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Factors associated with treatment outcome of tuberculosis in Bale Robe General Hospital, Southeastern Ethiopia: A retrospective study

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ABSTRACT

Aims: This study investigated the treatment success rate and the associated factors in patients with different forms of tuberculosis (TB) at Bale Robe General Hospital (BRGH), southeastern Ethiopia from 2012 to 2016.

Methods: An institution-based retrospective study was conducted. The study population was patients with TB registered at BRGH. The inclusion criteria were TB diagnosis with Ziehl-Neelsen staining for acid-fast bacillus and/or radiography and having treatment initiated from 2012 through 2016. Subjects with incomplete information were excluded.

Results: Among 807 patients with TB, 665 (82.4%) had successful treatment outcome (cure: 25.5%, treatment completion: 56.9%) and 142 (17.6%) patients had unsuccessful treatment outcome. In multivariate logistic regression analysis, age 65 years or older, being unemployed, having treatment after a previous failure, and receiving treatment during 2014 were associated with a reduced probability of treatment success. TB patients who were HIV-negative and treated during 2015 had higher treatment success. In multinomial logistic regression analysis, patients younger than 65 years of age showed a lower risk of death, whereas HIV-positive patients and patients treated during 2012 were more likely to experience death. New patients with TB were less likely to have treatment failure, but patients with TB who had treatment after failure were more likely to be transferred.

Conclusions: This study showed that TB out treatment success rate was satisfactory but below the minimum target set by the World Health Organization (85%). Age 65 and over, being unemployed, having treatment after failure and HIV co-infection were associated with unsatisfactory treatment outcomes.

Introduction

Tuberculosis (TB) is the tenth leading cause of death worldwide and the leading cause of death from a single infectious agent, ranking above HIV/AIDS (1). According to the World Health Organization (WHO) Global TB Report, TB caused an estimated 1.3 million deaths among HIV-negative people and 300,000 deaths in HIV-positive people (1). The highest TB morbidity and mortality rates occur in Africa (2). The fatality rate exceeds 50% in some African countries with high HIV infection rates (3).

Ethiopia is listed among the top 30 countries with a high TB burden, TB-HIV co-infection (TB/HIV), and multidrug-resistant TB (MDR-TB). Together, TB, TB/HIV, and MDR-TB accounted for 84% and 90% of the global burden during 2015 and 2016, respectively (4,5). Ethiopia is also a country achieving treatment success rates (TSRs) above 70% (6).

In 1992, WHO promoted the Directly Observed Treatment, Short-Course (DOTS), a treatment scheme where the physicians observe patients while the patients take prescribed TB medications. This strategy was subsequently adopted by nearly

all the countries (6). In Thailand, for instance, DOTS provided by health care workers has improved the treatment success of TB compared to self-administered therapy (SAT), consolidating the relevance of DOTS over SAT (7). Using the DOTS strategy, the highest treatment success of 95% was attained in Anqing, China (8). DOTS remains a core element of its successor, the Stop TB strategy (9), for which the WHO set targets of 84% case detection rate and 87% TSR by 2015.

In Ethiopia, DOTS was started in 1992 as pilots in the Arsi and Bale zones (10). The DOTS strategy was scaled up and implemented at the national level in 1997, and almost in all public, private, and non-governmental health facilities (11). However, the treatment success for patients with TB treated with DOTS varies from one country to another, and TSRs below the WHO target of 85% for cases of drug-susceptible TB are regularly reported by WHO's 194 member states, including Ethiopia (12-15). The DOTS program could not be optimized in Ethiopia due to poor treatment-seeking behavior; incomplete treatment or poor compliance; and treatment interruption or default, a phenomenon that contributes to prolonged infectiousness and increasing risk of drug resistance, relapsed TB, and death (16). Additionally, low literacy levels, discriminatory behavior of healthcare professionals, self-denial due to stigma, long treatment duration, inaccessibility of public health facilities, and shortage of drugs jeopardize successful treatment outcomes (17,18).

Previous studies conducted in different parts of Ethiopia revealed socio-demographic and clinical factors affecting the treatment outcomes of TB (19-21). Except for a single cohort study of TB treatment outcomes between 2007 and 2012 in Bale Robe town (14), information on treatment outcomes is lacking. Therefore, the purpose of this study was to determine the treatment outcome of all forms of TB cases and to identify associated factors for all types of TB cases involved in the DOTS program reported from 2012 to 2016 at Bale General Regional Hospital (BRGH).

Methods

Patients

The study was conducted at BRGH located in Robe Town in Bale Zone from January 2012 to December 2016. The town is located 430 km Southeastern of Addis Ababa, Ethiopia. Currently, the BRGH delivers clinical services to more than half a million urban and rural people. The hospital also serves as a training center for Madda Walabu University and provides clinical services to students, prisoners, and students of private and public colleges in the town. The Hospital's DOTS clinic operates within the National TB and Leprosy Control Program (NTBLCP) of Ethiopia (10,11,14). The DOTS clinic provides basic treatment and diagnostic services for all forms of TB through clinical diagnosis using the Ziehl-Nielsen staining method for acid-fast bacilli (AFB) and chest radiographs.

Study design, period, and data collection

An Institutional-based retrospective design was used for studying the TSR of TB and associated factors. The research participants were drawn from all patients with TB registered at the BRGH DOTS clinic in Bale Robe. The inclusion criteria were all TB cases diagnosed with Ziehl-Neelsen Staining for AFB and/or radiography and initiated TB treatment at the BRGH DOTS clinic from January 2012 through December 2016; cases with incomplete information were excluded. Data on various variables, including socio-demographic data (patient's gender, age, residence, and occupation), HIV serology status, TB types, TB patient category, outcomes of each study participant's NTBLCP-recommended treatment (10,11), and year of treatment, were recorded by trained nurses.

TB types, patient category, and treatment outcome definitions

Type of TB, patient category and treatment outcomes were defined according to the NTBLCP guideline (10) and Guidelines for Clinical and Programmatic Management of TB, TB/HIV, and Leprosy (11) adapted from the WHO. Types of TB were defined as the site of the lesions as either smear-positive pulmonary TB (PTB+) or smear-negative pulmonary TB (PTB-) or extra-pulmonary (EPTB). Patients were defined as having PTB+ if they had one of the following 3 conditions: (i) at least 2 initial sputum smears positive for AFB by direct microscopy, (ii) one initial smear positive for AFB by direct microscopy and positive culture, or (iii) one initial smear positive for AFB by direct microscope and radiographic abnormalities consistent with active TB. Patients were defined as having PTB- if they met one of the following 3 conditions: (i) had symptoms suggestive of TB with at least 3 initial smears negative for AFB by direct microscopy and no response to a course of broad-spectrum antibiotics; (ii) had 3 negative smears by direct microscopy, radiological abnormalities consistent with PTB, and a decision by a clinician to treat with a full course of anti-TB therapy; or (iii) had a diagnosis based on culture positive for *M. tuberculosis* but 3 initial smears negative by direct microscopy. EPTB is TB in organs other than the lungs, diagnosed by one culture-positive specimen from an extra-pulmonary site, histopathological evidence from a biopsy, or strong clinical evidence consistent with active EPTB and the decision by a physician to treat with a full course of anti-TB therapy.

Patients with TB fell into the following six case categories. New case: A patient who never had treatment for TB, or has been on anti-TB treatment for less than four weeks in the past; Relapse: A patient declared cured or treatment completed of any form of TB in the past, but who reports back to the health service and is now found to be AFB smear-positive or culture-positive; Treatment after failure: A patient who, while on treatment, is smear-positive at the end of the fifth month or

later, after starting. Treatment after failure includes patients who were initially sputum smear-negative, but who became smear-positive during treatment at 2 months or later; Default: A patient previously recorded as default from treatment and returns to the health facility with smear-positive sputum. Transfer-in: A patient who is transferred from a particular treatment unit with continued treatment after starting treatment in another treatment unit for at least four weeks; Other: A patient who does not fit into any above categories.

Treatment outcomes are defined as the following. Cured: A patient whose sputum smear or culture was positive at the beginning of the treatment but who was smear- or culture-negative in the last month of treatment and on at least one previous occasion; Treatment completed: A patient who completed treatment but who does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion; Treatment failure: A patient whose sputum smear or culture is positive at 5 months or later during treatment or patients found to harbor a MDR strain at any point of time during the treatment, whether they are smear-negative or -positive; Defaulter: A patient who has been on treatment for at least four weeks and whose treatment was interrupted for eight or more consecutive weeks; Died: A patient died from any cause during the course of treatment; Transferred out: A patient who started treatment and has been transferred to another reporting unit and for whom the treatment outcome is not known at the time of evaluation of treatment results. Treatment success is the sum of cured patients and patients who complete treatment. The TSR is defined as the ratio, expressed as a percentage, of the sum of cured patients and patients who completed treatment to the total number of patients studied.

Data quality assurance

Data were collected after training was provided to data collectors (trained nurses in the DOTS clinic of BRGH). This pretest was conducted at BRGH. The completed data were supervised by the principal investigator for completeness, and 5% of the samples were randomly selected and validated against the registration book. Data entry was done to the Epi-Info version to check data consistency.

All procedures were accomplished following the Declaration of Helsinki. Approval was received from the Institutional Research Ethics Committee of the College of Natural and Computational Science of Madda Walabu University (ref. no. CNCS/234/2017; September 26, 2017). Permission to conduct the research was obtained from the Robe Hospital administration before data collection. Because of the retrospective nature of the study, informed consent from the study participants was not needed not requested. Patient records were identified before analysis and kept confidential to ensure the confidentiality of patient information.

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS for Windows, version 21.0, IBM. Corp., Armonk, NY, 2012). Univariate analysis and multivariate logistic regression analyses were used to analyze factors associated with TSR in patients with TB. The independent variables were checked for the presence of multicollinearity using the variance inflation factor. The goodness of fit of the employed model was evaluated using the Hosmer-Lemeshow test, which compares observed with expected frequencies of the outcome and computes a test statistic that is distributed according to the chi-squared distribution. A p-value >0.05 implies there is no evidence that the observed and expected frequencies differ and the model fits well to run the multivariate logistic regression analysis. Marginal variables with p≤0.2 in univariate analysis were exported into a multivariate logistic regression model to detect independent predictors associated with TSR of patients with TB. In multivariate logistic regression analysis, the independent variables with a 95% confidence interval (CI) excluding one were significantly associated with TSR of TB (p<0.05). Multinomial logistic regression analysis was performed to evaluate independent predictor factors associated with treatment outcomes (dependent variables). In unadjusted multinomial logistic regression “crude relative risk ratio (CRRR)”, independent variables with p-value <0.05 and the 95% CIs, excluding one were exported to adjusted multinomial logistic regression “adjusted relative risk ratio (ARRR)”. Six outcome variables were used; the cure was used as the reference category and the remaining five variables (completed, failure, default, death, and transferred out) as separate variables. In ARRR, independent factors whose 95% CIs excluding one were significantly associated with the treatment outcome and the strength was significant at a p-value <0.05.

Results

Socio-demographic and clinical characteristics

The demographic and clinical characteristics of the study participants are shown in Table 1. A total of 807 patients with TB were registered at the DOTS clinic of BRGH from January 2012 to December 2016. Most were males (57.4%) and lived in urban areas (80.8%). More than three-fourths (75.8%) of the patients were 15-44 years old, mean age was 31.8 years (standard deviation ± 10.7 years). The study participants were students, self-employed, employed, unemployed, prisoners, and farmers. The majority were new cases (79.6%). Of the study subjects treated for TB, 79.2% were HIV-negative and 20.8% were HIV-positive. The patients with TB were PTB- (43.5%), PTB+ (28.0%) and EPTB (28.5%) cases. New patients with TB had the highest percentage of all TB forms (Table 1).

Treatment outcome of the patients

The treatment outcomes for patients who were registered in the DOTS program at the BRGH from January 2012 through December 2016 are shown in Table 2. Among the patients, 25.5% were cured and 56.9% completed their treatment. However, 2.1%, 3.3%, 6.2%, and 5.9% of the patients with TB had treatment failure, defaulted, died, or were transferred, respectively. The highest and lowest percentages of cured patients were recorded in pairs of patients with TB in the age groups 15-24 years and 54-64 years, in PTB+ and EPTB patients, and during 2015 (29.8%) and 2014 (21.1%).

Treatment failure was considerably higher in treatment after failure (28.6%) compared to the other TB patient categories. Treatment failure (3.9%), defaulters (10.6%), and transferred-out (13.3 %) cases had generally higher rates in 2014. More deaths were recorded for patients with TB ≥65 years (21.2%), PTB- patients (8.3%), relapsed cases (8.3%), and HIV-positive patients with TB (10.8%) and in 2012 (12.1%) compared to their corresponding counterparts (Table 2).

Treatment success rate

The TSR of the TB patients treated during the study period was 82.4% (Table 3). The TSRs of males (82.5%) and females (82.3%), and of PTB+ (84.1%) and EPTB patients (83.9%) were similar. The TSR of TB was higher in HIV-negative patients with TB (83.7%) than in HIV-positive patients with TB (77.8%). TSR increased or decreased inconsistently over the years of study; the lowest was in 2014 (66.7%) and the highest in 2015 (90.1%) (Table 3).

Factors associated with TSR in TB

Results of the univariate analysis and multivariate logistic regression are summarized in Table 3. In univariate analysis, variables significantly associated with TSR were age group, occupation, HIV status, and year of treatment of patients with TB (all at $p<0.05$), and patient residence and TB patient category (at $p\leq0.2$). These variables were fitted to the multivariate logistic regression analysis. In multivariate logistic regression, age ≥65 years [Odds ratio (OR): 0.17 (95% CI: 0.06-0.45)], being unemployed [OR: 0.86 (95% CI: 0.44-0.97)], having treatment after failure [OR: 0.37 (95% CI: 0.15-0.91)], and receiving treatment during 2014 [OR: 0.47 (95% CI: 0.23-0.96)] were associated with reduced probability of treatment success. However, HIV-negative patients with TB [OR: 1.62 (95% CI: 1.13-2.34)] and patients treated during 2015 [OR: 2.29 (95% CI: 1.32-3.98)] had a higher odds of treatment success than their counterparts (Table 3). Sex and residence of the patients and TB type had no significant association with treatment success ($p>0.05$) (Table 3).

Factors associated with treatment outcome of TB

Independent variables that were significantly associated with the treatment outcome in CRRR analysis were fitted to the ARRR model to determine the treatment outcome of TB. In the ARRR analysis, patients below 65 years of age had a significantly lower relative risk of death than the reference category (Table 4). However, HIV- positive patients with TB [ARRR: 2.18 (95% CI: 1.18-4.04)] and patients treated during 2012 [ARRR: 2.70 (95% CI: 1.14-6.39) had a higher relative risk ratio of death to HIV-negative patients with TB and patients treated during 2016, respectively. Patients with TB with PTB+ had a significantly lower relative risk ratio of completion, and transferring-out than those in the reference category (EPTB patients, $p<0.05$). New patients with TB also had a significantly lower relative risk of failure than patients in the reference category [ARRR: 0.10 (95% CI: 0.015-0.72)]. Patients with TB who were treated in 2014 had a significantly higher relative risk of default [ARRR: 11.46 (95% CI: 4.16-31.54)], and being transferred out [ARRR: 3.01 (95% CI: 1.35-6.72)] than those treated in 2016 (the reference year). Unemployed patients with TB had a significantly higher relative risk of failure [ARRR: 7.97 (95% CI: 1.13-55.8)] and being transferred out [ARRR: 4.27 (95% CI: 1.25-14.61)] than patients with TB who were farmers (the reference occupation) (Table 4).

Discussion

This study found satisfactory TSR of TB (82.4%) in BRGH. Patients with TB aged 65 and above, unemployed, having treatment after failure, TB-HIV co-infection, and receiving treatment during 2014 significantly reduced the probability of successful treatment of TB. Death from TB was considerably higher in patients with TB aged 65 and above, TB-HIV co-infection, and those having treatment during 2012. The treatment failure was significantly lower in new patients with TB, but transfer out was higher in patients having treatment after failure and treated during 2014.

The percentage of male patients with TB was higher than that of females (Tables 1). The underuse of the health facility by female patients due to socio-economic and cultural factors or gender-based biological differences accounted for differences in susceptibility to active disease (22,23). Most patients with TB were in the productive age group (15-44 years), in agreement with patients with TB attending other health facilities in Ethiopia (78%) (12) and Dilla University Referral Hospital (79.4%) (24). TB-associated morbidity and mortality occur mainly in the economically productive age (25). This may be due to the high mobility and interaction of the study population of the productive age group and thereby exposing them to TB infection.

Among patients with TB, PTB- was higher than PTB+ and EPTB (Table 1). A previous study in the BRGH (14) also reported higher percentages of PTB- (40.7%) than PTB+ (33.3%) and EPTB (26%). The higher percentage of PTB- than other TB types might be related to a diagnosis failure in the hospital where the clinicians rush to designate TB cases, as PTB- cases are also

more common in patients with HIV (4,5,26). A higher prevalence of PTB- (44.8%) and PTB+ (37.0%) was also reported from surrounding communities in Gambella Regional State (27).

We found a significantly higher prevalence of all forms of TB in urban areas than in rural areas (Table 1), contrasting with findings from a study in southern Ethiopia that reported more patients with TB in rural (66%) than in urban areas (44%) (12). This discrepancy might be due to high-density housing and associated exposure risk in urban areas. The rate of TB-HIV co-infection (Table 1) was higher than in a study in Debre Tabor (12.7%) (28) but slightly lower than that reported by BRGH (22.2%) (14).

The results of our analysis revealed that the percentage of cured patients (Table 2) was higher than the rate in the BRGH (19.7%) (14) but lower than the result in a recent systematic review and meta-analysis for Ethiopia (33.9%) (29). Most of the patients with TB in BRGH had completed the treatment outcome in agreement with similar studies in Ethiopia (12,15,20). The rate of treatment failure was slightly higher than the results in BRGH for 2007-2011 (1%) (14) and Asella Teaching Hospital (0.2%) (30). The rate of defaulters in our study was lower than the previous results in BRGH (6%) (14) and South Africa (9.8%) (22). The percentage of dead patients was similar at Asella Hospital (6%) (30) but higher than that at Dilla University Referral Hospital (3.4%) (24) and lower than at BRGH (9%) (14). This indicates a considerable improvement in the rate of dead patients with TB in our study compared to a previous study in the same hospital (14), which might be related to the improvements in DOTS service in the BRGH. The lower percentage of failure and defaulted patients might be due to the deployment of health extension workers who provide treatment and prevention services to the public in all zones in Ethiopia, including BRGH (31).

The TSR in our study (Table 3) was similar to that reported in a study of global TSRs (83%) in a 2015 cohort) (4) but slightly higher than the TSR in the BRGH (78.2%) (14). The TSR of PTB-, PTB+ and EPTB patients in our study was slightly higher than the rate in BRGH (PTB-, 79.5%; PTB+, 76.1% and EPTB, 79.3%) (14). The TSR of new cases in our study was higher than the rate in 2007-2012 in BRGH (78.9%) (14) but lower than the national TSR in new patients registered during 2016 (90%) (5). The TSR of patients with TB among HIV-negative and HIV-positive patients was similar to the TSRs at Asella Teaching Hospital (83.4% in HIV-negative and 79.8% in HIV-positive) (30), but higher than the TSRs in the BRGH (80.8% in HIV-negative patients with TB and 67.1% among HIV-positive patients) (14). Variation in DOTS performance in various study areas, socio-economic characteristics of the patients, geographic setting, sample size, study period, and the TB clinic management may have contributed to differences in TSR for patients with TB (20).

Table 1. Characteristics of tuberculosis patients at Bale Robe General Hospital, Ethiopia (n=807)

Age, mean±SD	31.8±1.07
Age groups, n (%)	
0-14	56 (6.9)
15-24	300 (37.2)
25-34	204 (25.3)
35-44	108 (13.4)
45-54	60 (7.4)
55-64	27 (3.3)
≥65	52 (6.4)
Sex, n (%)	
Male	463 (57.4)
Female	344 (42.6)
Residence, n (%)	
Urban	652 (80.8)
Rural	155 (19.2)
Job status, n (%)	
Student	246 (30.5)
Self-employee	258 (32)
Employed	91 (11.3)
Unemployed	104 (12.9)
Prisoner	30 (3.7)
Farmer	78 (9.7)
TB type, n (%)	
PTB-	351 (43.5)
PTB+	226 (28.0)
EPTB	230 (28.5)
TB patient category, n (%)	
New	642 (79.6)
Relapse	36 (4.5)
Defaulted	14 (1.7)
Failure	7 (0.9)
Transfer-in	89 (11.0)
Others	19 (2.4)
HIV status, n (%)	
Positive	168 (20.8)
Negative	639 (79.2)
Treatment year, n (%)	
2012	140 (17.3)
2013	149 (18.5)
2014	180 (22.3)
2015	151 (18.7)
2016	187 (23.2)

TB: Tuberculosis, PTB: Pulmonary tuberculosis, PTB-: Smear negative pulmonary tuberculosis, PTB+: Smear positive pulmonary tuberculosis, EPTB: Extra-pulmonary tuberculosis; SD: Standard deviation

Table 2. Treatment outcomes in tuberculosis patients at Bale Robe General Hospital, Ethiopia

	Cured	Completed	Failure	Defaulted	Death	Transferred out	Total
Age groups, n (%)							
0-14	7 (12.5)	45 (80.4)	0 (0)	2 (3.6)	0 (0)	2 (3.6)	56
15-24	99 (33.0)	157 (52.3)	7 (2.3)	14 (4.7)	8 (2.7)	15 (5.0)	300
25-34	51 (25.0)	111 (54.4)	4 (2.0)	6 (2.9)	16 (7.8)	16 (7.8)	204
35-44	24 (22.2)	67 (62.0)	3 (2.8)	0 (0)	7 (6.5)	7 (6.5)	108
45-54	15 (25.0)	28 (46.7)	2 (3.3)	3 (5.0)	7 (11.7)	5 (8.3)	60
55-64	3 (11.1)	19 (70.4)	0 (0)	1 (3.7)	1 (3.7)	3 (11.1)	27
≥65	7 (13.5)	32 (61.5)	1(1.9)	1 (1.9)	11 (21.2)	0 (0)	52
Sex, n (%)							
Male	107 (23.1)	275 (59.4)	8 (1.7)	14(3.0)	33 (7.1)	26 (5.6)	463
Female	99 (28.8)	184 (53.5)	9 (2.6)	13 (3.8)	17 (4.9)	22 (6.4)	344
Residence, n (%)							
Urban	168 (25.8)	365 (56.0)	16 (2.5)	22 (3.4)	43 (6.6)	38 (5.8)	652
Rural	38 (24.5)	94 (60.6)	1 (0.6)	5 (3.2)	7 (4.5)	10 (6.5)	155
Job status, n (%)							
Student	88 (35.8)	130 (52.8)	4 (1.6)	9 (3.7)	2 (0.8)	13 (5.3)	246
Self-employee	59 (22.9)	150 (58.1)	5 (1.9)	7 (2.7)	22 (8.5)	15 (5.8)	258
Employed	21 (23.1)	49 (53.8)	2 (2.2)	5 (5.5)	8 (8.8)	6 (6.6)	91
Unemployed	13 (12.5)	65 (62.5)	4 (3.8)	5 (4.8)	7 (6.7)	10 (9.6)	104
Prisoner	8 (26.7)	19 (63.3)	1 (3.3)	0 (0)	2 (6.7)	0 (0)	30
Farmer	17 (21.8)	46 (59.0)	1 (1.3)	1 (1.3)	9 (11.5)	4 (5.1)	78
TB type, n (%)							
PTB-	43 (12.3)	239 (68.1)	8 (2.3)	13 (3.7)	29 (8.3)	19 (5.4)	351
PTB+	148 (65.5)	42 (18.6)	5 (2.2)	8 (3.5)	11 (4.9)	12 (5.3)	226
EPTB	15 (6.5)	178 (77.4)	4 (1.7)	6 (2.6)	10 (4.3)	17 (7.4)	230
TB patient category, n (%)							
New	159 (24.8)	373 (58.1)	10 (1.6)	23 (3.6)	44 (6.9)	33 (5.1)	642
Relapse	18 (50.0)	11 (30.6)	1 (2.8)	0 (0)	3 (8.3)	3 (8.3)	36
Defaulted	5 (35.7)	8 (57.1)	0 (0)	1 (7.1)	0 (0)	0 (0)	14
Treatment after failure	2 (28.6)	2 (28.6)	2 (28.6)	0 (0)	0 (0)	1 (14.3)	7
Transfer-in	20 (22.5)	53 (59.6)	3 (3.4)	2 (2.2)	2 (2.2)	9 (10.1)	89
Others	2 (10.5)	12 (63.2)	1 (5.3)	1 (5.3)	1 (5.3)	2 (10.5)	19
HIV status, n (%)							
Positive	43 (25.7)	87 (52.1)	2(1.20)	2 (1.2)	18 (10.8)	16 (9.6)	168
Negative	163 (25.5)	372 (58.2)	15 (2.3)	25 (3.9)	32 (5.0)	32 (5.0)	639
Treatment year, n (%)							
2012	38 (27.1)	76 (54.3)	2 (1.4)	1 (0.7)	17 (12.1)	6 (4.3)	140
2013	36 (24.2)	91 (61.1)	2 (1.3)	3 (2.0)	10 (6.7)	7 (4.7)	149
2014	38 (21.1)	82 (45.6)	7 (3.9)	19 (10.6)	10 (5.6)	24 (13.3)	180
2015	45 (29.8)	91 (60.3)	1(0.7)	2 (1.3)	9 (6.0)	3 (2.0)	151
2016	49 (26.2)	119 (63.6)	5 (2.7)	2 (1.1)	4 (2.1)	8 (4.3)	187
Total	206 (25.5)	459 (56.9)	17 (2.1)	27 (3.3)	50 (6.2)	48 (5.9)	807

TB: Tuberculosis, PTB: Pulmonary tuberculosis, PTB-: Smear negative pulmonary tuberculosis, PTB+: Smear positive pulmonary tuberculosis, EPTB: Extra pulmonary tuberculosis

Table 3. Univariate and multivariate analysis of treatment success rate

Variables	Treatment success n (%)	Univariate analysis OR (95% CI)	p	Multivariate analysis OR (95% CI)	p
Age in groups					
0-14	52 (92.9)	1		1	
15-24	256 (85.3)	0.68 (0.27-1.67)	0.403	0.53 (0.20-1.43)	0.214
25-34	162 (79.4)	0.56 (0.29-1.05)	0.073	0.48 (0.22-1.01)	0.055
35-44	91 (84.3)	0.77 (0.44-1.36)	0.381	0.71 (0.36-1.40)	0.326
45-54	43 (71.7)	0.51 (0.29-0.89)	0.019	0.54 (0.27-1.09)	0.087
55-64	22 (81.5)	1.18 (0.60-2.31)	0.618	0.99 (0.47-2.08)	0.990
≥65	39 (75.0)	**0.23 (0.94-0.56)**	**0.001**	**0.17 (0.06-0.45)**	**0.001**
Gender					
Male	382 (82.5)	1		-	-
Female	283 (82.3)	0.984 (0.74-1.30)	0.909	-	-
Residence					
Urban	533 (81.7)	1	1		
Rural	132 (85.2)	1.28 (0.88-1.85)	0.188	1.16 (0.7 -1.74)	0.460
Occupation					
Student	218 (88.6)	1		1	
Self-employed	209 (81.0)	0.26 (0.70-2.24)	0.430	0.94 (0.99-3.81)	0.052
Gov. employed	70 (76.9)	0.98 (0.60-1.62)	0.950	1.17 (0.65-2.10)	0.590
Unemployed	78 (75)	**0.54 (0.32-0.91)**	**0.021**	**0.86 (0.44-0.97)**	**0.036**
Prisoner	27 (90.0)	1.40 (0.80-2.44)	0.240	1.89 (0.99-3.61)	0.051
Farmer	63 (80.8)	0.46 (0.17-1.25)	0.130	0.74 (0.25-2.20)	0.593
TB type					
PTB-	282 (80.3)	1		-	-
PTB+	190 (84.1)	1.27 (0.91-1.78)	0.155	-	-
EPTB	193 (83.9)	0.98 (0.67-1.44)	0.950	-	-
TB patient category					
New	532 (82.9)	1		1	
Relapse	29 (80.6)	0.21 (0.04-1.17)	0.076	0.20 (0.36-1.17)	0.075
Defaulted	13 (92.9)	0.67 (0.24-1.89)	0.457	0.56 (0.18-1.66)	0.297
Treatment after failure	4 (57.1)	0.58 (0.25-1.32)	0.195	**0.37 (0.15-0.91)**	**0.030**
Transfer-in	73 (82.0)	2.10 (0.46-9.44)	0.330	2.35 (0.44-12.61)	0.318
Others	14 (73.7)	0.61 (0.24-1.52)	0.294	0.48 (0.18-1.28)	0.145
HIV status					
Positive	130 (77.8)	1		1	
Negative	535 (83.7)	**1.50 (1.08-2.08)**	**0.014**	**1.62 (1.13-2.34)**	**0.009**
Year of treatment					
2012	114 (81.4)	1		1	
2013	127 (85.2)	2.01 (1.24-3.26)	0.350	1.52 (0.96-3.03)	0.200
2014	120 (66.7)	**0.93 (0.53-2.50)**	**0.046**	**0.47 (0.23-0.96)**	**0.038**
2015	136 (90.1)	**4.42 (2.86-6.82)**	**0.001**	**2.29 (1.32-3.98)**	**0.003**
2016	168 (89.8)	0.97 (0.57-1.65)	0.920	1.73 (0.88-4.40)	0.445

TB: Tuberculosis, PTB-: Smear negative pulmonary tuberculosis, PTB+: Smear positive pulmonary tuberculosis, EPTB: Extra pulmonary tuberculosis, HIV: Human immune deficiency virus, OR: Odds ratio, CI: Confidence interval

In multivariate logistic regression, TSR was significantly lower in patients with TB ≥65 years of age (Table 3), in concordance with similar studies in Ethiopia (21,27,30). Individuals at a higher age experience increased co-infections with other diseases and develop immune-compromised situations that might contribute to poorer treatment outcomes (18,30). Unemployed patients with TB exhibited a significantly lower TSR than the students (the reference category) (Table 3), in agreement with studies in the Tigray Region (20) and Anqing, China (8). Unemployed patients with TB may interrupt the DOTS treatment for socio-economic reasons and thereby reducing the TSR of TB. Patients with TB with treatment after failure exhibited lower TSR than new patients (Table 3). Other studies linked a previously treated TB with MDR (6,32) and unsuccessful treatment outcomes (18). HIV-negative patients with TB had significantly higher TSR than HIV-positive counterparts (Table 3), in agreement with related studies in Ethiopia (29,33). HIV co-infection increases the risk of latent TB reactivation 20-fold (33). Patients with TB treated

Table 4. Multinomial logistic regression analysis of factors associated with treatment outcomes

Variable	Completed	Failure	Default	Death	Transferred out
Age (years)					
0-14	1.32 (0.34-5.06)	0.28 (0.01-6.01)	1.16 (0.15-8.97)	**0.042 (0.006-0.269)**	1.20 (0.13-10.54)
15-24	0.83 (0.26-2.62)	1.20 (0.14-9.86)	1.38 (0.23-8.28)	**0.078 (0.020-0.275)**	1.79 (0.26-12.25)
25-34	0.98 (0.31-3.14)	1.44 (0.17-11.79)	1.17 (0.19-7.18)	**0.097 (0.028-0.330)**	4.23 (0.63-28.39)
35-44	0.88 (0.26-2.97)	2.02 (0.23-17.84)	0.41 (0.054-3.19)	**0.065 (0.017-0.240)**	2.92 (0.40-21.28)
45-54	0.71 (0.20-2.51)	1.91 (0.21-17.20)	1.73 (0.26-11.1)	**0.13 (0.035-0.480)**	2.97 (0.40-22.0)
55-64	1.21 (0.25-5.88)	0.34 (0.008-14.18)	1.57 (0.15-16.10)	**0.80 (0.011-0.628)**	4.73 (0.50-44.88)
>65 (Ref.)	1	1	1	1	1
Occupation					
Student	0.76 (0.32-1.82)	0.96 (0.12-7.45)	1.48 (0.32-6.7)	0.33 (0.10-1.08)	1.21 (0.36-4.00)
Self-employee	1.23 (0.56-2.73)	1.71 (0.26-11.08)	1.89 (0.045-7.95)	1.33 (0.52-3.34)	1.08 (0.36-3.22)
Gov. employee	1.02 (0.40-2.61)	2.19 (0.27-17.54)	4.33 (0.92-20.45)	1.40 (0.46-4.22)	1.57 (0.43-5.68)
Unemployed	1.55 (0.57-4.22)	**7.97 (1.13-55.8)**	2.55 (0.57-11.41)	1.02 (0.32-3.23)	**4.27 (1.25-14.61)**
Prisoners	0.76 (0.21-2.65)	1.85 (0.17-19.9)	0.50 (0.02-5.92)	0.84 (0.16-4.20)	0.39 (0.04-3.74)
Farmers (Ref.)	1	1	1	1	1
TB type					
PTB-	0.62 (0.35-1.08)	1.06 (0.37-3.03)	1.10 (0.49-2.45)	1.28 (0.62-2.64)	0.59 (0.29-1.20)
PTB+	**0.34 (0.02-0.61)**	1.29 (0.54-4.36)	1.75 (0.76-5.24)	1.14 (0.86-1.27)	**0.069 (0.032-0.14)**
EPTB (Ref.)	1	1	1	1	1
TB patient category					
New	0.71 (0.15-3.23)	**0.10 (0.015-0.72)**	0.33 (0.047-2.41)	0.69 (0.09-5.28)	0.23 (0.04-1.31)
Relapse	0.28 (0.05-1.67)	0.12 (0.01-1.51)	0.10 (0.05-1.82)	0.49 (0.05-4.89)	0.28 (0.038-2.204)
Default	0.29 (0.036-2.30)	0.21 (0.06-6.76)	0.67 (0.05-8.97)	0.12 (0.04-4.18)	0.54 (0.01-2.22)
Treatment after failure	0.17 (0.08-1.06)	0.1 (0.08-1.34)	0.05 (0.01-1.07)	0.4 (0.03-1.07)	**2.91 (1.25-13.63)**
Transfer in	1.16 (0.23-5.84)	0.40 (0.05-3.31)	0.28 (0.033-2.54)	0.71 (0.07-6.61)	0.78 (0.12-4.91)
Others (Ref.)	1	1	1	1	1
HIV Status					
HIV(+)	0.79 (0.47-1.31)	0.41 (0.62-0.199)	0.49 (0.20-1.18)	**2.18 (1.18-4.04)**	1.77 (0.94-3.32)
HIV (-) (Ref.)	1	1	1	1	1
Year of treatment					
2012	0.58 (0.30-1.10)	0.46 (0.11-1.8)	0.71 (0.17-2.97)	**2.70 (1.14-6.39)**	0.73 (0.28-1.90)
2013	0.88 (0.47-1.65)	0.49 (0.12-1.95)	1.21 (0.35-4.19)	1.54 (0.61-3.84)	0.92 (0.37-2.27)
2014	0.58 (0.308-1.09)	1.23 (0.40-3.71)	**11.46 (4.16-31.54)**	1.48 (0.58-3.72)	**3.01 (1.35-6.72)**
2015	0.61 (0.33-1.14)	0.24 (0.05-1.06)	0.70 (0.18-2.65)	1.40 (0.50-3.52)	0.33 (0.11-1.93)
2016 (Ref.)	1	1	1	1	1

TB: Tuberculosis, CI: Confidence interval, ARRR: Adjusted relative risk ratio in multinomial logistic regression analysis. NB. Ref.: Reference category for each independent factor used in multinomial logistic regression analysis. Values indicated in bold are significantly associated with treatment outcome at $p<0.05$

during 2014 had lower TSRs, but those who were treated during 2015 had higher TSRs than the reference year (Table 3). The Federal Ministry of Health assessment in 2013/2014 showed that the coverage of the DOTS program reached 79% in health centers and 98.4% in hospitals nationwide (34), indicating a large gap in the TSR among health institutions in Ethiopia. A global TB report showed that the TSR for TB in Ethiopia during 2014 was 89% (1) and lower than that during 2012 (91%) (2). Therefore, the national TSR of TB was impeded by some unexplained factors that might have affected the TSR in BRGH during 2014.

The ARRR analysis revealed that death from TB was lower in patients with TB in the <65 years of the age group (Table 4). Higher death rates from TB have also been reported in people of older age groups (18-21,35). Age-related co-infections and physiological deterioration may lead to poor treatment adherence, which, with less access of older people to health facilities, may lead to poor outcomes (30,36). We also found more deaths among PTB- patients than among PTB+ and EPTB patients. Diagnosis and treatment delays and HIV infection among PTB- cases were suggestive of higher death in PTB- TB cases than in PTB+ and EPTB (21,26). The relative risk ratio of treatment failure was lower in new patients with TB than in their counterparts (Table 4). Drug resistance due to the prevalence of MDR-TB in Ethiopia was low (1.6%) among new cases and relatively higher (12%) among retreatment cases (10,11). The relative risk of death in patients with TB was significantly higher in HIV-positive than in HIV-negative patients with TB. This finding was in concordance with other studies in Ethiopia (30) and South Africa (37), which found strong associations between HIV infection and TB mortality. The reduction in death and improvement of the success rate of TB has been in connection to antiretroviral treatment in TB-HIV co-infected individuals (38). In the adjusted multinomial logistic regression analysis, patients with TB who were treated during 2012 had a higher relative risk of death. At the global level, an estimated 8.6 million people developed TB and 1.3 million died of the disease in 2012 (9). A higher death rate was also reported for patients with TB who were treated during September 2012-May to 2013 in southern Ethiopia than in other years (24). A similar study in Ethiopia reported a higher rate of transfer for patients with treatment failure (12).

This study has several limitations. Because of its retrospective design, several socio-demographic characteristics such as educational status, income, family size, and distance from the treatment center were not available. Additionally, data on clinical characteristics were missing, including the presence of co-morbidities, complications related to the treatment, drug resistance, and patients' awareness levels. Therefore, the interpretation of the results should cautiously be made. Despite these limitations, the large sample size and follow-up of internationally accepted ethical guidelines were the strengths.

Conclusion

This study showed that the rate of cure in patients with TB was 25.5%, and the rate of treatment completion was 56.9%. The rate of patients who died of TB was 6.2%, transferred was 5.9%, treatment failure was 2.1%, and defaulted was 3.3%. The TSR in all forms of TB in BRGH (82.4%) was satisfactory but below the minimum target (85.0%) established by the WHO. Age, occupation, treatment category, HIV status, and year of treatment were independently associated with treatment success of TB. Age and HIV status were independently associated with the risk of death, whereas occupation of the patients with TB was significantly associated with the risk of treatment failure and transfer. TB type was associated with the risk of treatment completion and transfer; and the year of treatment was associated with the risk of treatment outcomes such as default, death, and transfer. Based on the findings of this study, continuous monitoring of patients with unsuccessful treatment outcomes and TB-HIV co-infection, supervision of the implementation of the DOTS program, and targeted interventions may be recommended.

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Ethics

Ethics Committee Approval: An approval was received from the Institutional Research Ethics Committee of the College of Natural and Computational Science of Madda Walabu University (ref. no. CNCS/234/2017; date: 26.09.2017).

Informed Consent: Retrospective study.

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Authorship Contributions

Concept: A.A.T., Y.B.G., Design: A.A.T., Y.B.G., H.K., Data Collection or Processing: A.A.T., Y.B.G., Analysis or Interpretation: A.A.T., Y.B.G., H.K., Literature Search: A.A.T., Y.B.G., Writing: A.A.T., Y.B.G., H.K.

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