FACTORS ASSOCIATED WITH DELAY IN TUBERCULOSIS TREATMENT AT 10 TERTIARY LEVEL CARE HOSPITALS IN THAILAND

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Abstract. Tuberculosis (TB) is common in Thailand. Delay in initiating tuberculosis treatment is a major public health problem. Delay in treatment can result in more severe diseases, risk for death, and greater risk of tuberculosis transmission in the community. We attempted to determine the duration from onset of TB symptoms to the date of first consultation (patient delay) and the factors associated with that delay at 10 tertiary level care hospitals in Thailand. All participants aged ≥18 years who were willing to participate were included in the study, which was conducted from January to December 2012. A structured questionnaire and medical records were used to collect data. One hundred ninety-nine TB patients were included in the study. The mean age of subjects was 48 years (SD=15.9); 69.8% were male. The median duration from onset of symptoms to first medical consultation was 30 days. On multivariate analysis, living in an urban area (adjusted odds ratio=2.81; 95% CI: 1.29-6.14) was an independent risk factor for the delay. Delay in seeking help is a common problem among TB patients in Thailand. At risk populations need to be educated on the importance of presenting for early medical consultation if they have symptoms of TB.

Keywords: TB infection, patient delay, Thailand

INTRODUCTION

Thailand is ranked eighteenth in the countries with the most TB cases (WHO, 2013). The estimated incidence of tuberculosis in Thailand during 2012 was 119 cases out of 100,000 population; 30,998 cases (54%) were new smear-positive cases (WHO, 2013). In 1966, the National TB Program (NTP) for Thailand was established; in 1996 directly observed therapy and then in 2008 directly observed therapy-short course (DOTS) was adopted in Thailand (Department of Disease Control, 2008). During a ministerial conference of the 22 highest TB burden countries in Amsterdam in 2001, Thailand committed itself to the goal of detecting 70% of the estimated TB cases and a treatment success rate of 85% of the cases detected (WHO, 2013).

The TB case detection rate increased

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from 60% in 1990 to 76% in 2012 (WHO, 2013). Some studies reported a delay in seeking healthcare by TB patients (Huong *et al*, 2007; Leung *et al*, 2007; Ngadaya *et al*, 2009). Some active TB patients "shop around for health". They may be misdiagnosed or receive ineffective treatment (Bawankule *et al*, 2010). A delay in treatment can allow the disease to get worse, increase the risk of death or lead to TB transmission in the community (Chin *et al*, 2000; Zahar *et al*, 2001; Golub *et al*, 2006).

We aimed to determine the average length of time from onset of symptoms to the first consultation and factors associated this delay.

MATERIALS AND METHODS

This study was conducted from January to December 2012 at 10 tertiary level care hospitals in Thailand. All TB patients aged ≥18 years capable of understanding the Thai language were included in the study. Participants with changes in diagnosis were excluded from the study. After obtaining written informed consent, all participants were given a self-administered questionnaire. Interviews occurred within 2 weeks of diagnosis and were conducted by nurses or health officers. The questionnaire included questions about demographics and socioeconomic characteristics. Medical records were reviewed to collect data about the symptoms associated with TB, patient factors, such as age, sex, socioeconomic characteristics, alcohol consumption and smoking, and clinical factors, such as HIV co-infection, underlying disease, microbiologic results showing resistance to isoniazid or rifampicin, and symptoms associated with TB. The time of onset of symptoms was self-reported and as were the symptoms the subject suspected were due to TB.

The socioeconomic status of participants were categorized as sufficient (income above or equal poverty line) and poor (income below poverty line). The poverty line for rural Thailand in 2011 was USD84.35 and urban Thailand USD69.21 (Office of the National Economic and Social Development Board, 2013).

MDR-TB case was defined as resistance to at least both isoniazid and rifampicin (Department of Disease Control, 2008; WHO, 2013). Suspected case of MDR-TB was defined as cases diagnosed by a physician and/or who received second line anti-TB drugs without microbiologic results showing resistance to isoniazid and rifampicin. The subject of interest was duration between date of onset of symptoms and date of first medical consultation. The symptoms were self-reported and the most commonly reported symptom was cough. Delay was defined by the median delay; therefore, patient were categorized as having either delay, taking longer than the median or no delay, taking less than the median time to seek consultation.

Statistical analysis

The data were entered into a computerized database using blinded double-entry. The two databases were compared to ensure accuracy. Categorical data were presented as percentages. For continuous data, normally distributed data were expressed as means and standard deviations, while freely distributed data were expressed as medians and interquartile ranges (IQR). Variables with a *p*-value<0.25 on bivariate analysis were included in multiple logistic regression analysis (Hosmer and Lameshow, 1989). Forward stepwise multiple logistic regression analysis was used to select variables to be included in the final model. The

probabilities for removal and entry of factors in the final model were set at 0.10 and 0.05, respectively. A *p*-value<0.05 was considered significant. On multiple logistic regression analysis, we calculated odds ratios (ORs) and 95% confidence intervals (95% CI). All statistical analyses were performed with STATA 11.0 (Stata corp, College Station, TX).

This study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University and the Ethics Review Committee for Research in Human Subjects of the Ministry of Public Health, Thailand.

RESULTS

One hundred ninety-nine participants were included in the study; 69.8% were males. The mean (SD) age was 48 (15) years old (range: 18-85 years). Twenty-five point seven percent of participants were single; 57.1% were married. Twenty-seven point two percent of participants reported a monthly income less than the poverty line. Current smokers and ex-smokers comprised 61.9%. Seventy point two percent reported using alcohol. Despite the availability of universal health care coverage in Thailand, 17.3% of participants were not covered by any health insurance at the health facilities they visited (Table 1). Diabetes mellitus was presented in 22.9% and HIV 6.8% (Table 2).

Median time duration from onset of symptoms to seeking medical consultation was 30 days (IQR 14, 60), 62 participants (31.2%) took longer than 30 days to seek a medical consultation. For MDR-TB the length of time was the same (Table 3).

Factors associated with waiting longer than 30 days were urban living (OR=2.18; 95% CI: 1.17-4.06) and distance

Table 1
Socio-demographic characteristics of 199 participants.

Variables	*n* (%)
Gender	
Male	139 (69.8)
Female	60 (30.2)
Age group (years)	
18-34	46 (23.1)
35-59	116 (58.3)
≥60	37 (18.6)
Mean (SD)	48.00 (15.89)
Marital status	
Single	51 (25.7)
Married	113 (57.1)
Divorced/widowed	34 (17.2)
Education level	
Grade 1-9	147 (74.2)
Grade10-unversity level	51 (25.8)
Residence area	
Urban	69 (35.0)
Rural	128 (65.0)
Socioeconomic status	
Sufficient	115 (72.8)
Poverty	43 (27.2)
Smoking status	
Never smoked	75 (38.1)
Current or ex-smoker	122 (61.9)
Alcohol use	
Never drank	59 (29.8)
Current or ex-drinker	139 (70.2)
Health insurance	
No	33 (17.3)
Yes	158 (82.7)
Distance from residence to health facility (km)	
<15	94 (69.1)
≥15	42 (30.9)

from home to the nearest health facility was <15 km (OR=2.76; 95% CI: 1.15-6.61) (Table 4). On multivariate analysis, the only factor associated with delay was living in rural area (adjusted OR=2.81; 95% CI: 1.29-6.14).

Table 2
Clinical characteristics of 199
participants.

Variables	n (%)
Underlying disease	
Diabetes mellitus	
No	91 (77.1)
Yes	27 (22.9)
HIV infection	
Negative	123 (93.2)
Positive	9 (6.8)
TB symptoms	
Hemoptysis	
No	146 (73.4)
Yes	53 (26.6)
Fever	
No	86 (43.2)
Yes	113 (56.8)
Chest pain	
No	173 (86.9)
Yes	26 (13.1)
Weight loss	
No	81 (40.7)
Yes	118 (59.3)
Dyspnea	
No	98 (49.3)
Yes	101 (50.7)
Type of TB infection	
Regular TB infection	146 (73.4)
MDR-TB with confirmed resistance to isoniazid and rifampicin	32 (16.1)
MDR-TB clinically diagnosed	21 (10.5)

DISCUSSION

The delay in seeking treatment of 30 days seen in our study is similar to studies from Ethiopia (30 days) and and Brazil (30 days) (Mesfin *et al*, 2009; Machado *et al*, 2011) but shorter than studies from Nepal (50 days), Tanzania (90 days) and India (55 days) (Basnet *et al*, 2009; Ngadaya *et al*, 2009; Bawankule *et al*, 2010). A possible explanation for the shorter time in our study could be easier access to health care in Thailand.

The association between delay and location of residence in our study is consistent with findings from Vietnam and Ethiopia (Huong *et al*, 2007; Mesfin *et al*, 2009), but not in studies from Vietnam (Lönnroth *et al*, 1999), Cameroon (Cambanis *et al*, 2007) and China (Tobe *et al*, 2013). The delay seen in those living in an urban area in our study is similar to a study from Gambia (Lienhardt *et al*, 2001). The delay in urban dwellers could be due to work obligations preventing them from having time to seek care. In our study those who lived <15 km from a health facility had a greater delay than those who lived ≥15 km from a health facility, but this finding did not reach significance. Similar findings were seen in a study from Ethiopia (Yimer *et al*, 2009). Our study found significant association between residence area and

Table 3
Duration between symptom onset and first medical consultation.

Type of TB infection	Days			
	Mean	(SD)	Median	(IQR)
Regular TB infection	47.23	(65.03)	30	(14, 60)
MDR-TB with confirmed resistance to isoniazid and rifampicin	50.81	(85.30)	30	(11, 52.50)
MDR-TB clinically diagnosed	48.95	(77.90)	30	(7, 60)

SD, standard deviation; IQR, interquartile range.

Table 4
Socio-demographic factors associated with length of delay in seeking treatment.

Factors	≤30 days n (%)	>30 days n (%)	Crude odds ratio	(95% CI)
Gender				
Male	97 (69.8)	42 (30.2)	1.00	Reference group
Female	40 (66.7)	20 (33.3)	1.15	(0.60-2.21)
Age group (years)				
18-34	35 (76.1)	11 (23.9)	0.70	(0.32-1.53)
35-59	80 (69.0)	36 (31.0)	1.00	Reference group
≥60	22 (59.5)	15 (40.5)	1.51	(0.71-3.26)
Marital status				
Single	39 (76.5)	12 (23.5)	1.00	Reference group
Married	76 (67.3)	37 (32.7)	1.58	(0.74-3.37)
Divorced/widowed	22 (64.7)	12 (35.3)	1.77	(0.68-4.61)
Education level				
Grade1-9	96 (65.3)	51 (34.7)	1.93	(0.91-4.09)
Grade10-unversity level	40 (78.4)	11 (21.6)	1.00	Reference group
Residence area				
Rural	96 (75.0)	32 (25.0)	1.00	Reference group
Urban	40 (58.0)	29 (42.0)	2.18	(1.17-4.06)
Socioeconomic status				
Sufficient	79 (68.7)	36 (31.3)	1.00	Reference group
Poverty	30 (69.8)	13 (30.2)	0.95	(0.44-2.04)
Smoking status				
Never smoked	53 (70.7)	22 (29.3)	1.00	Reference group
Current or ex-smoker	82 (67.2)	40 (32.8)	1.18	(0.63-2.19)
Alcohol use				
Never drank	43 (72.9)	16 (27.1)	1.00	Reference group
Current or ex-drinker	93 (66.9)	46 (33.1)	1.33	(0.68-2.61)
Health insurance				
No	20 (60.6)	13 (39.4)	1.58	(0.73-3.45)
Yes	112 (70.9)	46 (29.1)	1.00	Reference group
Distance from home to the health facility (km)				
<15	57 (62.6)	37 (39.4)	2.76	(1.15-6.61)
≥15	34 (80.9)	8 (19.1)	1.00	Reference group

CI, confidence interval.

distance from residence to the health facility. In our study those who live <15 km from a health facility and living in an urban area had more proportion than living in a rural area. Therefore, the explanation for these findings could also be due to work obligations preventing them from having time to seek health care.

In our study, gender was not significantly associated with delay, similar to studies from numerous countries (Wang *et al*, 2007; Sendagire *et al*, 2010; Lock *et al*, 2011; Belay *et al*, 2012; Jurcev-Savicevic and Kardum, 2012; Deponti

Table 5
Clinical characteristic factors associated with delay in seeking treatment.

Factors	≤30 days n (%)	>30 days n (%)	Crude odds ratio	(95% CI)
Underlying disease				
Diabetes mellitus				
No	68 (74.7)	23 (25.3)	1.00	Reference group
Yes	20 (74.1)	7 (25.9)	1.03	(0.39-2.76)
HIV infection				
Negative	87 (70.7)	36 (29.3)	1.00	Reference group
Positive	5 (55.6)	4 (44.4)	1.93	(0.49-7.62)
TB symptoms				
Hemoptysis				
No	97 (66.4)	49 (33.6)	1.00	Reference group
Yes	40 (75.5)	13 (24.5)	0.64	(0.32-1.31)
Fever				
No	61 (70.9)	25 (29.1)	1.00	Reference group
Yes	76 (67.3)	37 (32.7)	1.19	(0.65-2.18)
Chest pain				
No	123 (71.1)	50 (28.9)	1.00	Reference group
Yes	14 (53.9)	12 (46.1)	2.11	(0.91-4.88)
Weight loss				
No	62 (76.5)	19 (23.5)	1.00	Reference group
Yes	75 (63.6)	43 (36.4)	1.87	(0.99-3.53)
Dyspnea				
No	70 (71.4)	28 (28.6)	1.00	Reference group
Yes	67 (66.3)	34 (33.7)	1.27	(0.70-2.32)
Type of TB infection				
Regular TB infection	100 (68.5)	46 (31.5)	1.00	Reference group
MDR-TB with confirmed resistance to isoniazid and rifampicin	23 (71.9)	9 (28.1)	0.85	(0.37-1.98)
MDR-TB clinically diagnosed	14 (66.7)	7 (33.3)	1.09	(0.41-2.87)

CI, confidence interval.

et al, 2013; Wysocki *et al*, 2013). However, studies from Brazil and China found an association between delay and gender (Wang *et al*, 2008; Machado *et al*, 2011). The explanation for these findings is that females currently have to work outside their homes so it is easier for them to obtain knowledge and information about TB.

In Thailand, all patients with a diagnosis of TB are recommended to be tested for HIV (Department of Disease Control, 2008), in this study 66.3% of our participants were checked for HIV. In our study, those with HIV co-infection had a slightly longer delay in seeking treatment but this was not significant, similar to studies from Brazil and Nigeria (Deponti *et al*, 2013; Ukwaja *et al*, 2013; Wysocki *et al*, 2013). Studies from Tanzania, Ethiopia, and Brazil found no significant association between delay and HIV status (Mesfin *et al*, 2009; Ngadaya *et al*, 2009;

Deponti *et al*, 2013).

An advantage of our study was we determined delay for TB and suspected case of MDR-TB. Our study had some limitations. First, the questionnaire did not address what was done at the first medical consultation (*eg*, sputum smear microscopy, chest x-ray). Second, the onset of symptoms and first consultation were based on patient recall, which is subject to error and recall bias.

Delay in the diagnosis and treatment of tuberculosis is a serious public health problem in Thailand. The median duration of delay in our study was 30 days. The factor significantly associated with delay in seeking treatment was residence in an urban area. There was no difference in delay among patients with TB and MDR-TB. Delay in treatment can increase the risk of transmission. Hence, careful consideration should be taken to improve the TB case detection, especially in those living in an urban area.

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