

Adherence to TB Treatment Remains Low During Continuation Phase Among Adult Patients in Northwest Ethiopia

Kassahun Dessie Gashu (✉ kassahundessie@gmail.com)

University of Gondar College of Medicine and Health Sciences <https://orcid.org/0000-0002-7812-3743>

Kassahun Alemu Gelaye

University of Gondar College of Medicine and Health Sciences

Binyam Tilahun

University of Gondar College of Medicine and Health Sciences

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Abstract

Background: Adherence to Tuberculosis (TB) treatment remained a challenge for TB treatment programs. However, paucity of evidences specifically during continuation phase where the treatment is mainly patient-centered. This study aimed to determine the level and determinants of adherence to TB treatment among adult patients during continuation phase.

Methods: We deployed a facility-based cross-sectional study design supplemented with lived experiences and perspectives of focal care providers. The study population included all adult (≥ 18 years) TB patients enrolled in the continuation treatment phase and TB focal care providers (for key-informant interviews). The study included 307 participants from 22 health facilities. Nine TB focal care providers were purposively selected for key-informant interviews. A shorter form, 11-item ARMS (adherence to refill and medication scale) was used for measuring adherence. Binary logistic regression was applied to identify factors associated with patient adherence. The audio data was transcribed, coded and categorized into themes using OpenCode software. The interpretation and analysis were conducted using thematic analysis.

Results: Among 307 participants, 197 (64.2%) [95% CI (58.6% - 69.4%)] were adhere to TB treatment. A multi-variable analysis shown that secondary education (AOR = 4.138, 95% CI; 1.594-10.74); good provider-patient relationship (AOR=1.863, 95% CI; 1.014-3.423); good knowledge on TB treatment (AOR=1.845, 95% CI; 1.012-3.362) and middle family wealth (AOR= 2.646, 95% CI; 1.360-5.148) have shown significant association with adherence. Many patients mentioned that forgetfulness, traveling away from home without pills, and feeling sick were major reasons for non-adherence to TB treatment.

Conclusions: The study indicated that patients' adherence to TB treatment remains low during continuation phase. The patient's education level, knowledge, family wealth, and provider-patient relationship were found positively associated with patient adherence. Forgetfulness, traveling away, and feeling sick were major reasons for non-adherence to TB treatment. Interventional studies are needed on those factors to improve patient adherence to TB treatment during continuation phase.

Introduction

TB treatment requires a prolonged and combined course of antibiotics for 2 months of intensive followed by 4 months continuation phase [1–3]. Stop TB Strategy emphasized on universal access to patient-centered treatment and high-quality care and treatment support as the cornerstone of Directly Observed Treatment, Short-course (DOTS) to improve treatment success rate [3]. Patients' failure to adhere to TB treatment has been a global problem that results in poor health outcomes like, drug resistance, relapse, death, and increased health care costs [4–6].

Adherence to TB treatment is a regular and complete medication intake that gives individual TB patients the best chance of cure and also protects the community from the spread of TB [3]. Whereas, non-adherence to TB treatment has remained a major challenge in Ethiopia [7–12]. Studies in Ethiopia

indicated that forgetfulness [13–16]; poor provider-patient relationship as well as communication [15, 17, 18], poor knowledge towards TB treatment, distance to the health facility, and adverse clinical experiences [9, 13, 15, 19–22] were most commonly reported reasons for non-adherence to Anti-TB treatment.

Evidence showed that continuation phase was a risk factor for non-adherence, however, little is known about factors associated with the problem [13, 15, 23]. Previous studies focused on patients on both intensive and continuation phases, however, the treatment approach for intensive and continuation phases have been quite different. During the intensive phase, patients attend the nearby clinic every morning to swallow their pills under direct observation of care providers for two months. Whereas, a continuation TB treatment phase is a self-managed (patient-centered) approach in which anti-TB pills are daily taken by the patient at home with a weekly pill refilling schedule from the nearby health facility. The national TB treatment guideline suggests assigning treatment supporters including, family, health extension workers for each patient to support the treatment follow-up [23]. However, little is known about the challenges of community-based treatment support systems during the continuation phase. Above all, evidences were limited on factors affecting adherence to TB treatment during continuation phase.

Measuring adherence to TB treatment in a group of study subjects from both intensive and continuation phases could underestimate the problem. Also, it may not be an appropriate approach to identify factors specific to each phase that hinder patient adherence to TB treatment. Most studies involved patients as study population, and care providers' perspectives have gotten little attention. Pill count has been used predominantly for measuring adherence by many studies, despite, its proven limitation of overestimating the level of patient adherence to TB treatment [24].

Therefore, this study aimed to determine level of adherence and associated factors among adult TB patients enrolled in the continuation phase. It also aimed to explore TB focal person's perceptions of patient adherence to TB treatment during the continuation treatment phase.

Methods

Study design

An Institutional based cross-sectional study was conducted with adult TB patients in the continuation treatment phase from March 9 to May 30, 2019. It was supplemented with qualitative data to explore the lived experiences and prospects of the care provider's on patient adherence during the continuation phase.

Study setting and participants

Nationally, TB prevention and control programm is one of the priority services delivered integrated with Leprosy and HIV. The programm relies on supervisory staff at National, Regional, Zonal, Sub-cities, City Administration, Woreda, and treatment and Hospitals, Health Centres, and Health Post levels with staff equipped with expertise and skills. According to the national TB and Leprosy Control Programm (TLCP)

guideline, the functions of TB control program involve the community, patient, and management programmes. The community programme function incorporates creating public awareness, case finding and referral, supporting treatment adherence, and tracking defaulters mainly undertaken by Health Extension Workers and community volunteers. Patient management function focused on also engaged in case finding, case management, education, counseling, and controlling the transmission of the disease. The management programme function consists of planning, developing strategic policy and guidelines, training, coordination, and Advocacy, Communication and Social Mobilization (ACSM) [25]. In each health facility, a TB clinic has been established with at least one trained focal care provider to regularly manage cases and follow their treatment.

The study was conducted in 9 districts of Central Gondar Zone including Gondar town administration in Northwestern Ethiopia. The districts include Gondar Zuria, Tach Armachio, Wegera, East Dembia, West Belesa, Takusa, East Belesa, Alefa, and Gondar town administration. The study area consists of 74 functional public health facilities (Health centers and Hospitals) serving an estimated more than 2.9 million population overall in the area.

The study population included all adult (≥ 18 years) TB patients enrolled in the continuation treatment phase as eligible participants. Patients with Multi-drug-resistant Tuberculosis (MDR-TB) and Extensively Drug-resistant Tuberculosis (XDR TB) were not included in the study. TB focal care providers were involved in the key-informant interviews.

Sample size and sampling techniques

We calculated the sample size using a single population proportion formula with assumptions, including, proportion of patients adherent to TB medications ($P = 66\%$) on the continuation phase [15]; margin of error ($d = 5\%$), and a design effect of 1.5 were used to calculate the sample size. Considering the finite population and 10% non-response rate, the final sample size was 331 TB patients. A total of 22 (30%) health facilities (19 Health Center and 3 Hospitals) were selected from 9 districts. A total of 22 (30%) health facilities (19 Health Center and 3 Hospitals) were selected from 9 district. The selection of facilities involved both urban and rural (random selection of at least one) facilities depending on the size of the districts. All eligible participants were included in the study in open cohort during the study period. Nine TB focal care providers were involved for key-informant interview from nine different health facilities. We selected each key-informants purposively from each districts.

Data collection tools and procedures

In this study, socio-demographic characteristics, disease characteristics, TB treatment-related knowledge, and attitude, provider-patient relationship, and family wealth quantiles were included as predictor variables. All the assessment tools including, the 8-item TB treatment-related knowledge assessment questions [12, 15, 26–28], a 4-item attitude questions [15, 17, 26] and a 6-item provider-patient relationship [15] questions were adapted from literatures. The family wealth index assessment tool was constructed from multiple household assets, services, and facilities [29].

The current study deployed the Adherence to Refill and Medication Scale (ARMS) to measure patient adherence to TB treatment during the continuation phase. The original ARMS consists of 12 items including two subscales, an 8-item medication-taking subscale, and a 4-item refill subscale. Each item was structured as a Likert scale with responses of “none,” “some,” “most,” or “all” of the time, which were given values from 1 to 4 [30]. For this study, a shorter form of ARMS (11-item) was implemented to assess the dependent variable (adherence to TB medication and refilling). One of the items, “How often do you forget to take your medicine when you are supposed to take it more than once a day?” was not relevant to TB medication. Since TB pills often are taken once a day as it was used in a similar study in Diabetes mellitus [31].

A structured interviewer-administered questionnaire was translated into Amharic (local language) and piloted before data collection. The internal consistency of the tool was approaching well with Cronbach’s α value 0.769, according to the cut of value [32]. We trained and employed six data collectors and two supervisors. For the qualitative data, a semi-structured key informant interview guide was used to explore the existing provider-patient relationship and support during the continuation treatment phase. Participants were asked mainly about their opinion on which TB treatment phase is the risk for non-adherence? How non-adherence to TB treatment was high on the specified phase? How was the communication and relationship between patients and care providers? And how effective was the community-based treatment support system?

Data analysis

We used a Principal Component Analysis (PCA) technique to compute the family wealth index quantile separately for urban and rural depending on assets and services specific to the urban and rural population [29].

Adherence to TB treatment was measured the 11-item ARMS values range from 1= “none of the time” to 4=“all of the time”. One item was reverse coded then the overall adherence score ranges from 11–44. The lower scores indicate better adherence and the higher score represents a higher level of non-adherence, items were asking about how frequently failed to adhere to specific elements [30]. The scales were further transformed into dichotomous outcomes using the recommended classification (scored 11 as adhered and > 11 as non-adhered) [30, 31]. We used the Variance Inflation Factor (VIF) to check the multicollinearity effect among predictor variables [33]. We conducted a single-level analysis after assessing the nature of the data that did not fit to multilevel analysis for the reason of lack of substantial clustering effect with (ICC = 0.0179). A binary logistic regression analysis was deployed to identify factors that are associated with adherence to TB treatment during the continuation phase using STATA version 14 software. The COR and AOR with 95% CI and p value < 0.05 were used for determining statistical significance of the association between predictor and outcome variables.

For the qualitative data analysis, we transcribed the audio data into the Amharic language by experts in the field and translated into English by fluent speakers. After familiarization with the transcript, we assigned codes inductively and deductively and categorized into themes. We examine patterns,

relationships, contradictory responses, and gaps in understanding in each theme. Quotes were selected and presented for norms of the participants' shared perceptions.

Results

Socio-demographic and economic characteristics of participants

In this study, a total of 307 study participants (92% response rate) were interviewed. Of these participants, the majority 110 (35.8%) of them were aged between 35 and 44 years. The median age of the participants was 29.0 years with a minimum of 18 and a maximum of 84 years. More than half of the participants 178 (58.0%) were males. Regarding marital status, 142 (46.3%) of the participants were single. The majority, 285 (92.8%) of them were Orthodox Christian followers. Of the total participants, 220 (71.7%) were urban residents. Among the participants, 101 (32.9%) of them could not read and write. Only 40 (13%) of the participants have a higher level of education. Among all married participants, 47 (39.5%) of their partners had no education at all. The family asset was calculated in quantiles, and the finding has shown that 62 (20.2%) and 61 (19.9%) fall in lowest and highest wealth quantiles respectively. About 122 (39.7%) of the participants did not have a mobile phone at all (Table 1).

Table 1
Socio-demographic and economic characteristics of participants, northwest Ethiopia (n = 307)

Characteristics	n (%)
Age	
Below 25	84 (27.4)
25–34	110 (35.8)
35–44	60 (19.5)
45+	53 (17.3)
Sex	
Male	178 (58.0)
Female	129 (42.0)
Marital status	
Single	142 (46.3)
Married	119 (38.8)
Divorced	34 (11.1)
Widowed	12 (3.9)
Religion	
Orthodox	285 (92.8)
Muslim	20 (6.5)
Others	2 (.7)
Residence	
Urban	220 (71.7)
Rural	87 (28.3)
Educational level	
Can't read and write	101 (32.9)
Informally educated	37 (12.1)
Primary	73 (23.8)
Secondary	56 (18.2)
Higher	40 (13.0)

Characteristics	n (%)
Partner's educational level	
Can't read and write	47 (39.5)
Informally educated	10 (8.4)
Primary	33 (27.7)
Secondary	17 (14.3)
Higher	12 (10.1)
Type of facility enrolled for treatment	
Health Center	267 (86.9)
Hospital	40 (13.1)
Wealth quantile	
Lowest	62 (20.2)
Second	61 (19.9)
Middle	62 (20.2)
Fourth	61 (19.9)
Highest	61 (19.9)
Own a mobile phone	
Yes, smartphone	55 (17.9)
Yes, basic phone	130 (42.4)
Not at all	122 (39.7)

In the qualitative interview, nine TB focal care providers have participated from seven Health Centers and two Hospitals. Of the total participants, 6 of them were males. The age of the participants ranges from 26 to 40 years. Only three of the participants had a first degree and above education and the rest were diploma holders. Participants' experience as TB focal person ranges from 6 months to 7 years.

Clinical characteristics of participants

Among all study participants, 187 (60.9%) of them were infected with pulmonary TB and 120 (39.1%) were with extra pulmonary patients. Twenty (6.8%) of the participants were relapsing cases. Thirteen (4.2) participants did not disclose their TB status to their family members. Twenty-six (8.5%) of the participants were TB/HIV co-infected (Table 2).

Table 2
Clinical characteristics of study participants,
northwest Ethiopia (n = 307)

Characteristics	Number (%)
Type of TB	
Sputum positive pulmonary TB	126 (41.0)
Sputum negative pulmonary TB	61 (19.9)
Extra pulmonary TB	120 (39.1)
Treatment category	
New	287 (93.5)
Relapse	20 (6.5)
Disclosed TB status to family	
Yes	294 (95.8)
No	13 (4.2)
TB/HIV co-infected	
Yes	26 (8.5)
No	281 (91.5)
Adhered to treatment	
yes	197 (64.2)
No	110 (35.8)

Adherence to TB treatment

The overall score of ARMS ranged from 11 to 44 with a median value of 11. We used the dichotomous classification after checking the data was not normally distributed. The finding indicated that 197 (64.2%) with [95% CI (58.6% – 69.4%)] were found to be adhered and 110 (35.8%) with [95% CI (30.6% – 41.4%)] were non-adhered to TB treatment (Table 2).

Focal TB care providers were asked about “which treatment phase has a higher risk of non-adherence to the treatment?” Many focal care providers agreed that non-adherence to TB treatment worsens during the continuation phase as compared with the intensive phase, where patients take their daily pills at the clinic directly observed by the care provider. A 23 years male TB focal person replied that:

...when patients enrolled in the continuation phase, they often get reluctant to their pills. Let alone daily medication, they even miss weekly refilling appointments, however, during the intensive phase, they come to take their pills on time

Determinants of adherence to TB treatment during continuation phase

The bi-variable binary logistic regression analysis showed that patient age, educational level, distance to the health facility, provider-patient relationship, patient knowledge on TB treatment, and family wealth index were associated with adherence to TB treatment during the continuation phase.

Whereas, in the multivariable binary logistic regression analysis, patients' educational level, provider-patient relationship, patient knowledge on TB treatment, and family wealth index were associated with the outcome variable. Secondary level educated patients were four times more likely to adhere to TB treatment as compared to non-educated patients (AOR = 4.138, 95% CI; 1.594–10.74). Similarly, patients who reported good provider-patient relationships were 2 times more likely to adhere to the treatment than their counterparts, with (AOR = 1.863, 95% CI; 1.014–3.423). Those who have good knowledge of TB treatment were also more likely to adhere (AOR = 1.845, 95% CI; 1.012–3.362). Patients with middle family wealth were 3 times more likely to adhere than patients with poor family wealth (AOR = 2.646, 95% CI; 1.360–5.148) (Table 3).

Table 3

Factors associated with adherence to TB medication and pill refilling during continuation phase in Northwest Ethiopia (n = 307)

Variables	Adherent		COR(95%CI)	AOR(95%CI)
	Yes	No		
Patient age				
24 years and below	58	26	2.317 (1.139–4.712)*	1.533 (.642-3.661)
25–34 years	81	29	2.901 (1.461–5.757)*	2.123 (.937-4.813)
35–44 years	32	28	1.187 (.566-2.487)	.879 (.378-2.043)
45+ years	26	27	1	1
Sex				
Male	113	65	1	1
Female	84	45	1.074 (.669-1.724)	1.251 (.707-2.214)
Residence				
Urban	146	74	1.393 (.836 – 2.320)	.764 (.374-1.559)
Rural	51	36	1	1
Educational level				
No education	53	48	1	1
Informal education	20	17	1.065 (.501-2.268)	.729 (.299-1.773)
Primary	45	28	1.456 (.789-2.685)	1.057 (.501-2.231)
Secondary	46	10	4.166 (1.895–9.157)*	4.138 (1.594–10.74)*
Higher	33	7	4.27 (1.728–10.55)*	2.795 (.970-8.052)
Distance to the health facility				
Less than 5 km	72	156	2.708 (1.206–6.081)*	2.275 (.877-5.903)
5–10 km	23	29	1.576 (.618-4.018)*	1.672 (.589-4.746)
Greater than 10 km	15	12	1	1
Treatment supporter assigned				
Yes	74	123	1	1
No	36	73	1.22 (.746-1.996)	1.375 (.769-2.457)
Disclosed TB status to family				

Variables	Adherent		COR(95%CI)	AOR(95%CI)
	Yes	No		
Yes	105	189	1.125 (.359-3.527)	.744 (.191-2.902)
No	5	8	1	1
Provider-patient relationship				
Good	112	45	1.903 (1.186–3.055)*	1.863 (1.014–3.423)*
Poor	85	65	1	1
Knowledge on TB treatment				
Good	157	72	2.072 (1.226-3.5)*	1.845 (1.012–3.362)*
Poor	40	38	1	1
Attitude on TB treatment				
Favorable	121	59	1.376 (.858-2.206)	1.272 (.702-2.305)
Unfavorable	76	51	1	
Wealth index				
Poor	54	49	1	1
Middle	71	31	2.078 (1.173–3.683)*	2.646 (1.360–5.148)*
Rich	72	30	2.178 (1.225–3.871)*	1.949 (.957-3.968)

*p-value less than 0.05

Patients who were non-adherent to their TB medication were asked for their reasons for failure to treatment adherence. More than half 58% (n = 110, non-adherent participants) reported forgetfulness to daily medication, 17.3% reported traveling away from home without pills, 8.2% and 5.5% were due to feeling sick and fearing side effects of the drugs, respectively (Fig. 1).

TB focal care providers were also asked for their perspectives about contributing factors for non-adherence to TB treatment. Poor communication and relationship with their patients, transportation and related costs for pill refilling, relapsing of the disease, political unrest, and poor treatment support at the community were found major contributing factors for non-adherence to TB treatment during the continuation phase.

All respondents agreed that good communication and relationship was essential for patient adherence to TB medications. However, about half (4/9) of participants reported that their communication with

patients decline as the patients shifted from the intensive phase (facility-based treatment) to the continuation phase. A 23 years old, male participant also added that:

During the continuation phase, we do not have daily contact with patients as we do on intensive phase. Even, weekly attendance was not easy. Some patients did not come, they send their supporter/family member to the clinic for refilling, and they were busy with family matters, social events like a funeral.

In the key-informant interview, the majority of TB focal providers also exemplified that patients with low income tend to miss and/or interrupt refilling due to transportation and related costs. Besides, relapse cases tend to default treatments. A 39 years female focal provider replied that

"TB patients on continuation phase often miss refilling and from my experience, their reasons are mainly related to transportation cost and unintended social events".

Participants also mentioned that relapsing cases tend to lost-to-follow-up. A 37 years female focal provider added that:

"This year alone we lost two patients due to relapse of the case [TB]. One female insisted not to take the pills anymore and decided to go to Monastery. Similarly, one male patient lost from treatment follow-up..."

Political unrest and security problems were among the challenges for the patient, the care providers, and central drug suppliers. A 40 years male focal provider replied that

Our community was victimized with frequent political turmoil and security problems which results in lost-to-follow due to massive displacement, migration of care-providers, and interruption of drug supply from the center.

Respondents were also asked their opinion on whether the assigned treatment supporters were helpful during the continuation treatment phase. Many participants replied that they were not helpful as intended, and (2/9) reported as helpful. The problem begins with assigning treatment supporters. A 32 years old participant replied that:

"During assigning treatment supporters, patients often choose educated relatives without considering the distance away from their home: mostly, they choose their relatives in urban while the patient living in rural."

In addition, the commitment of treatment supporters was confronted by their income level and their prior commitments as reported by the respondents. A 23 years old, male participant mentioned that:

Treatment supporters very rarely accompany patients during refilling, they mention transportation cost, own family, and social commitments.

A 40 years male TB focal provider also added that:

During the continuation phase, we assign treatment supporters but in practice, most did not follow and most focal providers lack skills to influence patients to take their pills at home

Discussion

This study identified that adherence to TB treatment was low. Patients' educational level, knowledge, family wealth, and provider-patient relationship were positively associated with adherence to TB treatment. From the care providers' perspectives, poor communication and relationship with patients, transportation and related costs for refilling, relapsing of the disease, political unrest, and poor treatment support at the community were major underlying factors for non-adherence to TB treatment during the continuation phase.

The study has shown that patients' adherence to Tb treatment was lower as compared to the pooled estimate of the national level of adherence to TB treatment [16]. It also lower as compared with other studies conducted in different parts of Ethiopia including in Arba Minch town [9], in Sidama [34], in Addis Ababa [10], in Alamata [14] and Gondar town [15]. The discrepancy could be due to the subjects in which the current study included only from the continuation phase and other studies involved both intensive and continuation phases. And evidences indicated that non-adherence to Tb treatment worsens during the continuation phase [13, 15, 23]. In this study, TB focal care providers also have shown their agreement that the continuation phase was a risk for patients' failure to adhere to TB treatment. Besides, we used a composite items to measure adherence to Tb treatment. While, previous studies used pill count as a measure of adherence that often shown overestimation of patient adherence to TB medications [24].

This study has shown that educational level was positively associated with adherence to TB treatment. The finding was in line with a study conducted in Equatorial Guinea [35] and Nepal [36] indicated that patient literacy was a significant factor for non-adherence to TB treatment. The current study has shown that patients with the middle family wealth index were about 3 times more likely to adhere to their TB medication as compared to patients in poor family wealth index. Patients with rich family wealth have also shown higher adherence as compared to patients in the poor category, however, it was marginally insignificant. The finding was in line with a study in Nepal [36]. Our qualitative finding also supported that transportation and related expenses during traveling for pill refilling were among the challenges that directly influence their adherence to the treatment.

Similarly, a good provider-patient relationship was also significantly associated with patient adherence during the continuation phase. The finding was consistent with previous studies which reported that provider-patient relationship was associated with adherence to TB treatment in Ethiopia [15, 17, 18]. Our qualitative analysis also revealed that care providers did not have a strong relationship with their patients. Provider-patient relationship is considered as the core element of ethical principles of medicine that establish trust and motivation to engage patients on their treatment. The relationship could be a driver of good clinical outcomes. It promotes desired treatment results and also prevents adverse treatment outcomes [37, 38].

Patients with good knowledge related to TB treatment were about 2 times more likely to adhere to their medication and refilling. Similarly, studies in Ethiopia [12, 15] and China [28] also reported that poor knowledge about TB and anti-TB therapy was significantly associated with non-adherence. It implies that the provision of TB treatment-related information is an essential component of the service.

Generally, this study shown non-adherence to TB treatment was a problem in the continuation phase. It needs to conduct interventional studies with innovative strategies and evaluate its effectiveness in improving patient adherence to TB treatment during the continuation phase.

Limitation of the study

We determined the level of adherence using a patient self-report that often underestimate the problem due to recall and social desirability biases. Our study participants were enrolled from public health centres and hospitals. We did not address patients at private health facilities and health post levels. This could affect the generalizability of the study findings to the wider context.

Conclusion

TB treatment adherence was low during the continuation phase. Patients' educational level, family wealth, provider-patient relationship, and patient knowledge related to TB treatment were positively associated with patient adherence. Innovative strategies needed to be scientifically evaluated and implemented to support and improve adherence to TB treatment during the continuation phase.

Abbreviations

ACSM

Advocacy, Communication and Social Mobilization

ARMS

Adherence to Refill and Medication Scale

DOTS

Directly Observed Treatment, Short-course

HIV

Human Immunodeficiency Virus

MDR-TB

Multi-drug-resistant Tuberculosis

PCA

Principal Component Analysis

TB

Tuberculosis

TLCP

TB and Leprosy Control Programm

Declarations

Ethical approval and consent to participate

Ethical clearance was obtained from the Institutional Review Board (IRB) of the University of Gondar with an approval number O/V/P/RCS/05/1077/2018. Written informed consent was obtained from study participants after discussing with participants' rights and responsibilities, possible harms, and benefits of participating in the study. The study did not use personal identifiers during data collection, storage, and dissemination.

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declared that there is no competing interest.

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Authors' contributions

All authors made a substantial contribution to the conception, design, and write-up of the protocol. All authors read and approved the final manuscript.

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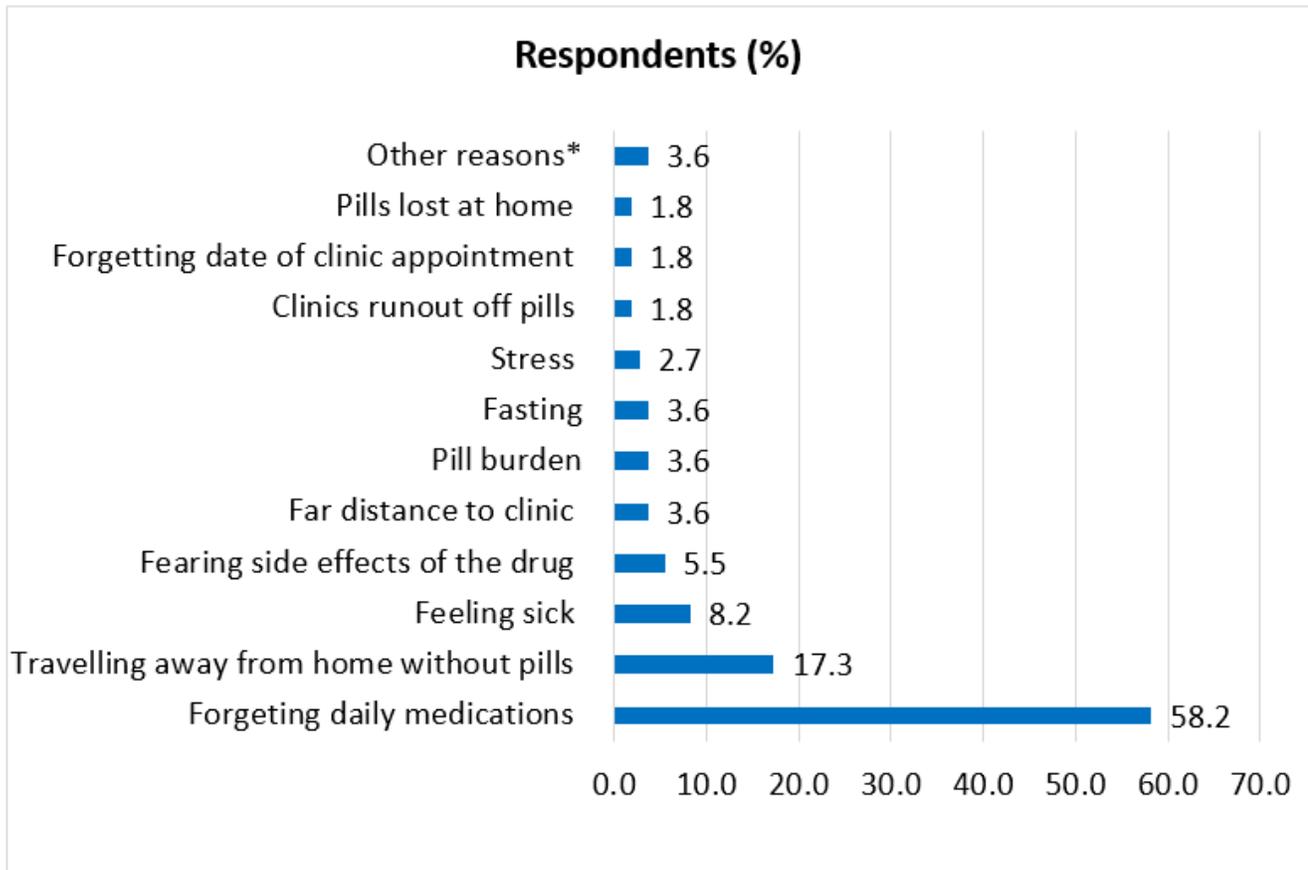
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Figures



**Other reasons include: perceiving as completed, feeling recovered, clinics closed and rodents spoil pills at home*

Figure 1

Patients' reasons for non-adherence to TB treatment during continuation phase (n=110)