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# Association of TB treatment initiation delay with clinical severity and risk of transmission among pulmonary tuberculosis patients in Tigray, Northern Ethiopia: Cross-sectional study

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## Abstract

Background Delayed treatment initiation of tuberculosis (TB) increases disease progression and development of complications which may lead to a higher risk of transmission, clinical severity and increased mortality. But, published evidences that investigated the effect of delayed initiation of treatment on clinical severity and risk of transmission of pulmonary tuberculosis patients is scarce in Tigray, Northern Ethiopia.

Objective To investigate the association of delayed treatment initiation of Pulmonary Tuberculosis with clinical severity and risk of transmission. Methods In this cross-sectional study design, a total of 875 newly diagnosed adult pulmonary tuberculosis patients were recruited from 21 health facilities from October 2018 to October 2019. Health facilities were selected by simple random sampling method and the study participants were enrolled consecutively. Data were collected using questionnaires through face-to-face interviews of patients within the first 2 weeks of treatment initiation. Clinical severity was assessed by Bandim tuberculosis score and risk of transmission was assessed by smear positivity or lung cavitations. Data were analyzed using SPSS version 21 software program. Logistic regression analysis was used to ascertain the association of delay with clinical severity and risk of transmission. P-value of less than 0.05 was reported as being statistically significant.

Results Those who had initiating treatment without delay and those who were initiated treatment after a medium delay of 31 to 60 days were significantly associated with decreased clinical score compared to those who initiated treatment after a delay of more than two months. Compared with patients who were initiated treatment within one month, the risk of transmission was greater for delay of 30-60 days and above 60 days. Patients having more than 3 family members have higher risk to transmit TB as compared to those who have maximum of 3 family members. Whereas, patients having at least two rooms and being HIV negative have lower risk to transmit TB compared to their counter patients.

Conclusion Narrowing the gap between initial occurrence of TB symptoms and treatment initiation is the way forward to improve clinical courses of TB patients and to reduce the risk of transmission of TB to other people from these patients.

## Introduction

Delayed treatment initiation of tuberculosis (TB) has a potential to increase the risk of morbidity and mortality because of disease progression and development of complications (1). This rapid disease progression also increase disease transmission within the community and creates favorable condition for TB epidemic (2, 3). Most transmissions occur between the appearance of cough and initiation of treatment as patients become more contagious with prolonged because of highest bacillary numbers on sputum smears (4).

TB delay can be due to patient delay (late presentation with symptoms), health provider delay (failure of the health system to diagnosis tuberculosis) or total treatment delay (delay due to late presentation and

late diagnosis of tuberculosis) (5). In a systematic review of delays in the diagnosis of pulmonary TB, the mean total delay ranged from 25 to 185 days, with patient and health system delay contributing roughly equally (6). Few studies have explored the effects of treatment initiation delay of tuberculosis (TB) patients on the risk of infection among their close contacts, clinical severity, and treatment outcome (7, 8). Studies had also reported the relationship between duration of total delay of smear-positive TB patients and TB infection with a turning point at 30 days after which the risk of TB infection and clinical severity increased significantly (1, 5, 9). There are also contradicting results showing that delay was not related with increased transmission (10, 11).

In Ethiopia where TB is a major public health problem, TB patient's treatment initiation ranges from 60– 120 days (12, 13). The median patient and provider delay were 20–90 days and 6–34 days (12–16), respectively and there is also a fourfold-difference in the time of first contact and diagnosis (12). A prevalence survey in Ethiopia had also indicated that two-thirds of active TB cases were not detected timely (17). In Tigray, northern Ethiopia the median patient delay of smear-positive patients was 90 days, while the overall median health service delay was 9 days (13). Previous studies did not investigate the effect of total delay on the risk of transmission and clinical severity in Ethiopia which would be important for setting interventions to successfully control TB. The aim of the current study was to investigate if the delay in treatment initiation is associated with the risk of transmission and clinical severity.

## Methodology

## Study area

The study was conducted in two zones (Mekelle and Eastern zones) of Tigray Region, Northern Ethiopia. Mekelle is the Regional capital which is located 778km from Addis-Ababa. The region has seven administrative zones: comprising a total of 53 Weredas (districts) and 673 Tibias (sub-districts). The population is above 5.3 million which is about 6% of the total population of Ethiopia and the rate of urbanization is about 20% per year. Economically active age group accounts for about 51.8 % of the total population, 95.5% of the population are Orthodox Christians, 4.1% are Muslims and 0.4% are Catholics (18). There are 712 health posts, 214 health centers and 38 hospitals (1 specialized hospital, 15 general hospitals, 22 primary hospitals) in the region. There are also well-organized community-based structures that support the health system at the grass-root level (health extension workers and women development army). The private health sector also plays a significant role in relieving the burden of the patient load from the public facilities with strong policy support (19, 20). Currently, almost all health facilities are providing directly observed short-course tuberculosis treatment by trained health workers (TB focal persons). The program was introduced in all hospitals, health centers and in most of the health posts for the past years (19).

## Study design, population, period and inclusion

A cross-sectional survey was conducted to investigate the effect of total delay of PTB patients on clinical severity and risk of transmission in health facilities of two zones of Tigray Region, Northern Ethiopia.

Study participants were bacteriologically positive or x-ray positive pulmonary tuberculosis new cases during one year period (i.e. October 2018 to October 2019) in the health facilities of the two zones of the Tigray region. PTB patients whose age is 18 years and above, with no previous history of TB, non-MDR-TB cases and who are diagnosed and initiated treatment within the study settings were included in the study.

### Sample size

In calculating the sample size that enable us to estimate the effect of delay on clinical severity and risk of transmission, we considered 95% confidence interval, 80% power, equal number of exposed and non-exposed (delay was exposer). The calculated sample size for the objective was 850 and we have considered 425 TB patients as non-exposed and the remaining 425 as exposed.

## Recruitment of study participants

Out of the seven zones of the region, two zones (i.e. Eastern zone and Mekelle zone) were selected because of their proximity to the research Institute where the TB culture is performed, and logistical reasons that emanates from the need to have frequent visit to the study sites. Furthermore, the only functional specialized hospital is located in Mekelle. Within the selected zones, there were 26 health centers and 6 hospitals that reported an average monthly cases of 3 and above in the years 2016/2017 and 2017/18 (20). Hence, of the 26 health centers and 6 hospitals, 16 were selected by lottery method and five hospitals were included in the study excluding one hospital as it become for ophthalmological service only. The planned sample size was proportionally allocated to each health facility based on the average number of TB cases reported by the facility in the prior two years. Study participants within each facility were consecutively enrolled until the allocated sample size was attained.

## Data collection

The data collection tool was drafted from previously tested instruments and from reviewed literature (12, 21, 22) and then modified to fit to the context of the research interest. Study participants were identified during their treatment start and invited for consultation and enrolment. The samples for laboratory investigations were collected before treatment initiation. Data were collected on socio-demographic and lifestyle factors, clinical and diagnosis related factors, outcome measurement using Bandim TB score, and measurement of risk of transmission as described below.

**Socio-demographic and lifestyle data:** Background data collected from study participants include gender, age, residence, occupation, marital status, education, family size, income as indebt (poor), income=expense, and saving; smoking history as smoker and non-smoker, and alcohol intake (Yes, No).

**Clinical and diagnostics data:** Clinical examination and interviews of patients were carried out at recruitment or inclusion. During this time Symptoms (respiratory symptoms, constitutional symptoms, or both), smear status (as positive and negative), pulmonary cavity by chest x-ray (yes/no), and patient delay duration by (<30 days, 31–60 days, and >60 days) were collected. Respiratory symptoms included

dyspnea, hemoptysis, cough, or expectoration while constitutional symptoms included malaise, loss of appetite, weight loss, fatigue, fever, chills, chest pain or night sweats.

Smear microscopy of all the study participants was done at three GeneXpert sites of the study area. Three slides per individual were prepared and examined by two laboratory technologists independently. Xray of the study participants was done in five of the study hospitals who have X-ray machine. These results were examined by a medical doctors specialized in radiology

**Bandim TB score:** Clinical severity was assessed by the Bandim TB score (8). The Bandim TB score is a newly developed tool to assess clinical status of patients with TB. Its value is expressed as a numeric index based on cough, hemoptysis, dyspnoea, chest pain, night sweating, anemic conjunctivae, tachycardia, positive lung auscultation, increased temperature, body mass index (BMI) and middle-upper arm circumference (MUAC). A Bandim TB scores  $\geq$ 8 correlates with mortality and lower TB score correlates with favorable outcomes, with cure and treatment success (23, 24). In these studies and in other settings (8) severe TB was defined as TB score  $\geq$ 8, which has a strong predictive capacity for mortality.

Scoring and severity classes: The score was based on 11 clinical variables (i.e. cough, hemoptysis, dyspnoea, chest pain and night sweating, anemic conjunctivae, tachycardia, positive lung auscultation, increased temperature, body mass index (BMI≤16 and BMI≤18) and middle-upper arm circumference (MUAC≤200mm and MUAC≤220mm). Each of the 11 variables is scored 0/1 point; the total score was generated resulting the maximum score of 13 points. For all variables examined and used in the score, missing values were coded as zero. The patients were classified into two severity classes as TB score <8 as having less severe and TB score having ≥8 as having a higher severity class.

### Measurement of risk of transmission and definitions

In this study sputum smear positivity and presence of pulmonary cavity were used as proxy measures for the risk of TB transmission (22, 25, 26). Patients who were smear-positive and had cavitation or smear-positive but had no lung cavitations or smear-negative but had lung cavitation was considered as having risk of transmission. Whereas those patients who were smear-negative and had no lung cavitations were considered as having no risk of transmission. Lung cavitations were defined as the presence of at least one cavity on a chest radiograph taken during the episode of TB (25). Total delay is the time period from the onset of TB symptoms to first start of anti-TB treatment and classified as <30 days, 31-60 days and >60 days.

#### Data quality and management

The questionnaire was pretested before the actual data collection. During sample collection for laboratory investigation, patients were advised to submit thick sputum rather than saliva and the sputum sample was collected as per standards (27). Before smearing, specimens were assessed macroscopically for quality and recorded as purulent with whitish color or bloody. The study numbers or codes were

covered with wrap around stickers before microscopy. As part of internal quality control (IQC), all the positive slides and randomly selected 50% of negative slides were re-examined by a different laboratory technologist.

## Data analysis

Data was computerized and analyzed using SPSS version 21. For categorical variables, univariate analysis was performed by using frequencies and percentages whereas mean or standard deviation was employed for continuous variables. Normality was checked for those continuous variables and the total treatment initiation delay was not normally distributed. Hence, Mann-Whitney U and Kruskal Wali's tests were used to compare median delay across the clinical spectrum of the study participants. Initially bivariate logistic regressions was used to model association of pre-specified characteristics and the odds of delayed treatment initiation and then those variables with p-value of at most 0.2 were entered into the multivariate model. A comparison of the proportion of smear-positive tuberculosis and the presence of a pulmonary cavity (risk of transmission) with the duration of patient delay was modeled using a multivariate logistic regression model. Similarly, the association between clinical severity and the total delay was modeled using multivariate logistic regression model. In both logistic regression models the goodness of fit was checked using Hosmer and Lemeshow test. In all analysis any result with the p-value less than 5% was considered as being statistically significant.

## Result

## Characteristics of the study participants

A total of 875 pulmonary tuberculosis patients were included in this study with a response rate of 100%. The mean ages of the participants were 38.2 (sd=15.1) with a median age of 35 years. From the total respondents, 58.1% were males, 54.5% were from urban areas, 27.2% were farmers, 21.6% were housewives, 18.9% were employed, 10.4% were daily laborer, 11.4% were of students and the remaining 10.5% were Unemployed. In terms of socio-economic status, 37.7% were poor (living in debt), 35.6% had income equal to their expense (had medium income) and the remaining 25.8% earned for covering their expenses and savings. With regard to education, 39.9% were illiterate, 37.1% primary school (1-8 grade), 12.5% secondary school (9-12 grade) and 10.5% completed college and above. Regarding marital status, 55.1% were married, 8% were divorced or widowed and 26.7% were single. Of all the study participants 36.6% were AFB positive, 88.2% were GeneXpert positive and 45.5% had suggestive X-ray (like cavitations in the lung)..

### Self-reported clinical symptoms and other clinical profiles

The major self-reported clinical symptoms were cough (99.2%), and fever (48.6%).Of all the study participants 28.7% and 26.6% had a BMI of below 18 and 16, respectively. Similarly, 39.6% had MUAC below 220mm and 23.5% had MUAC measurement of below 200mm. The clinical score of 61.6% of the study participants was lower than eight (Table 1)

Table 1: self-reported clinical symptoms and other clinical profile of the study participants from selected health facilities of two zones of Tigray, Northern Ethiopia, October 2018 to October 2019

Variable		Number (N=875)	Percent
	Symptoms		
Self reported clinical symptoms	cough	868	99.2
	fever	425	48.6
	chest pain	389	44.5
	weight loss	398	45.5
	haemoptysis	204	23.3
	others <sup>a</sup>	449	51.3
Other clinical profiles	<b>Presence of other chronic diseases<sup>b</sup></b> (excluding HIV)		
	Yes	23	2.6
	No	852	97.4
	HIV status		
	Pos	99	11.3
	Neg	776	88.7
	BMI		
	Normal (>18)	391	44.7
	16-18	251	28.7
	<u>&lt;</u> 16	233	26.6
	MUAC (in MM)		
	Normal (>220)	323	36.9
	200-220	346	39.6
	<u>&lt;</u> 200	206	23.5
	Clinical score		
	<8	445	50.9
	<u>&gt;</u> 8	430	49.1

<sup>a</sup> Sweating, loss of appetite, fatigue, chill, malaise <sup>b</sup> diabetes, arthritis, epilepsy, chronic liver disease, Visceral leishmaniasis, COPD; BMI (Body Mass Index); MUAC (Mid-Upper Arm Circumference)

#### Behavioral And Environmental Factors Of The Study Participants

Significant proportion of the study participants had history of alcohol intake and lives in crowed situation (large family living in small number of rooms) and smoking, respectively. Prevalence of reporting history of smoking and contact with known TB patients is not very large (Table 2).

Table 2 Behavioral and environmental factors of the study participants in selected health facilities of two zones of Tigray, Northern Ethiopia, October 2018 to October 2019

Variable		Number (N = 875)	Percent		
Behavioral and environmental factors	Alcohol use Yes No History of smoking Yes No Previous TB contact Yes No Family size 1-3 >3 Number of rooms <2 $\leq 2$	464 411 89 786 128 747 477 398 358 517	53 47 10.2 89.8 13.3 77.8 54.5 45.5 40.9 59.1		
The effect of total delay on clinical severity and risk of transmission					

#### The Effect Of Total Delay On Clinical Severity

The median total delay of the study participants was 62 days with an inter-quartile range of 16-221 days. Of all the study participants 26.2% came to a health facility and got diagnosis and treatment within 30 days and of those who delayed for more than 60 days, 80% had a clinical score of eight and above. The difference in median total delay was associated with patients having hemoptysis, fever, chest pain, weight loss and others like night sweating or other constitutional symptoms (Kruskal-Wallis test; P < 0.05; Mann-Whitney test; P < 0.05) (see Table 3 ).

#### Table 3

Non-parametric test results of total delay and clinical profile of TB cases in two zones of Tigray, Northern Ethiopia, October 2018 to October 2019

Variable		Total delay	
		Median	P value
Cough	Yes	59	0.518
	No	62	
BMI	<16 16-18 >18	69 55 54	0.105
Hemoptysis	Yes No	147 40	< 0.001
Chest pain	Yes No	74 46	< 0.001
Weight loss	Yes	83	< 0.001
	No	41	
Fever Others	Yes No	74 43	< 0.001
	Yes No	73 43	< 0.001
MUAC (in MM)	< 200 200-2200 > 2200	69 49 61	0.134

In multivariate logistic regression analysis (Table4), those who had not delayed to initiate treatment (AOR = 0.04, 95%Cl 0.04-0.11) and those who were initiated treatment after medium delay or from 30 to 60 days (AOR = 0.17, 95%Cl 0.06-0.15) were significantly associated with decreased clinical score or mild disease compared to those who initiated treatment after delay for more than two months.

#### Table 4

Clinical severity score and associated factors among study participants in selected health facilities of two zones of Tigray, Northern Ethiopia, October 2018 to October 2019

Variables	Clinical sev	verity	COR	AOR
	Mild (< 8)	Severe ( $\geq$ 8)		
Sex Female Male	229 310	138 198	0.68(0.81-1.4) 1.00	0.9(0.64-1.27) 1.00
Age 18-34 35-44 45-54 ≥ 55	139 254 93 42	79 148 67 53	0.58(0.36-0.94) 0.57(0.34-0.95) 0.64(0.38-1.1) 1.00	0.58(0.32-1.03) 0.61(0.33-1.13) 0.55(0.29-1.03) 1.00
Income Indebt Income = expense saving	313 204 122	114 128 94	1.4(1.01-2.05) 1.2(0.85-1.61) 1.00	1.3(0.86-2.03) 0.96(0.65-1.4) 1.00
Delay in days No delay (≤ 30) Medium delay (31-60) Long delay (>60) HIV status Positive Negative	233 112 147 63 476	32 74 277 36 300	0.07(0.05-0.11) 0.09(0.06-0.15) 1.00 0.91(0.59-1.4) 1.00	0.04(0.04-0.11) 0.17(0.06-0.15) 1.00 0.91(0.54-1.54) 1.00
Smoking history Yes No	53 486	36 300	0.91(0.50-1.42) 1.00	1.4(0.81-2.41) 1.00
Alcohol consumption Yes No	300 239	164 172	0.76(0.58–0.99) 1.00	0.84(0.61-1.17) 1.00
COR = crude odds ratio, AOR = adjusted odds ratio,				

#### The effect of delay on the risk of TB transmission

In multivariate logistic regression analysis (Table 5), the risk of transmission was 4.2 fold (95%Cl, 2.82-6.01pv < 0.001) in a group that delayed for 30–60 days and 6.2 fold (95%Cl 4.32–8.83, pv < 0.001) for those who delayed for more than 60 days as compared to patients who were initiated treatment within one month. Similarly having more than 3 family members has 1.6 fold (95%Cl 1.16–2.14) risk of transmission compared to those who have at most three family members. Whereas, having lower number of rooms and being HIV negative were more likely to present with a lower risk of transmission Whereas, having two and above a number of rooms and being HIV negative were less likely to present with a lower risk of transmission by 55% (95%Cl 0.33–0.61) and 43% (95%Cl 0.36–0.91) compared to those who have one room and HIV positive TB patients, respectively.

#### Table 5

Variables	Risk of transmission Odds ratio (OR)			
	Yes	No	Crude OR	Adjusted OR
Sex Male Female	250 171	258 196	1.00 1.1(0.85-1.54)	1.00 0.8(0.59-1.31)
Age 18-34 35-44 45-54 ≥ 55	199 100 79 43	203 118 92 41	1.00 1.1(0.66-1.71) 1.2(0.52-1.7) 1.2(0.72-2.1)	1.00 0.63(.35-1.15) 1.1(0.61-1.92) 1.2(0.68-2.16)
Educational status No formal education Primary education Secondary education College and above	178 161 45 37	178 164 64 55	1.00 0.65(0.41-1.03) 0.69(0.43-1.1) 0.96(0.54-1.68)	1.00 0.4(0.22-0.81) 0.7(0.38-1.3) 0.9(0.52-1.93)
Family size 1-3 >3 Number of rooms <2 ≥2	196 225 212 209	202 252 146 308	1.00 1.07(0.83-1.42) 1.00 0.47(0.36-0.62)	1.00 1.6(1.16-2.14) 1.00 0.45(0.33-0.61)
HIV status Positive Negative	57 364	42 412	1.00 0.65(0.43-0.99)	1.00 0.57(0.36-0.91)
Delay in days No delay (≤ 30) Medium delay (31−60) Long delay (>60)	68 67 286	197 119 138	1.00 3.7(2.56-5.29) 6(4.26-8.46)	1.00 4.2(2.82-6.01) 6.2(4.32-8.83)
OR = odds ratio, * indicates statistically significant variables with P-value less than 0.05				

Risk of tuberculosis transmission among study participants in selected health facilities of two zones of Tigray, Northern Ethiopia, October 2018 to October 2019

## Discussion

Significant association of delayed treatment initiation in the current study with clinical severity is in line with previous studies in Guinea Bissau (21, 28, 29), Ghana (30), Italy (31) and Spain (6). In Guinea Bissau the proportion of clinical severity was higher among patients who had long and very long delays. The study in Ghana (30) indicated that a higher risk of hospitalization for TB patients was associated with longer treatment delay. The studies in Italy and Spain shown that delayed TB patients to initiate treatment had resulted in more severe clinical presentation and extensive disease condition (31, 7). This might be because the bacteria had got time to multiply, which would lead to further infection and this also allows the MTB to continue growing and overwhelm the cells it has infected which would be resulted

in worse clinical symptoms like the presence of a mixture of blood and sputum in the lungs over time (32). This implies the need of interventions targeted to those delayed treatment initiated patients while they are on follow up.

Compared with patients who initiated treatment within one month, the odds of patients presenting with smear-positive tuberculosis and the pulmonary cavity or risk of transmission was higher among patients who delayed treatment initiation beyond a month. This finding is consistent with other studies from the USA (33) and china (22) in which delay was associated with increased smear positivity and lung cavitations. Thus, the presence of a higher proportion of smear positivity and lung cavitations among delayed TB patients indicates that delayed TB patients had increased risk of transmission. This is supported by previous studies (25, 26) which showed that TB patients with smear positivity and lung cavitations. This could be due to a long duration of delay that would affect the number of bacilli in the lung and sputum which leads to a higher reproductive rate of the bacteria. Status and grade of sputum smear, lung cavitations and time of treatment initiation determine the infectiousness of the index cases (34, 35). The number of bacilli found in the sputum of smear-positive patients makes the patients more infectious (4, 36). This implies that policy makers should design the way families of TB patients could be screened regularly.

High proportion of overcrowding described by few numbers of rooms and larger family size with the presence of a higher proportion of smear-positive and lung cavitations among the delayed TB patients would farther intensify TB transmission in the study area. The risk of TB transmission varies depending on the closeness of contact with an infectious TB index case where the increased closeness of contact, poorly ventilated and overcrowded dwellings were associated with the increased transmission (37, 38).

In this study HIV positive patients had a higher rate of risk of transmission compared to HIV negative TB patients which was similar with studies from Kenya (39) and US () but contrary to Tanzania (37). A study in Kenya and US indicated that risk of TB infection was increased with increasing HIV prevalence over time and in Tanzania the TB annual risk of infection remained unchanged despite an increase in HIV prevalence (39, 40). Furthermore; contrary to our findings studies had also indicated lower rate of smear positivity and lung cavitations among HIV positive patients due to the absence of delayed-type hypersensitivity response (41, 42). The observed difference or contrary might be due to all of HIV infected patients participated in this study had started antiretroviral therapy which could improved immune status of the patients and this leads to the increased risk of transmission or lung cavitations.

The findings of the current study should be interpreted with the following limitations. The duration of treatment delay may be influenced by recall bias which may affect the magnitude of patient delay. Effort was made to minimize the bias using different methods. Firstly, we have used local calendars of holidays, special events (marriage, death, birth date and epiphany) which enable the patients to remember the exact date. Second, the study participants were recruited and interviewed immediately after their diagnosis. Furthermore, we do not believe that this bias would affect the association between

sputum smear positivity, having a pulmonary cavity and clinical severity with increasing duration of treatment delay as it would be the same for all patients. Rather than using actual disease transmission measures, we used two proxy measures which could potently bring a worry. However, these two measures have been well associated with TB transmission and have been used by previous studies to measure the risk of transmission (22, 25, 26).

## **Conclusion And Recommendations**

Delayed initiation of TB treatment increases clinical severity and risk of transmission (i.e, increased smear positivity and lung cavitations). Furthermore; the risk of transmission was higher among those who have more than three family members, lower in TB patients having at least two rooms and among HIV negative TB patients. These findings imply that the regional government should work to reduce the long-delayed treatment initiation through strengthening its diagnostic efficiency and implementation of rapid diagnostic tools at the primary health care units. Delayed and non-delayed patients should be clearly identified during treatment initiation for better clinical management during the treatment follow up period. Future study on the same topic should use real transmission measures so that it addresses one of the limitations of the current study.

## Declarations

### Authors' contributions

KT wrote the proposal, participated in data collection and drafted the manuscript. AM, GB, GM and NB commented the proposal with great revisions, participated in data analysis and revised drafts of the manuscript.

### Conflict of interest

There is no financial and non-financial conflict among the authors.

## Funding

No external funder.

### Availability of data and materials

All data is contained in the manuscript and other raw data will be provided to readers upon the request to the corresponding author.

### Consent for publication

Not applicable.

### Ethical consideration

Ethical approval for this study was obtained from Research and Ethical Committee of Addis Ababa University, Aklillu Lemma Institute of Pathobiology. A formal permission letter was also obtained from regional health bureau of Tigray to the selected district health office. Each health facility selected for the study was contacted with permission letter from district health office. Each case diagnosed as TB according to the national guideline was consented in a written form before the interview. To assure confidentiality interview with TB case was held in a private room and the information collected were recorded anonymously.

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