

Non-Adherence to Anti-TB Drugs and Its Predictors among TB/HIV Co-Infected Patients in Mekelle, Ethiopia

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Abstract

Background: Non-adherence to tuberculosis (TB) treatment in TB/human immunodeficiency virus (HIV) co-infected patients greatly affect treatment outcome. It can lead to an increased risk of drug resistance which is difficult to treat and contribute to increased mortality. Therefore, this study was aimed to determine the prevalence and factors associated with non-adherence to anti-TB drugs among TB/HIV co-infected patients in Mekelle, Ethiopia.

Methods: A health institution based cross-sectional study was conducted in Mekelle from March to April 2013. Consecutive sampling was used to select respondents. Data were collected with the help of a structured questionnaire and analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0 software.

Results: The prevalence of non-adherence to anti-TB medications among TB/HIV co-infected patients was 55.8% in a 5-day period prior to the interview. From logistic regression models, patients who had no caregivers (Adjusted Odds Ratio (AOR)=3.73, 95% CI=1.15-12.11) and people to remind them to take their medications (AOR=11.15, 95% CI=1.66-74.91) were more likely to be non-adherent. The major reasons cited for missing medicines were forgetting to take medications, felt sick when take the medications and far away from health facilities.

Conclusions: The prevalence of non-adherence was high. TB/HIV co-infected patients should be targeted with interventions to improve medication adherence, particularly by supporting them to continue their treatment.

Keywords: Co-infection; Factors; Non-adherence; Tuberculosis

Introduction

Tuberculosis (TB) remains an important problem in human immunodeficiency virus (HIV) infected patients worldwide. TB is the most common opportunistic infection among HIV-infected individuals, and co-infected individuals are at high risk of death. TB and HIV co-infections have added to the disease burden [1]. According to the World Health Organization (WHO) Global TB Report 2013, 1.1 million of the 8.6 million people who developed TB worldwide were HIV-positive; 75% of these HIV-positive TB cases were in the African Region. Ethiopia is one of the highly affected countries by the TB/HIV co-epidemic. WHO Global Report 2013 estimates that 10% of TB patients are HIV positive in Ethiopia [2].

HIV-associated TB patients take in increased morbidity and mortality due to TB and other HIV related diseases. The appropriate management of HIV-associated TB remains extremely challenging due to diagnostic difficulties, adherence concerns, the overlapping drug side effects, drug-drug interactions, and the occurrence of immune reconstitution inflammatory syndrome. Concomitant treatment also leads to a higher pill burden [3]. This may lead to poorer adherence among these patients. Poor adherence to anti-TB drugs can lead to an increased risk of drug resistance, including multi-drug and extensively drug resistant TB, which is difficult to treat and contribute to increased mortality [1]. Adherence to anti-TB treatment, a major determinant of outcome, is of special concern in HIV positive patients [4]. Patients with TB are expected to have adherence levels greater than 90% in order to facilitate a cure [5].

The present study was therefore conducted to determine the prevalence of non-adherence to anti-TB drugs among TB/HIV co-infected patients under treatment of TB in Mekelle, Ethiopia and to identify determining factors associated with these events. Understanding the epidemiology and determinants of non-adherence is important for program planning and targeting resources to increase

adherence among such vulnerable population.

Methods and Materials**Study design and area**

A cross-sectional study was conducted in Mekelle, Tigray region, Ethiopia from March to April 2013. Two public hospitals and three health centres were selected among three public hospitals and nine health centres found in Mekelle zone based on the proportion of people come to get their TB and/or HIV treatment.

Study population and sample

All TB/HIV co-infected patients aged 18 years and older, and patients who had been on concomitant treatment for both TB and HIV were included in this study. TB/HIV co-infected patients who were less than eighteen years old, not receiving concomitant ART, unwilling to participate and not mentally fit were excluded. Consecutive sampling was employed to select respondents who came to refill at the time of data collection. The total study participants fulfilled the criteria was 120. The study was approved by the Health Research Ethics Review Committee of College of Health Sciences, Mekelle University. Prior to data collection, the purpose of the study was explained to the study

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Received November 18, 2014; Accepted December 16, 2014; Published December 19, 2014

Citation: Eticha T, Kassa E (2014) Non-Adherence to Anti-TB Drugs and Its Predictors among TB/HIV Co-Infected Patients in Mekelle, Ethiopia. J Bioanal Biomed 6: 061-064. doi:[10.4172/1948-593X.1000113](https://doi.org/10.4172/1948-593X.1000113)

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population, confidentiality was ensured and written consent was obtained.

Data collection methods and analysis

A structured questionnaire to assess non-adherence to anti-TB drugs and its determinants was developed in English, then translated into the local language (Tigrigna) and back into English to check the accuracy. The standardized questionnaire was pre-tested before the actual data collection. The questionnaire consisted of three parts: socio-demographic information, factors related to non-adherence (patient factors, program factors, social support and drug related factors) and reasons of missing doses. The patients were interviewed based on the questionnaire. Non-adherence was measured using patients' self-reports of how they had been taking their drugs in the three and five days preceding the interview. Adherence was calculated as the percentage of prescribed drugs over the three and five day periods that a patient took. Patients who reported a missing more than 10% (had taken less than 90%) of the prescribed medicines were considered to be non-adherent.

Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0. Categorical data were summarized as frequencies and percentages. Logistic regression analysis was performed to determine potential predictors of non-adherence to anti-TB drugs. Statistical significance was set at $p < 0.05$.

Results

Socio-demographic characteristics of study participants

The study sample consisted of 66(55.0%) men and 54(45.0%) women. The overall age of the respondents ranged from 18 to 69 years with the mean age of 34.6 ± 11.3 SD years and about 42% of them were above 35 years. The majority (40.8%) of the respondents were employed and 64.2% had a monthly income of 500-1000 Ethiopian Birr (ETB) (exchange rate: 1 USD=18.8 ETB). More than a quarter 35 (29.2%) of the study participants could read and write; while 30(25.0%) of them were illiterate (Table 1).

The Prevalence of non-adherence to Anti-TB treatment

This study found a prevalence of non-adherence to anti-TB medications among TB/HIV co-infected patients was 53.3% in three days and 55.8% in the five days prior to the interview. More than half (59.7%) of the non-adherent patients in the five days were males.

Factors associated with non-adherence to Anti-TB treatment

Socio-demographic factors were found to not be associated with adherence (Tables 1). On the other hand, patients who had no caregivers were more likely to be non-adherent to anti-TB drugs compared to those who had (AOR=3.73, 95% CI=1.15-12.11). Similarly, patients who had no reminders to take their medications were more likely to be non-adherent compared to those who had someone to remind them all the time (AOR=11.15, 95% CI=1.66-74.91) (Table 2).

Reasons for non-adherence to Anti TB treatment

Various reasons for non-adherence to anti-TB treatment are listed in (Table 3). The most common reasons cited by the study participants for missing doses were forgetting to take medications (67.2%), felt sick when take the medications (49.3%) and far away from health facilities (37.3%).

Characteristics	n (%)	Non-adherence, n (%)		AOR (95% CI) [¶]	p value
		Yes	No		
Gender					
Male	66 (55.0)	40 (60.6)	26 (39.4)	1	
Female	54 (45.0)	27 (50.0)	27 (50.0)	0.53 (0.24, 1.21)	0.131
Age					
<25	25 (20.8)	13 (52.0)	12 (48.0)	1	
25-35	45 (37.5)	26 (57.8)	19 (42.2)	1.12 (0.34, 3.68)	0.852
>35	50 (41.7)	28 (56.0)	22 (44.0)	0.74 (0.19, 2.86)	0.666
Marital status					
Unmarried	46 (38.3)	26 (56.5)	20 (43.5)	1	
Married	41 (34.2)	24 (58.5)	17 (41.5)	0.80 (0.28, 2.29)	0.677
Divorced	19 (15.8)	10 (52.6)	9 (47.4)	0.56 (0.16, 1.96)	0.363
Separated	14 (11.7)	7 (50.0)	7 (50.0)	0.50 (0.13, 2.01)	0.332
Education status					
Illiterate	30 (25.0)	17 (56.7)	13 (43.3)	1	
Read & write	35 (29.2)	22 (62.9)	13 (37.5)	1.16 (0.41, 3.29)	0.776
Primary	17 (14.2)	12 (70.6)	5 (29.4)	1.59 (0.41, 6.16)	0.504
Secondary	22 (18.3)	10 (45.5)	12 (54.5)	0.58 (0.16, 2.07)	0.400
Tertiary	16 (13.3)	6 (37.5)	10 (62.5)	0.46 (0.11, 1.91)	0.284
Employment status					
Student	29 (24.2)	13 (42.9)	16 (57.1)	1	
Employed	49 (40.8)	26 (53.1)	23 (46.9)	2.03 (0.63, 6.57)	0.239
Unemployed	42 (35.0)	28 (66.7)	14 (33.3)	2.86 (0.87, 9.40)	0.084
Monthly income in ETB*					
<500	77 (64.2)	46 (59.7)	31 (40.3)	1	
500-1000	31 (25.8)	15 (48.4)	16 (51.6)	0.66 (0.24, 1.83)	0.421
>1000	12 (10.0)	6 (50.0)	6 (50.0)	0.90 (0.18, 4.23)	0.888

[¶]AOR—Adjusted Odds Ratio, CI—Confidence Interval, * Exchange rate: 1 USD=18.8 Ethiopian Birr (ETB).

Table 1: Socio-demographic characteristics of TB/HIV co-infected patients and non-adherence.

Discussion

In the present work, 53.3% and 55.8% of patients among the entire sample were non-adherent to the anti-TB therapy in the three and five days before the interview, respectively. This finding was markedly higher than the levels of non-adherence reported from other studies conducted in Uganda (25%) [6], Northern and Southern Ethiopia (10%, 13.6%, 20.8%) [7,8]. However, it was similar to the study conducted in India, where the prevalence of non-adherence was 50% [9]. The possible explanation for greater non-adherence in this study might be attributable to the differences in sample size, study populations and period of time over which adherence was assessed. In this study, only TB/HIV co-infected patients who were receiving treatment for both infections were included. The study conducted in Northern Ethiopia included both HIV-positive and HIV-negative patients. Although the study participants in the survey conducted in Mbarara Hospital, Uganda were TB/HIV co-infected patients, those who were not on antiretroviral treatment were included. TB/HIV co-infected patients, particularly those who are taking concomitant treatment for both infections, are much more likely to be non-adherent for multiple reasons. Moreover, this fluctuation could also be referable to the duration in which the adherence was assessed. In the latter studies, adherence was calculated over one month and it was also over the last four days in the case of Northern Ethiopia. However, interventions and greater attention to patients who reported their non-adherence are needed in order to improve treatment adherence. This level of non-adherence is very concerning since the likelihood of development of multi-drug and extensively drug resistant TB is increased. This will

Characteristics	Non-adherence, n (%)		AOR (95% CI)	p value
	Yes	No		
Patients' feeling about TB				
Feel ashamed	34 (63.0)	20 (37.0)	2.72 (0.76, 9.70)	0.124
Don't feel ashamed	33 (50.0)	33 (50.0)	1	
Knowledge of TB spread				
Have some knowledge	59 (55.7)	47 (44.3)	0.34 (0.07, 1.71)	0.192
Don't know	8 (57.1)	6 (42.9)	1	
Alcohol consumption				
Yes	43 (58.9)	30 (41.1)	1.00 (0.32, 3.13)	0.998
No	24 (51.1)	23 (48.9)	1	
Smoking				
Yes	27 (67.5)	13 (32.5)	1.36 (0.38, 4.80)	0.637
No	40 (50.0)	40 (50.0)	1	
Who gives care to patient				
Self	45 (63.4)	26 (36.6)	3.73 (1.15, 12.11)	0.028
Others	22 (44.9)	27 (55.1)	1	
Has someone to remind to take medicine				
All the time	17 (40.5)	25 (59.9)	1	
Sometimes	25 (43.9)	32 (56.1)	1.76 (0.43, 7.20)	0.430
Not at all	11 (52.4)	10 (47.6)	11.15 (1.66, 74.91)	0.013
Cost of travel in ETB				
≤10	40 (52.6)	36 (47.4)	0.86 (0.24, 3.12)	0.819
>10	27 (61.4)	17 (38.6)	1	
Long waiting time				
Yes	29 (52.7)	26 (47.3)	0.46 (0.15, 1.44)	0.182
No	38 (58.5)	27 (41.5)	1	
Feel distance is long				
Yes	37 (49.3)	38 (50.7)	0.36 (0.10, 1.26)	0.110
No	30 (66.7)	15 (33.3)	1	
Relation with health provider				
Excellent	4 (44.4)	5 (55.6)	0.24 (0.02, 2.86)	0.258
Very good	15 (60.0)	10 (40.0)	1.90 (0.51, 7.04)	0.337
Good	48 (55.8)	38 (44.2)	1	
High drug burden				
Yes	56 (53.3)	49 (46.7)	0.25 (0.04, 1.44)	0.121
No	11 (73.3)	4 (26.7)	1	
Any side effect				
Yes	25 (65.8)	31 (34.2)	2.08 (0.62, 6.95)	0.236
No	42 (51.2)	40 (48.8)	1	
Treatment phase				
Intensive	49 (60.5)	32 (39.5)	2.36 (0.77, 7.27)	0.135
Continuous	18 (46.2)	21 (53.8)	1	

Table 2: Patient factors, program factors, drug factors and non-adherence.

Reason	Frequency (%)
Forget it	45 (67.2)
Felt sick when take the medication	33 (49.3)
Far away from health facility	25 (37.3)
Change in their daily routine activity	17 (25.4)
Felt depressed/overwhelmed	12 (17.9)
Had problem taking medication orally	11 (16.4)
Too many pills to take	11 (16.4)
Felt the drug is toxic and want to avoid the side effect	5 (7.5)

Table 3: Reasons for non-adherence cited by TB/HIV co-infected patients (n=67).

further increase the burden of a disease that is already very big and increase the costs of its management. It is thus necessary to institute adherence support measures to lower the non-adherence levels [6].

There was no association between social demographic factors and non-adherence like another study [6]. However, some factors were considered to be significantly associated with non-adherence. Lack of caregivers and people who remind the TB patients to take their medications were associated with non-adherence in this work. Nevertheless, Amuha et al. reported that these factors were not related to non-adherence to treatment [6]. Social support was found to be crucial for patients' treatment. It has been investigated that patients who have family support and come to the clinics accompanied are usually those who successfully complete their treatment [10]. Therefore, patients who missed their medications require an increased support for the improvement of medication adherence.

In this study, gender of the patient did not significantly affect non-adherence to treatment like other studies [6,11,12]. However, some studies have shown an association between non-adherence and gender of the patients [9,13]. Some studies indicated that educational status [8,14] and marital status [15] were associated with anti-TB medication adherence unlike this study. Failure to detect an association between socio-demographic factors and non-adherence in this survey could have been due to the small sample size and cross-sectional study employed.

The primary reason of non-adherence reported by the patients was forgetting to take medications, mainly because of their daily routine activities in the area, as described in other studies [8,9,16]. However, this was not the main reason for non-adherence in the study conducted in Jiangsu Province of China [14]. The second reason was that patients felt sick when they took the medications. This possibly related to the overlapping antiretroviral and anti-TB drugs side effects. Both anti-TB and antiretroviral drugs have similar side effect profiles. When they are given together, there is a potential of added toxicity [17]. The other reason was being far away from the health facilities. This finding was consistent with the results reported from the study conducted in India, where the distance from directly observed treatment centres to the patient's residence was the reason reported by the patients for non-adherence to treatment [18]. Lack of access to the health facility to pick up medications due to distance to the facility could lead to poor adherence to treatment [19].

This study was limited in that a cross sectional study was employed, which might suffer from temporal relationship establishment with some variables and could not provide much more substantial evidence of causality. In addition, self-reports were used which usually overestimate adherence levels. The sample size was too small to detect important associations between variables.

In conclusion, non-adherence rate among the study participants was high. Interventions focusing on the identified predictors of non-adherence could improve medication adherence in TB/HIV co-infected patients. Further study with a larger sample size and more rigorous study designs over a longer period of time needs to be done to assess adherence and detect associations.

Acknowledgement

We gratefully acknowledge the staff of the health facilities for their invaluable assistance during data collection. We would also like to acknowledge the respondents for their time.

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Citation: Eticha T, Kassa E (2014) Non-Adherence to Anti-TB Drugs and Its Predictors among TB/HIV Co-Infected Patients in Mekelle, Ethiopia. *J Bioanal Biomed* 6: 061-064. doi:[10.4172/1948-593X.1000113](https://doi.org/10.4172/1948-593X.1000113)

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