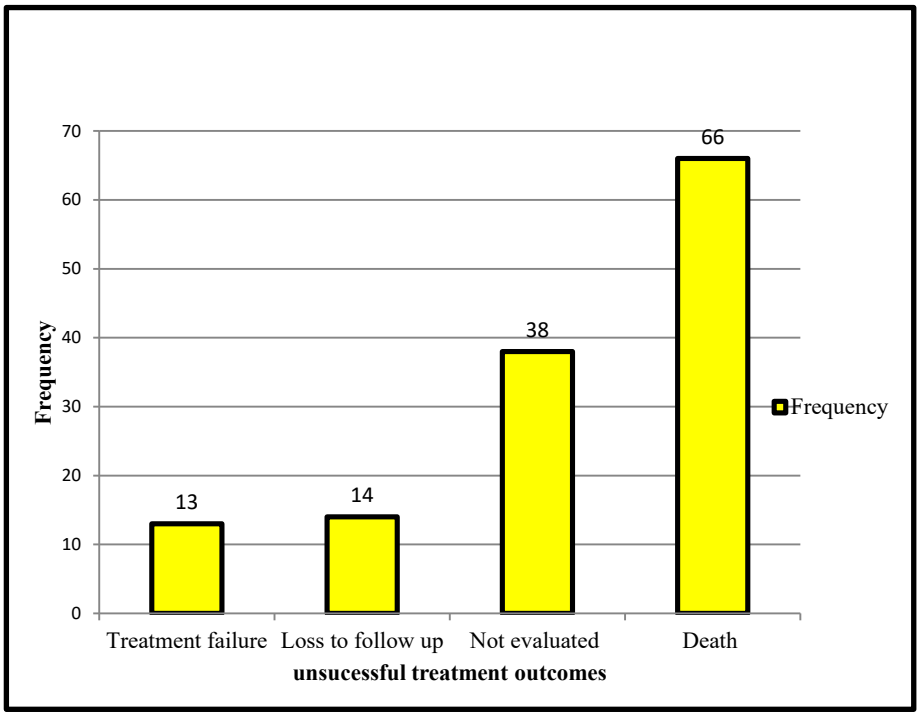

Figure 1. Shows the frequency of unsuccessful treatment outcomes among TB patients in two public hospitals of Bale Zone, Southeast Ethiopia, 2020.

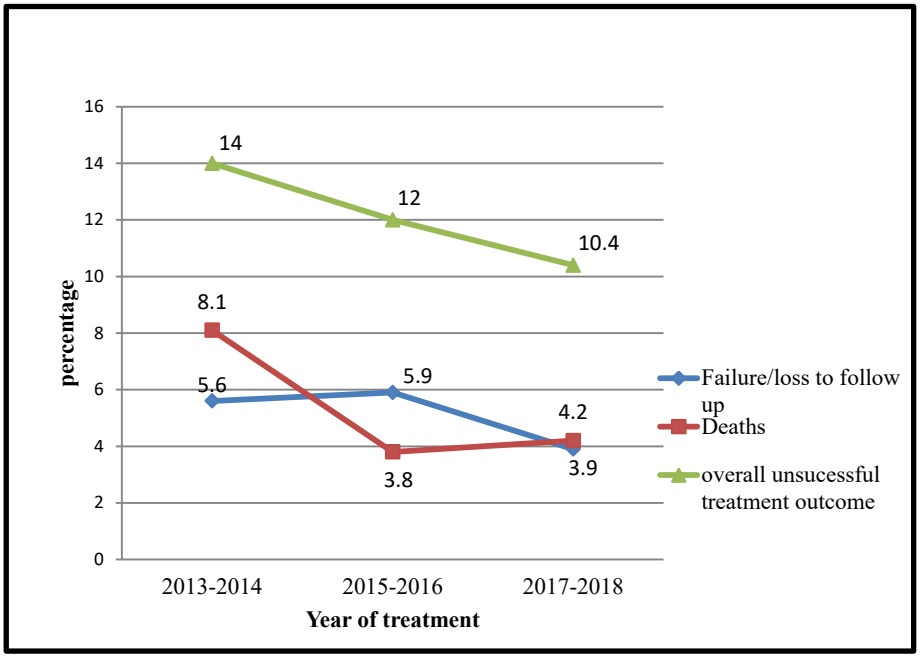

Figure 2. Trends of unsuccessful treatment outcomes over years of treatment in two public hospitals, Southeast Ethiopia, 2020.

our study, patients with TB aged 45 years and greater were at a 4.2 times higher risk of death than the below 24 year age category. The comparable study findings were reported from studies conducted at Felege Hiwot Hospital, Ethiopia and Eastern Taiwan [28, 31]. The possible explanation for this similarity might be related to the continuing loss of competent immune response, which might increase the risk of death if an individual is infected with TB at their late age [32]. In this study, HIV infection incidence was 19.6%, which is comparable and slightly higher than the study finding in the southern part of Ethiopia, which was 20.1% [33] and 13.9% [34]. Thus, the incidence of HIV infection determined in this study was lower than that of similar study findings in different parts of Ethiopia: Mizan hospital, 67% [35]; Debre Markos, 44% [36]; and 31% in the Oromia region [37]. The differences within study findings might be due to healthcare facilities' characteristics and study period. The risk of death among patients with TB who were HIV-negative was reduced by 68% when compared with coinfected patients with TB/HIV. This means

Table 2. Unadjusted and adjusted multinomial logistic regression analysis for determinants of the tuberculosis treatment outcome from July 2013 to June 2018 (n = 1257).

Variables	Treatment outcomes				
	Cured/ completed	Failure/loss to follow up		Death	
		COR (95% CI)	AOR (95% CI)	COR (95% CI)	AOR (95% CI)
Hospital-Level					
Referral hospital		1	1	1	
General hospital	Base outcome	4.34 (1.96, 9.60)	**4.21 (1.82, 9.75)**	1.20 (0.70, 2.07)	1.38 (0.77, 2.50)
Address patient					
Urban		1		1	
Rural	Base outcome	0.78 (0.42, 1.46)	1.26 (0.64, 2.48)	0.77 (0.41, 1.43)	0.94 (0.48, 1.84)
Prison	Base outcome	1.28 (0.38, 4.28)	1.34 (0.39, 4.69)	2.17 (0.82, 5.77)	2.26 (0.79, 6.38)
Sex					
Male		1		1	
Female	Base outcome	0.86 (0.51, 1.43)	0.88 (0.51, 1.50)	1.21 (0.74, 2.00)	1.18 (0.70, 1.99)
Age					
≤24		1		1	
25–44	Base outcome	0.90 (0.53, 1.54)	1.18 (0.66, 2.08)	2.42 (1.21, 4.83)	1.73 (0.84, 3.57)
≥45	Base outcome	0.57 (0.27, 1.30)	0.92 (0.40, 2.14)	5.11 (2.54,10.29)	4.20 (2.03, 8.70)
Type of TB					
Pulmonary TB positive		1		1	
Pulmonary TB negative	Base outcome	0.48 (0.26, 0.87)	**0.41 (0.22, 0.78)**	1.62 (0.92, 2.87)	1.41 (0.77, 2.57)
Extra pulmonary	Base outcome	0.50 (0.26, 0.95)	**0.48 (0.25, 0.92)**	0.73 (0.35, 1.51)	0.72 (0.34, 1.54)
Category of patients with TB					
New		1		1	
Retreated	Base outcome	2.33 (0.79, 6.71)	2.31 (0.76, 7.02)	1.17 (0.36, 3.83)	2.11 (0.76, 5.83)
Transferred in	Base outcome	4.92 (2.57, 9.44)	**3.62 (1.83, 7.16)**	2.72 (0.62, 12.03)	1.20 (0.35, 4.14)
HIV status					
Positive		1		1	
Negative		2.27 (0.97, 5.32)	2.05 (0.84, 4.99)	0.29 (0.18, 0.49)	**0.32 (0.19, 0.56)**
Year of treatment					
2013–2014		1		1	1
2015–2016	Base outcome	1.01 (0.57, 1.80)	0.94 (0.51, 1.71)	0.45 (0.25, 0.81)	**0.45 (0.24, 0.83)**
2017-2018/ 19	Base outcome	0.66 (0.33, 1.29)	0.67 (0.33,1.34)	0.48 (0.26, 0.90)	**0.42 (0.22, 0.80)**

AOR-adjusted odds ratio and COR-crude odds ratio. Bold indicates the significantly associated factors at $P < 0.05$.

more efforts are needed to strengthen the suggested world health organization TB/HIV collaborative activities at all levels of the health care provision system.

4.1. Limitations of the study

Some of the limitations of this study were treatment adherence and other disease conditions that might affect the outcome, which were not captured in the patient's file. Furthermore, the selected sites encompass a small geographic region, and hence, patients from these facilities might have a different profile than patients who reside in other parts of the country. Moreover, we recommend further studies, using a prospective study design, by focusing on primary data.

5. Conclusion

In this study period, unsuccessful treatment outcomes (failure, loss to follow-up, and death) were moderately reduced. Nearly 90% of patients with TB had successful or favorable treatment outcomes. Treatment failure rates were higher in patients with smear-positive pulmonary TB than in smear-negative and extrapulmonary TB. More proportions of deaths were recorded among patients with TB who were HIV positive and in the first years of treatment (from 2013 to 2014). The level of the hospital, age, TB type, category of patients with TB, HIV test status, and year of treatment were found to be associated with unsuccessful treatment outcomes (failure/loss to follow-up and death). To enhance successful TB treatment outcomes, efforts like supportive supervision and monitoring mechanisms need to be strengthened. Counseling during the intensive and continual phases of treatment, scheduled home visits to trace defaulters, and motivating patients and their supporters through providing health education to reduce unfavorable treatment outcomes are recommended.

Declarations

Author contribution statement

Demisu Zenbaba: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Mitiku Bonsa and Biniyam Sahiledengle: Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

Ethical consideration

The office of the institutional ethics review board of Madda Walabu University's Goba Referral Hospital provided ethical clearance. Two public hospitals in the Bale Zone granted written data access authorization. The study did not include any participants. We just took the data from the record and anonymized it.

Consent for publication

Not applicable.

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