

Predictors of Non-adherence to Anti-Tuberculosis Medication in Tuberculosis Patients in Thailand

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ABSTRACT The study aimed to assess the prevalence of and correlates the non-adherence to anti-tuberculosis (TB) medication in tuberculosis patients in Thailand. In 2014, a cross-sectional interview survey was conducted among 225 TB patients across 42 hospitals, 21 provinces, in all four regions in Thailand. Systematic sampling was used for all new TB and new retreatment patients within one month of the anti-TB treatment. The dependent variable was the self-reported TB medication non-adherence (<90% anti-TB medication). Results indicate that 15.6 percent of TB patients had been non-adherent to their TB medication in the past 10 days. In multivariate logistic regression, male gender, secondary or higher education, was diagnosed with TB through community screening, being a retreatment TB patient and not having chosen their own DOT supporter was associated with TB medication non-adherence. Findings can be used to apply to practice levels to improve TB treatment adherence.

INTRODUCTION

Thailand is a country with “high-burden” tuberculosis (TB) and the TB treatment success rate was eighty-one percent (WHO 2014a), which seems higher among Thai than non-Thai TB patients (WHO 2013). TB patients should have adherence levels of ninety percent or more to facilitate cure (Awofeso 2008). One of the factors contributing to the below target TB cure rates ($\geq 85\%$) in Thailand may be attributed to poor anti-TB medication adherence (Thai National AIDS Committee 2014). There is a lack of studies investigating medication adherence in TB patients in Thailand.

Studies conducted in developing countries found that the prevalence of TB medication non-adherence ranged from ten percent to fifty percent (Peltzer 2001; Amuha et al. 2009; Bagchi et al. 2010; Adane et al. 2013; Kulkarni et al. 2013; Naidoo et al. 2013). Based on literature review, with focus on low and middle countries, the following factors were found to be associated with TB treatment non-adherence:

- 1) Socio-economic factors like, lack of transportation cost, lack of material incentives and lack of social support (Jittimanee et al. 2007; Lutge et al. 2015; Tola et al. 2015).
- 2) Patients healthcare provider factors like, inadequate communication, lack of DOTS (Kapella et al. 2009; Suwankeeree and Picheansathian 2014; Tian et al. 2014; Tola et al. 2015).
- 3) Behavioral factors like, early recovery feelings, disbeliefs in the curability of TB, alcohol and tobacco use, poor knowledge about the TB treatment duration and the possible negative effects of TB medication non-adherence (Munro et al. 2007; Tola et al. 2015).

In order to improve TB medication adherence, it is vital to understand barriers and facilitators that influence patients to adhere to anti-TB medication treatment programs (Naidoo et al. 2013). Therefore, the study aimed to assess the prevalence and correlates of non-adherence to anti-TB medication in tuberculosis patients from 42 hospitals across Thailand.

METHODOLOGY

Sample and Procedure

TB outpatients were systematically sampled and interviewed, as they were visiting the TB clinic at a hospital. The target was to recruit 10 Thai TB patients from each of the 28 hospitals and 3 TB migrant patients for each of the 14 hospitals. Two hospitals were purposefully selected from 21 of 67 provinces across all four regions in Thailand. The recruitment of any new TB treatment and new TB retreatment patients (within one month of treatment) and 18 years or more of age was conducted by a healthcare professional who referred the patient for study participation if interested. Then, a trained external research assistant interviewed the TB patient after informed consent to participate in the study had been obtained. The study protocol received ethics approval from the Research Ethics Committee, Faculty of Social Sciences and Humanities, Mahidol University (COA No: 2014/222.1308), and the national Thai Ministry of Public Health of Thailand also approved the protocol.

Measures

Anti TB medication adherence was assessed with the question, "In the past 10 days, on how many days did you not take your TB medication?" Taking less than ninety percent anti-TB medication was classified as non-adherence to TB medication (Awofeso 2008).

Socioeconomic characteristics assessed included age, sex, formal education, migration status, income, and residential status (Pengpid and Peltzer 2015).

The status of TB treatment and HIV were elicited by a self-report (Peltzer et al. 2012; Pengpid and Peltzer 2015).

TB knowledge was assessed with six items, for example, "Do you know that TB can be cured?" (WHO 2008) The Cronbach alpha for the TB knowledge scale was 0.65 in this sample. In addition, it was assessed where and under what circumstances TB was diagnosed (WHO 2008).

Stigma in relation to TB was assessed with an 11-item validated scale in Thailand, for example, "Some people who have TB are afraid to go to TB clinics because other people may see them there." (Van Rie et al. 2008) Response options were from 0=strongly agree to 3=strongly agree.

The Cronbach alpha for this scale was 0.78 in this sample.

Alcohol use frequency was assessed with one item from *The Alcohol Use Disorders Identification Test* (AUDIT) (Babor et al. 2001).

Current tobacco use (in the form of cigarettes, chewing tobacco, snuff, cigars) was assessed with one question. Responses included a "yes" or "no" (WHO 1998).

Health system questions included five items on the accessibility of (TB) health services in relation to geographic distance, costs, and waiting time, for example, "Do they have to pay to see a health provider?" (USAID 2011) The Cronbach alpha for this healthcare accessibility scale was 0.68 in this sample. Five items assessed the satisfaction of services at the TB clinic, for example, "Are healthcare providers, supportive and respectful of people who have TB?" (USAID 2011) Response options ranged from 1=very dissatisfied to 5=very satisfied. The Cronbach alpha for this healthcare satisfaction scale was 0.87. Finally, patients were asked if they had a DOT supporter, who the DOT supporter was and if they had chosen their own DOT supporter.

Data Analysis

The International Business Machines Cooperation (IBM) Statistical Package for the Social Sciences (SPSS) for Windows software application program version 19.0 was utilized to analyze the data. Descriptive statistics were used to describe the sample. Data was checked for normality distribution and outliers, and non-parametric tests were used for non-normal distributions. Associations of non-adherence to anti-TB medication were examined using logistic regression analyses. The researchers used bivariate analysis, followed by multivariate backward conditional logistic regression. All variables with a bivariate test P value ≤ 0.25 were considered for inclusion in the multivariate logistic regression model (as recommended by Hosmer and Lemeshow 2000). The level of statistical significance was a two-sided p value < 0.05 .

RESULTS

Sample Characteristics

The final sample with complete data consisted of 225 TB patients, 75.1 percent were men with a mean age of 47.9 years (SD=16.0), ranging from 18 to 88 years. Almost two-thirds of the

participants (66.5%) were 41 years and older, the majority (89.3%) were Thai, and thirty-three percent had completed secondary education. Regarding TB diagnosis, 80.1 percent were diagnosed when they were sick, 10.7 percent were TB retreatment cases, and 81.8 percent had been on TB treatment for more than two months. Further, 6.7 percent were HIV positive, a few were using tobacco (14.2%) and alcohol in the past week (6.8%). The mean TB knowledge was 4.8,

with a range of 0-6, the mean TB stigma 11.3, with a range of 0-22, and the mean inaccessibility to health services was 3.4, with a range of 0-5. Almost all (93.2%) indicated that they had a DOT supporter, most of which was a member of the family (80.3%), and about two-thirds (66.8%) chose their own DOT supporter. In all, 15.6 percent of TB patients had been non-adherent to their TB medication in the past 10 days (see Tables 1a and 1b).

Table 1a: Sample characteristics by adherence status (N=225)

	<i>All N (%) Mean (SD)</i>	<i>Adherent N (%) or Mean (SD)</i>	<i>Non-adherent N (%) or Mean (SD)</i>	<i>Statistic t/χ^2, p-value</i>
<i>Socio-demographics</i>				
<i>All</i>				
<i>Age in years</i>	225	190 (84.4%)	35 (15.6%)	
18-40	75 (33.5%)	60 (80.0%)	15 (20.0%)	1.70;
41-60	93 (41.5%)	80 (86.0%)	13 (14.0%)	0.428
61 or more	56 (25.0%)	49 (87.5%)	7 (12.5%)	
<i>Gender</i>				
Female	56 (24.9%)	53 (94.6%)	3 (5.4%)	5.90;
Male	169 (75.1%)	137 (81.1%)	32 (18.9%)	0.015
<i>Nationality</i>				
Thai	201 (89.3%)	167 (83.1%)	34 (16.9%)	2.65;
Migrants	24 (10.7%)	23 (95.8%)	1 (4.2%)	0.103
<i>Education</i>				
None	26 (11.6%)	25 (96.2%)	1 (3.8%)	
Primary	124 (55.4%)	106 (85.5%)	18 (14.5%)	4.87;
Secondary or more	74 (33.0%)	58 (78.4%)	16 (21.6%)	0.088
<i>Residence</i>				
Rural	121 (53.8%)	99 (81.8%)	22 (18.2%)	1.38;
Urban	104 (46.2%)	91 (87.5%)	13 (12.5%)	0.241
<i>Patient related factors</i>				
<i>How TB was Diagnosed</i>				
Community screening	9 (4.1%)	6 (66.7%)	3 (33.3%)	6.86;
Sick	177 (80.1%)	146 (82.5%)	13 (17.5%)	0.032
When checking other diseases	35 (15.8%)	34 (97.1%)	1 (2.9%)	
TB knowledge (scale) (range 0-6)	4.8 (0.8)	4.9 (0.8)	4.5 (1.0)	1.80; 0.033
<i>TB Treatment Status</i>				
New TB	201 (89.3%)	172 (85.6%)	29 (14.4%)	1.82;
Retreatment	24 (10.7%)	18 (75.0%)	6 (25.0%)	0.177
<i>TB Treatment Duration</i>				
1-2 months	38 (18.2%)	32 (84.2%)	6 (15.8%) ²⁰	.18;
3-6 months	123 (58.9%)	103 (83.7%)	20 (16.3%)	0.912
7 or more months	48 (23.0%)	39 (81.3%)	9 (18.8%)	
<i>HIV Status</i>				
Negative or do not know	208 (93.3%)	174 (83.7%)	34 (16.3%)	.99
Positive	15 (6.7%)	14 (93.3%)	1 (6.7%)	;0.321
<i>On ART</i>				
No	5 (33.3%)	4 (80.0%)	1 (20.0%)	.10;
Yes	10 (66.7%)	9 (90.0%)	1 (10.0%)	0.747
<i>Tobacco Use (Current)</i>				
No	193 (85.8%)	164 (85.0%)	29 (15.0%)	.29;
Yes	32 (14.2%)	26 (81.3%)	6 (18.8%)	0.590
<i>Alcohol Use (Past Week)</i>				
No	205 (93.2%)	173 (84.4%)	32 (15.6%)	.88;
Yes	15 (6.8%)	14 (93.3%)	1 (6.7%)	0.349

Table 1b: Sample characteristics by adherence status (continued)

	All N (%) Mean (SD)	Adherent N (%) or Mean (SD)	Non-adherent N (%) or Mean (SD)	Statistic <i>t/χ², p-value</i>
<i>Health System and Community Factors</i>				
DOT supporter	15 (6.8%)	14 (93.3%)	1 (6.7%)	1.03;
No	205 (93.2%)	171 (83.4%)	34 (16.6%)	0.311
Yes				
<i>DOT Supporter</i>				
Family member	171 (80.3%)	144 (84.2%)	27 (15.8%)	1.44;
Village health volunteer	14 (6.6%)	13 (92.9%)	1 (7.1%)	0.487
Health care worker	28 (13.1%)	22 (78.2%)	6 (21.4%)	
<i>Chose DOT Supporter</i>				
No	2 (33.2%)	56 (77.8%)	16 (22.2%)	3.50;
Yes	7 145 (66.8%)	127 (87.6%)	18 (12.4%)	0.061
Inaccessibility of health care service (scale) (range 0-5)	3.4 (0.8)	3.4 (0.8)	3.3 (0.9)	.32; 0.313
<i>Health Care Service Satisfaction</i>				
Low	58 (26.7%)	46 (79.3%)	12 (20.7%)	1.85;
Medium	76 (35.0%)	66 (86.8%)	10 (13.2%)	0.397
High	83 (38.2%)	72 (86.7%)	11 (13.9%)	
TB stigma (scale) (range 0-22)	11.3 (3.9)	11.2 (4.0)	11.5 (3.5)	-.25; 0.229

Associations with TB Medication Non-adherence

In multivariate logistic regression, the male gender, secondary or higher education, was diagnosed with TB through community screening, being a retreatment TB patient and not having chosen their own DOT supporter was associated with TB medication non-adherence (see Table 2).

DISCUSSION

The study found that almost one in five patients were not adhering to their TB treatment. This finding is similar to most previous studies (Amuha et al. 2009; Bagchi et al. 2010; Adane et al. 2013; Naidoo et al. 2013; Tola et al. 2015). Since self-reported adherence was used in this study, the rate of reported non-adherence was

Table 2: Associations of non-adherence to TB medication of TB patients in Thailand

Variables	Adjusted odds ratio (95% Confidence Interval) ^a	P-value
<i>Gender</i>		
Female	1.00	0.020
Male	4.52 (1.27-16.17)	
<i>Education</i>		
None	1.00	0.008
Secondary or more	7.28 (1.69-31.36)	
<i>How TB was Diagnosed</i>		
Community screening		
Sick	1.00	0.030
By chance when checking other diseases	0.10 (0.01-0.80)	
<i>TB Treatment Status</i>		
New TB	1.00	0.036
Retreatment	3.38 (1.08-10.52)	
TB knowledge (scale)	0.48 (0.21-1.11)	0.086
<i>Chose DOT Supporter</i>		
No	1.00	0.050
Yes	0.23 (0.05-0.99)	

^a Hosmer and Lemeshow Test: Chi-square=24.19, P=0.001; Nagelkerke R²= 0.18

likely to be an underestimation (Adams et al. 1999). Nevertheless, the rate of non-adherence is cause for concern and it is necessary to improve adherence support measures to lower the non-adherence levels (Amuha et al. 2009).

In agreement with some previous studies (for example, Balbay et al. 2005), this study found that some socio-demographic factors (male gender) were associated with TB medication non-adherence. While generally studies found a lack of basic education to be associated with non-adherence, this study found that higher education (secondary or higher education) was associated with TB medication non-adherence. This finding is unclear and needs further investigation. Migrants seemed to show better medication adherence than Thais, yet due to the small sample size of migrants this did not reach significance.

Having been diagnosed with TB through community screening was found in this study to have a higher risk for non-adherence than being diagnosed with TB when sick or during another health examination. Contrary to this finding, a previous study found that family screening was associated with adherence (Balbay et al. 2005). It is possible that in this study, being diagnosed in the health facility (rather than passively getting diagnosed through a community screening) could be an admission for an indicator of responsibility facilitating successful completion of the treatment.

Patient factors of being a retreatment TB patient were associated with non-adherence. Persons who have previously failed to take anti-TB medication are at higher risk for non-adherence (Sevim et al. 2002). There was an association between poorer TB knowledge and non-adherence in bivariate analysis in this study. Other studies also found such an association (Munro et al. 2007; Tola et al. 2015). This result could mean that improved TB health education could be beneficial for TB treatment adherence. Unlike in other studies (Tola et al. 2015), this study did not find an association between alcohol, tobacco use and TB medication non-adherence. The reason why a significant association was not found may possibly be because of the overall low prevalence of tobacco and alcohol use in this study sample.

In terms of health system factors, not having chosen their own DOT supporter was in this study associated with TB medication non-ad-

herence. The implications of this finding may be that healthcare workers may allow TB patients to choose their own DOT supporter. Further, there was no association found between inaccessibility of health services, including costs of services, dissatisfaction of TB healthcare services, TB stigma and TB medication non-adherence. This finding is not in line with other studies (Jittimanee et al. 2007; Tesfahuneygn et al. 2015; Tola et al. 2015) that have shown that accessibility, patients healthcare worker factors and TB stigma influenced TB medication adherence.

CONCLUSION

The level of TB medication adherence among TB public healthcare patients in Thailand was found to be sub-optimal.

RECOMMENDATIONS

Interventions to improve TB medication adherence need to be intensified in Thailand, taking into account some of the risk factors identified in this study.

STUDY LIMITATIONS

The study had several limitations. Causality between compared study variables cannot be concluded, since this was a cross-sectional study. Further, study variables were mostly assessed by self-report so that it is possible that participants gave desirable responses. Failure to find an association between the study variables and TB medication non-adherence in this study could also be due to the low sample size, meaning that there was not sufficient power to detect an association.

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