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Determinants of Treatment Failure among New Smear Positive Pulmonary Tuberculosis Patients, Northwest Ethiopia: A Case-Control Study

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Abstract

Introduction: Despite the accessibility of curable anti-tuberculosis medications, tuberculosis (TB) treatment failure is still challenge to the health and economic burden. As a result the patient remains main source of infection in the public and may lead to develop Resistance TB, as a consequence less productivity and lack of ability to work.

Methods: Unmatched case control study design was conducted among 94 cases and 196 controls from January to May 2018. Cases and controls were selected from health centers and government hospitals using systematic random sampling. Binary logistic regression analysis was used to identify factors.

Results: Patients age 30-39 years were 20% more likely risk for treatment failure as compared with age 40 and above (AOR=0.80; 95% CI:0.73-0.92), patients with a family size of 5 and above were 2.81 times more likely risk for TB treatment failure as compared with a family size of less than three (AOR=2.81; 95% CI: 1.70-4.64), patients co-infected with HIV were 3.79 times more likely risk for TB treatment failure as compared with HIV negatives (AOR=3.79; 95% CI:1.67-8.60), and duration of cough greater than 9 weeks were 6.84 times more likely risk for TB treatment failure as compared with cough of less than 5 weeks (AOR=6.84; 95% CI: 4.31-9.37) and Patients with positive smear result at two months were also 7.92 times more likely risk for treatment failure (AOR=7.92; 95% CI: 3.56-17.60) as compared with negative smear result patients were factors significantly associated with treatment failure.

Conclusion: TB treatment failure was associated with older age, large family size, co-infected with HIV, long duration of cough before diagnosis and positive sputum smear at end of two months. Hence, service providers should provide strict follow up for TB patients co-infected with HIV and patients of positive smear at end of two months during the course of treatment.

Keywords: Pulmonary tuberculosis patients; TB treatment; HIV

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Abbreviations: DM: Diabetes Mellitus; DOTS: Directly Observed Treatment Short Course; FMoH: Federal Ministry of Health; HC: Health Center; HIV: Human Immune-Deficiency Virus; MDR: Multi Drug Resistance; NSP: New Smear Positive; PH: Primary Hospital; PTB: Pulmonary Tuberculosis; TB: Tuberculosis; TTF: Tuberculosis Treatment Failure; TTS: Tuberculosis Treatment Supporter; WHO: World Health Organization; ZHD: Zonal Health Department

Introduction

Despite the accessibility of curable anti-tuberculosis medications, tuberculosis (TB) still to be a global public health problem [1], with an estimated 10.4 million incident cases and the ninth leading cause of death worldwide ranking above HIV/AIDS with 1.8 million deaths in 2016: 74% were in Africa and 56% were in five countries including India, Indonesia, China, the Philippines and Pakistan [2]. According to WHO estimation South-East Asia Region incident cases were 45 percent, and in African Region 25 percent including Ethiopia similarly fastest decline in TB incidence were the European Region 4.6% and 82% of deaths were in the two regions [2]. Fourteen countries are in the three high-burden country lists for TB, TB/HIV and MDR [2]. Ethiopia is one of the countries among the 30 high TB burdened countries with treatment success rate of 83% from all forms of TB from those bacteriologically confirmed TB cases the cure rate was 78% [3].

Poor treatment outcome of TB patients would lead to the risk of treatment failure, drug resistance, relapse, death, continuous existence of infection, and could declines treatment outcomes in TB control programs [4].

Tuberculosis mostly affects in their most productive age group (15-54 years), poor socio-economic status individuals and those co-morbid with HIV, diabetes and severe kidney disease and also those individuals who used prolonged steroid therapy [5]. The vast majority of TB cases can be cured when early diagnosis and appropriate medications are provided and taken properly. Treatment failure is defined as a patient with sputum smear or sputum culture remaining smear-positive at 5 months of treatment or later after the initiation of anti TB treatment [6,7], is one of the unsuccessful treatment outcomes that challenges to control of TB. Patients with smear positive at five months or later during treatment have a higher mortality compared to cured [8].

According to WHO recommendation to diagnose Treatment failure in resource limited settings by using microscopic Acid Fast Bacilli examination at 5 months or later during treatment. However, detecting the risk of failure for treatment is essential before the 5 months in adhering and decreasing the spread TB, morbidity and mortality [6]. Treatment failure is still challenge to the health and economic burden as the patient remains a source of infection in the public and it may lead to develop Multi Drug Resistance TB, as a consequence less productivity and lack of ability to work [9]. The ideal tool for this is regular laboratory monitoring using sputum AFB microscopy or culture. However, factors such as socio demographic, behavioral and economic, and disease and treatment related factors might result in treatment failure [7].

Sputum monitoring for New smear positive (NSP) PTB patient should be done by taking sputum sample using microscopic Acid Fast Bacilli (AFB) examination at the end of 2rdmonth (1x) if the result was positive smear (2 samples) at the end of 3rd month should be done and also if the sputum result will also be positive at end of 5th month (1x)the patient consider as Treatment Failure and start medication as Retreatment regimen [6,7].

To treat the patient registered as new TB patients, treatment after failure, relapse and others the Ethiopian federal ministry of health (FMoH) and WHO strongly recommends patients should receive a drug regimen containing Rifampicin, Isoniazid, Pyrazinamide and Ethambutol for 2 months and Rifampicin and Isoniazid 4 months prepared as fixed dose combination based on weight of the patient [6,7].

Despite the fact that many activities have been done to end the TB epidemic, poor treatment adherence still makes a challenge to manage and achieve the global Targets to end TB (deaths, disease, and Zero suffering due to TB) by 2030 (21). Therefore, this study plans to identify the Determinants of treatment failure among NSPPTB patients in health centers and governmental hospitals and helps to increase the tuberculosis treatment cure rate under DOTS.

Materials and Methods

Unmatched case control study design was conducted. Both cases and controls were selected from selected health facilities registered from January 2016 to December 2017 in West Gojjam zone, Northwest Ethiopia. The study was conducted from January 2018 - May 2018.

During the study period there were 108 health centers and 6 hospitals in west Gojjam Zone. Ninety three health centers and 6 government hospitals were provide TB diagnosis with sputum microscopy and treat on DOTS, with a total of 742 NSP PTB patients cured from the disease and 114 treatment failure patients being on anti-TB treatment from January 2016 to December 2017. Sputum smear microscopy is a basic method for the diagnosing TB lower and middle income countries [10]. All of the 114 cases (67 were from 15 health centers and 47 from six hospitals) and from the total 742 cured patients (251 were from the above 15 health centers, 146 were take their medication from 6 hospitals) [11].

Patients were eligible for inclusion for cases - All NSP PTB patients (aged ≥ 18 years) who were smear positive at the beginning of the treatment from January 2016 to December 2017 at health centers and hospitals of west Gojjam zone and for Controls - All NSP PTB patients (aged ≥ 18 years) who were smear positive at the beginning of the treatment from January 2016 to December 2017 at health centers and hospitals of west Gojjam zone.

The sample size of the study was calculated by a two-population proportion formula by using Epi Info version 7.2.1.0 unmatched case control, 80% power with 1:2 ratio of case to control. By considering different determinant factors studied from Tigray, Ethiopia [12], the proportion of exposure among patients of family size 3-5 person at home compared with less than three person/home (OR=2.2, with 95% CI) and 53.17 percent controls exposed was taken as determinant variable to calculate the highest sample size of 275, from selected health centers and hospitals. After considering 10% of non-response a total sample size of 303 (101 cases and 202 controls) was required.

Ethical consideration

Ethical clearance was obtained from ethical review board of Bahir Dar University College of Medicine and Health Sciences and letter of permission was obtained from Amhara Public Health Institute and West Gojjam Zone Health Department. Written consent was also obtained from each selected health center and hospital. Similarly, informed consent was obtained from the participants prior to participation, and data collection procedure was anonymous for keeping the confidentiality of any information. The participants also informed to refuse or withdraw from the study.

Results

Socio-demographic characteristics

From the total population, 290 study participants were completed the interview with a response rate of 95.7%. Among these 94 (93.1%) were cases (failure) and 196 (97.0%) were controls (cured from tuberculosis). About 60 (63.8%) of failures and 61 (31.1%) of cured patients were age of 40 and above. From the total participants 74 (78.7%) of failures and 130 (66.3%) of cured from

tuberculosis were males. The majority 88 (93.6%) of treatment failure participants and 168 (85.7%) cured from tuberculosis were Orthodox Christians **(Table 1).**

Behavioral and economic factors

The majority 61 (64.9%) of failures and 83 (42.3%) of cured participants were monthly household income of less than one thousand birr. About 11 (11.7%) of failure patients and 8 (4.1%) cured participants were a distance of 10 km and above to reach the health facility, more of them 73 (77.8%) and 132 (67.3%) were going to the health facility with their foot. About 45 (47.8%) of failures and 49 (25%) cured participants were drink alcohol during treatment. From which 32 (71.1%) of cured participants were drink alcohol almost every day. About 4 (4.3%) of failures and 8 (4.1%) of cured participants were smoke cigarette, and 7 (7.4%) of failures and 8 (4.1%) of cured participants were chew chat during treatment **(Table 2).**

Table 1 Socio demographic characteristics, West Gojjam Zone, (January to May 2018).

Variables		Cases n= 94	Controls n=196	Total n=290
Age (years)	≤ 19 years	3 (3.2%)	30 (15.3%)	33 (11.4%)
	20-29 years	15 (15.9%)	61 (31.1%)	76 (26.2%)
	30-39 years	16 (17.0%)	44 (22.4%)	60 (20.7%)
	≥40 years	60 (63.8%)	61 (31.1%)	121 (41.7%)
Sex	Male	74 (78.7%)	130 (66.3%)	204 (70.3%)
	Female	20 (21.3%)	66 (33.7%)	86 (29.7%)
Religion	Orthodox	88 (93.6%)	168 (85.7%)	256 (88.3%)
	Muslim	4 (4.3%)	23 (11.7%)	27 (9.3%)
	Protestant	2 (2.1%)	5 (2.6%)	7 (2.4%)
Marital status	Married	68 (72.3%)	139 (70.9%)	207 (70.5%)
	Single	23 (24.5%)	50 (25.5%)	73 (25.1%)
	Divorced	3 (3.2%)	7 (3.6%)	10 (3.4%)
Family size	Less than 3	9 (9.6%)	41 (20.9%)	50 (17.2%)
	3-5 person	18 (19.1%)	43 (21.9%)	61 (21.0%)
	More than 5	67 (71.3%)	113 (57.7%)	180 (62.1%)
Ethnicity	Amhara	87 (92.6%)	180 (91.8%)	267 (92.1%)
	Tigre	4 (4.3%)	10 (5.1%)	14 (4.8%)
	Oromo	3 (3.2%)	6 (3.1%)	9 (3.1%)
Educational status	Not attend school	30 (31.9%1)	33 (16.8%)	63 (21.7%)
	Primary	40 (42.6%)	77 (39.3%)	117 (40.3%)
	Secondary and above	24 (25.5%)	86 (43.9%)	110 (37.9%)
Residence	Rural	82 (87.2%)	166 (84.7%)	248 (85.5%)
	Urban	12 (12.8%)	30 (15.3%)	42 (14.5%)
Occupation	Farmer	67 (71.3%)	143 (73.0%)	210 (72.4%)
	Housewife	13 (13.8%)	21 (10.7%)	34 (1.7%)
	Merchant	9 (9.6%)	21 (10.7%)	30 (10.3%)
	Student	5 (5.3%)	11 (5.6%)	16 (5.6%)
Treatment supporter	No	11 (11.7%)	13 (6.6%)	24 (8.3%)
	Yes	83 (88.3%)	183 (93.4%)	266 (91.7%)
HIV status	Positive	43 (45.7%)	41 (20.9%)	84 (28.9%)
	Negative	51 (54.3%)	155 (79.1%)	206 (71.0%)
Health facility	Hospital	34 (94.4%)	93 (96.8%)	127 (43.8%)
	Health center	60 (92.3%)	103 (97.2%)	163 (56.2%)

Table 2 Behavioral and economic factors of the respondents, West Gojjam Zone, (January to May 2018).

Variables		Cases n=94	Controls n=196	Total n=290
Monthly income (Birr)	Less than 1000	61 (64.9%)	83 (42.3%)	144 (49.6%)
	1000-3000 birr	22 (23.4%)	81 (41.3%)	103 (35.5%)
	More than 3000	11 (11.7%)	32 (16.3%)	43 (14.8%)
Distance from the nearby health facility	10km and above	3 (3.2%)	7 (3.6%)	10 (3.4%)
	5-9 km	23 (24.5%)	50 (25.5%)	73 (25.2%)
	Less than 5 km	68 (72.3%)	139 (70.9%)	202 (71.4%)
Mode of transport	Foot	73 (77.8%)	132 (67.3%)	207 (71.4%)
	Taxi	21 (22.3%)	64 (32.6%)	85(29.3%)
Money paid to reach health facility (Birr)	5 up to 10 birr	5 (5.3%)	22 (11.2%)	27 (9.3%)
	Less than 5 birr	16 (17.0%)	42 (21.4%)	58 (20.0%)
Drink alcohols during treatment	Yes	45 (47.9%)	49 (25.0%)	94 (32.4%)
	No	49 (52.1%)	147 (75.0%)	196 (67.6%)
Frequency of drink alcohol	Almost every day	32 (71.1%)	19 (38.8%)	51(54.9%)
	Once a week	13 (28.9%)	30 (61.2%)	43 (45.1%)
Cigarette Smoking	Yes	4 (4.3%)	8 (4.1%)	12 (4.1%)
	No	90 (95.7%)	188 (95.9%)	278 (95.9%)
Chat chewing	Yes	7 (7.4%)	8 (4.08%)	15 (5.2%)
	No	87 (92.6%)	188 (95.9%)	275 (94.8%)
Use of traditional medicines	Yes	2 (2.1%)	3 (1.5%)	5 (1.7%)
	No	92 (97.9%)	193 (98.5%)	285 (98.3%)
Attitude of patient toward health workers at TB clinic	Very good	45 (47.9%)	180 (91.8%)	225 (77.6%)
	Medium	30 (31.9%)	9 (4.6%)	39 (13.4%)
	Not good	19 (20.2%)	7 (3.6%)	26 (9.0%)

Disease and treatment related factors

About 54 (57.4%) of failures and 54 (27.6%) of cured participants were more than 8 weeks of cough duration before tuberculosis diagnosis. From the treatment participants 77 (81.9%) of failure and 180 (91.8%) of cured patients were loss of appetite during treatment. About 10 (10.6%) of failures and 8 (4.1%) of failures were not taking their anti TB medication on DOTS. About 10 (55.6%) of failures and 6 28.6%) of cured participants were failed to take anti-TB medication for more than 14 days and above. The majority 86 (91.5%) of failures and 168 (85.7%) of cured participants were take their medication before meal. Regarding comorbidity 9 (9.6%) of failure participants and 7 (3.5%) of cure participants were diabetes mellitus patients. About 27 (28.7%) of failures and 31 (15.8%) of cured participants were anti-TB drug side effect, from which 12 (44.44%) of failures and 14 (45.2%) of cured participants were had vomiting as side effect. About 90 (95.7%0 of failures and 22 (11.2%) of cured participants were a positive smear result during treatment **(Table 3).**

Table 3 Disease and treatment related factors of the respondents, West Gojjam Zone, (January to May 2018).

Variables		Case n= 94	Control n=196	Total n=290
Duration of cough before TB diagnosis	≤ 4 weeks	16 (17.0%)	110 (56.1%)	126 (43.4%)
	5-8 weeks	24 (25.5%)	32 (16.3%)	56 (18.6%)
	≥ 9 weeks	54 (57.4%)	54 (27.6%)	108 (37.2%)
Loss of appetite during treatment	Yes	77 (81.9%)	180 (91.8%)	257 (88.6%)
	No	17 (18.1%)	16 (8.2%)	33 (11.4%)
Not take drug on DOTS	Yes	10 (10.6%)	8 (4.1%)	18 (6.2%)
	No	84 (89.4%)	188 (95.9%)	272 (93.8%)
Frequency of fail to take TB drug	≤ 14 days	8 (44.4%)	15 (71.4%)	23 (58.9%)
	> 14 days	10 (55.6%)	6 (28.6%)	16 (41.0%)
Take the TB medication	Before meal	86 (91.5%)	168 (85.7%)	254 (87.6%)
	With meal	6 (6.4%)	19 (9.7%)	25 (8.6%)
	After meal	2 (2.1%)	9 (4.6%)	11 (3.8%)
Co-morbid with DM	Yes	9 (9.6%)	7 (3.6%)	16 (5.5%)
	No	85 (90.4%)	191 (97.4%)	276 (95.2%)
Vomiting as side effect	Yes	12 (12.8%)	14 (7.1%)	26 (8.9%)
	No	82 (87.2%)	182 (92.6%)	264 (91.0%)
Nausea as side effect	Yes	15 (15.9%)	17 (8.7%)	32 (11.0%)
	No	79 (84.1%)	179 (91.2%)	258 (88.9%)
Smear result at end of 2 month	Positive	90 (95.7%)	22 (11.2%)	112 (38.6%)
	Negative	4 (4.2%)	174 (88.8%)	178 (61.4%)

Determinant factors of treatment failure

The socio-demographic, behavioral, economic, disease and treatment related factors of treatment failure were analyzed using bivariate logistic regression as shown below **(Table 4-6).**

All variables with p-value of less than 0.2 in the bivariate analysis were transferred to multivariable logistic regression to identify determinant factors. By using multivariable logistic regression the determinant factors associated with treatment failure were age 30-39 years (AOR=0.80; 95% CI:0.73-0.92) were 0.8 times less likely developing treatment failure as compared with age 40 and above, tuberculosis patients with a family size of five and above were 2.81 times more likely risk for treatment failure as compared with a family size of less than three (AOR=2.81; 95% CI: 1.70-4.64), HIV positive tuberculosis patients also 3.79 times more likely risk for treatment failure (AOR=3.79; 95% CI:1.67-8.60) as compared with HIV negative patients, and also duration of cough greater than 9 weeks were 6.84 times more likely risk for treatment failure as compared with a cough of less than 5 weeks (AOR=6.84; 95% CI: 4.31-9.37). Patients with positive smear result at two months were also 7.92 times more likely risk for treatment failure (AOR=7.92; 95% CI: 3.56-17.60) as compared as compared with negative smear result patients **(Table 7).** The model goodness of the test was checked by Hosmer-Lemeshow statistic and p-value was 0.424.

Discussion

In this study determinants significantly associated with tuberculosis treatment failure were: patient age 40 and above, five and above family members live at home, co-infected with HIV, duration of cough more than 8 weeks before TB diagnosis and positive sputum smear result at end of two months were determinant factors for tuberculosis treatment failure.

In this study being age between 30-39 years as compared to 40 years and above had 0.8 times less likely risk of tuberculosis treatment failure. Similarly, a study carried out in Tigray the risk of treatment failure was higher among patients 40 years and above of age (adj. OR=2.50, 95% CI: 1.12-5.59) as compared with 15-40 years [13]. Another case control study in Tigray also showed age between 30-39 years compared to 40 years and above were a negatively risk factors for treatment failure [12]. Another study in Nigeria age greater than 40 years with (P<0.001) were a significant determinant factor [14]. Similarly on other studies in Thailand, Malaysia, and Portugal with (AOR=3.10, 95% CI: 1.33-7.24), (AOR=1.01, 95% CI: 1.01–1.02) and (AOR=4.37, 95% CI 2.64–7.22) age greater than 60 years consecutively were a high-risk factor for treatment failure [15-17]. This study was unlike with a study conducted in Uganda which revealed no socio-demographic factor was associated with treatment failure [18]. It is not clear that the differences do exist. However, being older in age has a risk for treatment failure may be due to less immunity, low socio-economic status and delay in early diagnosis and treatment leads to poor treatment adherence.

In this study the odds of treatment failure with a patient live in a family size greater than 5 persons were 2.81 times more likely higher risk as compared with a family of less than 3 person live at home. This is almost in between two studies conducted in Tigray with living in the same house with 5 or more family members AOR 2.2, 95 CI% 0.97-4.94 [12] and (adj. OR=3.26, 95% CI: 1.43-7.44) [13]. This being larger family size may have the relation of to low income, and patients with low economic status have a chance of malnutrition resulted in more drug side effects and as a consequence leads to poor adherence.

In this study HIV co-infected cases were 3.79 times more likely risk for treatment failure as compared with HIV negative patients. A retrospective cohort study in West Gojjam Zone was also showed

Table 4 Socio-demographic factors of treatment failure using bivariate logistic regression.

Variables		Cases	Controls	COR (95%CI)	P-Value
Age (years)	≤ 19 years	3	30	0.41 (0.11-1.54)	0.180*
	20-29 years	15	61	0.27 (0.07-1.03)	0.055*
	30-39 years	16	44	0.10 (0.03-0.35)	<0.001*
	≥ 40 years	60	61	1	
Sex	Male	74	130	1.88 (1.06-3.34)	0.032*
	Female	20	66	1	
Marital status	Single	68	139	1	
	Married	23	50	0.93 (0.22-3.93)	0.92
	Divorced	3	7	0.88 (0.22-3.49)	0.85
Family size	Less than 3	9	41	1	
	3-5 person	18	43	1.38 (0.73-2.59)	0.312
	More than 5	67	113	2.70 (1.23-5.91)	0.013*
Educational status	Not attend school	30	33	1.75 (0.93-3.26)	0.079*
	Primary	40	77	1.86 (1.02-3.36)	0.001*
	Secondary and above	24	86	1	
Residence	Rural	82	156	1.75 (0.87-3.52)	0.115*
	Urban	12	40	1	
Occupation	Farmer	67	143	1.06 (0.28-3.94)	0.93
	Housewife	13	21	0.73 (0.21-2.59)	0.63
	Merchant	9	21	0.97 (0.32-2.90)	0.95
	Student	5	11	1	
Treatment supporter	No	11	13	1.86 (0.80-4.34)	0.147*
	Yes	83	183	1	
Health facility	Hospital	34	93	0.06 (0.03-1.04)	0.070*
	Health center	60	103	1	
HIV status	Positive	42	41	3.05 (1.79-5.20)	<0.001*
	Negative	52	155	1	

Note: * significant for multivariable regression at P-value <0.2, 95% CI; 1=reference category.

Table 5 Behavioral and Economic factors of treatment failure using bivariate logistic regression.

Variables		Cases	Controls	COR (95%CI)	P-Value
Monthly income (in birr)	Less than 1000	61	83	2.70 (1.52-4.81)	0.001*
	1000-3000 birr	22	81	2.13 (0.99-4.57)	0.050*
	More than 3000	11	32	1	
Distance from the nearby HF	10 km and above	3	7	1.14 (0.28-4.55)	0.851
	5-9 km	23	50	1.06 (0.60-1.88)	0.833
	Less than 5km	68	139	1	
Mode of transport	Foot	73	132	1.68 (0.95-2.97)	0.072*
	Taxi	21	64	1	
Drink alcohol	Yes	45	49	2.75 (1.64-4.62)	<0.001*
	No	49	147	1	
Frequency of drink alcohol	Almost every day	32	19	3.88 (1.63-9.22)	0.002*
	At least once/week	13	30	1	
Cigarette Smoking	Yes	4	8	1.04 (0.30-3.56)	0.94
	No	90	188	1	
Chat chewing	Yes	7	8	1.89 (0.66-5.38)	0.23
	No	87	188	1	
Use traditional medicine	Yes	2	3	1.39 (0.22-8.51)	0.72
	No	92	193	1	

HIV co-infected cases were more likely to have unsuccessful treatment outcome compared to HIV negatives (AOR, 2.68; 95% CI: 1.92, 3.72) [19]. A case control study conducted in Eastern Ethiopia revealed HIV positive status (AOR=2.5; 95% CI 1.34-5.7) [20]. A study in Ukraine also showed HIV-positive individuals had a fifty percent higher risk to develop treatment failure [21] and a study in Portugal (AOR 4.93;95%CI 3.50–6.96) [16]. But studies in Tigray, Uganda and Thailand showed HIV status had no

Table 6 Disease and treatment related factors of treatment failure using bivariate logistic regression.

Variables		Cases	Controls	COR (95%CI)	P-Value
Duration of cough before TB Dx	≥ 9 weeks	54	54	6.87 (3.60-13.11)	<0.001*
	5-8 weeks	24	32	1.33 (0.69-2.55)	0.386
	≤ 4 weeks	16	110	1	
Loss of appetite	Yes	77	160	1.02 (0.54-1.93)	0.95
	No	17	36	1	
Not take on DOTS	Yes	10	8	2.79 (1.06-7.34)	0.036*
	No	84	188	1	
Take the medication with	After meal	86	168	2.30 (0.48-10.89)	0.29
	With meal	6	19	1.62 (0.62-4.21)	0.32
	Before meal	2	9	1	
Comorbid with DM	Yes	9	7	2.89 (1.04-8.01)	0.041*
	No	85	191	1	
Vomiting as side effect	Yes	12	14	1.90 (0.84-4.289)	0.120*
	No	82	182	1	
Nausea as side effect	Yes	15	17	1.99 (0.95-4.20)	0.067*
	No	79	179	1	
Smear result at two months	Positive	63	58	4.83 (2.85-8.20)	<0.001*
	Negative	31	138	1	

Note: * significant for multivariable regression at P-value <0.2, 95% CI; 1= reference category.

Table 7 Determinant factors of tuberculosis treatment failure using multivariable logistic regression analysis.

Variables		Cases	Controls	COR (95%CI)	AOR (95%CI)	P-Value
Age (years)	≤ 19 years	3	30	0.41 (0.11-1.54)	0.56 (0.02-1.10)	0.450
	20-29 years	15	61	0.27 (0.07-1.03)	0.69 (0.02-1.36)	0.314
	30-39 years	16	44	0.10 (0.03-0.35)	0.80 (0.73 0.92)	0.001*
	≥40 years	60	61	1	1	
Sex	Male	74	130	1.88 (1.06-3.34)	1.58 (0.67-3.76)	0.291
	Female	20	66	1	1	
Family size	Less than 3	9	41	1	1	
	3-5 person	18	43	1.38 (0.73-2.59)	2.2 (0.97-4.94)	0.34
	More than 5	67	113	2.70 (1.23-5.91)	2.81 (1.7-4.64)	0.001*
Educational status	Not attend school	30	33	1.75 (0.93-3.26)	8.62 (2.76-27.26)	0.08
	Primary	40	77	1.86 (1.02-3.36)	2.55 (0.89-7.23)	0.078
	Secondary and above	24	86	1	1	
Residence	Rural	82	166	1.75 (0.87-3.52)	1.91 (0.63-5.78)	0.25
	Urban	12	30	1	1	
Treatment supporter	No	11	13	1.86 (0.80-4.36)	0.73 (0.17-3.05)	0.66
	Yes	83	183	1	1	
Mode of transport	Foot	73	132	1.68 (0.95-2.97)	2.25 (0.89-5.68)	0.085
	Taxi	21	64	1	1	
Not take on DOTS	Yes	10	8	2.79 (1.06-7.34)	4.85 (0.88-26.76)	0.07
	No	84	188	1	1	
HIV status	Positive	42	41	3.05 (1.79-5.20)	3.79 (1.67-8.60)	0.001*
	Negative	52	155	1 (1.52-4.81)	1	
Monthly income (birr)	Less than 1000	61	83	2.70	4.36 (2.14-6.58)	0.95
	1000-3000 birr	22	81	2.13 (0.99-4.57)	1.32 (0.96-1.68)	0.45
	More than 3000	11	32	1	1	
Drink alcohol	Yes	45	49	2.75 (1.64-4.62)	3.45 (1.34-5.56)	0.341
	No	49	147	1	1	
Comorbid with DM	Yes	9	7	2.89 (1.04-8.01)	1.93 (0.37-10.02)	0.432
	No	85	191	1	1	
Duration of cough before TB Dx	≥ 9 weeks	54	54	6.87 (3.60-13.11)	1.41 (0.57-4.38)	0.445
	5-8 weeks	24	32	1.33 (0.69-2.55)	6.84 (4.31-9.37)	<0.001*
	≤ 4 weeks	16	110	1	1	
Vomiting as side effect	Yes	12	14	1.90 (0.84-4.29)	1.57 (0.42-5.93)	0.500
	No	182	182	1	1	
Smear result at two months	Positive	63	58	4.83 (2.85-8.20)	7.92 (3.56-17.60)	<0.001*
	Negative	31	138	1	1	

Note: * Statistically significant at P-value <0.05, 95% CI; 1=reference category.

association with treatment failure [12,18,22]. The reason for the difference not clear, however HIV suppress the immune system and malnutrition leads to treatment failure. As a result, critical follow-up is important for those patients co-infected with HIV may an advantage for a better treatment adherence.

In this study, those patients having greater than 8 weeks cough were 6.84 times more likely risk for developing treatment failure as compared with those who had cough of less than 5 weeks. Similarly, a study in Tigray showed having cough for more than 9 weeks before TB diagnosis were higher risk of treatment failure compared with those who had less than 4-week cough [12]. Coming early to the health facility for the diagnosis of tuberculosis has strong relationship with treatment success rather than coming late because of the patient has developed complications. Despite Ethiopia had set active case finding through cough surveillance at all service points as a standard to control TB infection; early detection and diagnosis of individuals with cough were still a challenge.

In the present study sputum smear positive at end of the second month after initiation anti-tuberculosis treatment was 7.92 times more likely risk for treatment failure as compared with sputum smear negative at end of the second month after initiation anti-tuberculosis. Similarly, a study in Eastern Ethiopia smear positive sputum test result at second month after initiation treatment showed (AOR=14; 95% CI 5.5-36) [20]. There are also studies which reveal smear positive at two months were as a significant determinant factor for tuberculosis treatment failure. Of which a study in Egypt positive sputum smear at 2nd month after initiation treatment (AOR 10.19; 95% CI 5.07–12.50) [23] and study conducted in Uganda a positive sputum smear at 2 months of TB treatment (AOR 20.63, 95%CI 5.42- 78.41) [18]. Similarly, a study in Nigeria positive sputum smears after two month of anti-tuberculosis treatment [14] and a study in Burkina-Faso positive at two months of treatment (adj. OR=11.52; 95%CI:5.18-25.60) also a factor for treatment failure. There are another studies in Iran positive sputum smear at end of the second month (AOR 14.33 95%CI: 6.77-30.33) [24], in India smear positivity at 2 months of treatment [25] and in a prospective cohort study conducted in China a positive smear test result two months after start of treatment (RR 4.2 95%CI: 2.0-9.1) [26]. This is an important finding since AFB Smear at end of second month should be regularly monitored based on the Flow Chart for Sputum AFB monitoring for bacteriologically confirmed PTB Patients in the national TB programs [5]. Therefore, critical follow-up is important for those patients who are smear positive at the beginning of treatment that may an advantage for the prevention of treatment failure.

Limitation of the study

There may be social desirability bias especially on behavior related variables since the participants more likely to answer a socially acceptable response, even if not true. More confidential data collection was done for each respondent to minimize this bias.

Conclusion

In this study patient aged 40 and above, family members of five and above live at home, co-infected with HIV, duration of cough more than 8 weeks before TB diagnosis and positive sputum smear result at end of two months were determinant factors for tuberculosis treatment failure. Being age 30-39 years were less likely risk for treatment failure as compared with age 40 and above, patients with a family size of 5 and above were more likely risk for treatment failure as compared with a family size of less than three, patients co-infected with HIV were more likely risk for treatment failure as compared with HIV negative patients, duration of cough greater than 9 weeks were more likely risk for treatment failure as compared with cough of less than 5 weeks and Patients with positive smear result at two months were more likely risk for treatment failure as compared with negative smear result patients.

Data availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

All authors (SM, KM, and WA) have substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data; drafting the article and revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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