

Original Article

Factors associated with the unsuccessful tuberculosis treatment of hill tribe patients in Thailand

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Abstract

Introduction: Tuberculosis (TB) remains a serious public-health problem worldwide. The successful tuberculosis treatment was in low rate among the hill tribes in Thailand. This study aimed to determine factors associated with the unsuccessful tuberculosis treatment among the hill tribe TB patients in northern Thailand.

Methodology: A retrospective cohort study was conducted using secondary data from the national TB reporting system. Data of newly registered hill tribe patients with TB receiving treatment were obtained from 18 government hospitals in Chiang Rai province, during 2014–2017. TB treatment outcomes and factors associated with unsuccessful were determined.

Results: A total of 770 hill tribe patients with TB registered during the study period. The majority were males aged 25–64 years. About 80% of the patients lived in rural areas and 53.9% worked in agriculture. The overall TB treatment success rate was 80.4%. Two factors were associated with unsuccessful TB treatment: ages 25–44 and ages 45–64 (aOR 3.14 (1.03–9.55) and 3.02 (1.01–9.03), respectively) and receiving antiretroviral drugs (proxy of HIV infection) (aOR 2.30 (1.02–5.15)).

Conclusion: Although the TB treatment success rate among hill tribe patients did not reach the national goal, it was still higher than that of other Thai TB patients in the area. In Thailand, hill tribe people can access health services free-of-charge under the national health insurance. This could influence the successful treatment. However, some barriers need to be considered, such as the high default rate and high death rate among those with HIV coinfection.

Key words: Tuberculosis; hill tribe; treatment success; TB treatment; minority.

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Introduction

Tuberculosis (TB) is a major public health problem world-wide [1]. Approximately 10.4 million TB patients and 1.6 million TB deaths were reported in 2017. Countries in South-East Asia and the Western Pacific regions, including Thailand, have some of the highest TB burdens, and about 62% of reported new cases are from these countries [2]. Many studies have found that, in minorities, a lower proportion of suspected TB cases undergo complete diagnostic evaluation and an even lower proportion of cases are successfully treated [3]. In 2013, 65% of TB cases reported in the United States were among foreign-born persons, despite immigrants only constituting 12.5% of the total US population [4]. The statistics are even more telling for the state of Utah, where 78.8% of the TB cases in 2013 were among foreign-born individuals, who comprised just 8.2% of the population from 2009

to 2013 [5]. China also reported there was a higher proportion of minorities among notified TB cases in big cities, ranging from 40%–80%; and the treatment completion rate among minorities was about 60% compared with over 85% of local residents with TB [6]. In addition, minority groups are more likely to live in overcrowded and poorly ventilated houses. The perceptions of health and illness in some ethnic minorities may also have a negative impact on treatment-seeking behaviors and a poor socioeconomic status and language barrier can also impact minorities' access to health services [7].

Thailand is recognized as having an excellent national health system that provides free health care to its citizens, despite being a developing country [3]. All TB patients are given the entire course of treatment free of charge, and this policy covers all Thai people and registered minorities who hold a national identification

card (ID). Despite this, Thailand had a reported 93,000 new TB cases, and 130,000 cumulative cases in 2017, among which 16% were HIV positive [8]. TB was more prevalent in the upper northern part of Thailand: among the 77 provinces in Thailand, just seven upper northern provinces contributed to a half of the overall TB cases reported in the country. Chiang Rai province had the highest TB morbidity rate with a prevalence of 119.5 per 100,000 people [9].

In Chiang Rai, there is a large hilly region at the border with Myanmar and Lao PDR, which is inhabited by a large number of hill tribe people [10]. In 2018, there were approximately 1.2 million people living in Chiang Rai Province, and 300,000 of those were classified as being of hill tribe origin with their own culture, belief, and language. Most hill tribes moved down from China many decades ago and settled in the hill and border areas of Chiang Rai [11]. Most of the tribal people are living in poverty and face a number of barriers preventing them accessing health and educational services [12] and, because of this, they have become vulnerable to poor health. In addition, poor living conditions increase their risk of contracting communicable diseases, particularly tuberculosis [13].

In 2016, about 16% of new sputum-positive TB cases in Chiang Rai were hill tribe patients, according to the report of the Ministry of Public Health, Thailand. The treatment success rate among the hill tribe patients has been reported to be lower than the goals of the National Tuberculosis Control Programme Guideline, Thailand (NTP) and World Health Organization (WHO) [14]. Factors related to this low treatment success rate have not been explored; therefore, this study aimed to determine TB treatment success rate and the factors associated with unsuccessful TB treatment among the hill tribes of Chiang Rai, Thailand.

Methodology

Study design

A retrospective cohort study was conducted to identify factors associated with unsuccessful TB treatment of hill tribe TB patients in Chiang Rai, Thailand.

Study setting

Secondary data on TB among hill tribes of Chiang Rai province were obtained from the national TB case management and reporting system (TBCM). All new TB patients diagnosed at government hospitals are required to register to the system. In Chiang Rai province, there are 18 government hospitals, including one regional hospital and 17 general hospitals. Hill

tribal people in the area are legal residents and, therefore, are under the national universal health coverage policy; therefore, they have access to free health services at these hospitals, including TB treatment.

Research instruments

Two sheets were developed and used for data collection. First, an excel sheet was developed and used for collecting the hill tribe TB patient individuals' characteristics and also treatment outcomes from the TBCM system. Second, world sheet was developed for collecting data from other medical records such as laboratory results and treatment plan in each visit. Two sheets of data collection were pooled into a single file in SPSS before analysis.

Data collection

Newly diagnosed patients registered with TB in Chiang Rai province during 2014–2017 were identified. Only data from hill tribe patients, as described in the ethnic variable, were extracted for analysis. There are six major hill tribes in the area, including Akha, Lahu, Hmong, Mein, Lisu, and Karen. Demographic and clinical characteristics as well as treatment outcomes were obtained. Type of tuberculosis, pulmonary or extrapulmonary, was determined according to the WHO's criteria. Patients diagnosed with both pulmonary and extrapulmonary TB were classified in pulmonary tuberculosis group. Patient's living area was defined as urban (living in a capital city of the province) and rural (living outside the capital city). In Thailand, directly observed therapy (DOT) is required for all TB patients. This would also allow healthcare providers to closely monitor the TB treatment outcome, particularly when death occurred in the patients. Unfortunately, we were not able to access information on HIV status due to a logistical barrier. Therefore, we used data on the prescription of antiretroviral drugs (ARV) as a proxy of HIV status. According to the national tuberculosis case management guideline, all TB-HIV patients must receive ARV drugs.

Data analyses

Categorical variables data were summarized into frequency and percentage. Missing data were not imputed in all analyses. We used TB treatment outcome definitions from the WHO guidelines: treatment outcomes were classified into cured, treatment completed, died, defaulted, treatment failed, and transferred out. Successful TB treatment was defined as cured and treatment completed, in which the patients

completed the course of treatment with evidence of at least one negative sputum result after treatment. Unsuccessful TB treatment outcomes were considered when the patients failed to respond to treatment (sputum remained positive at month five or later), died for any reason, or was lost to follow-up (default) [14]. Transfer-out outcome was classified in neither successful nor unsuccessful treatment outcome. Patients with transfer-out outcome were those who had transferred to another healthcare facility due to any reasons. According to the database system, the final treatment outcome of transferred patients cannot be retrieved. Characteristics of patients in the unsuccessful and successful TB treatment groups were analyzed and compared using Chi-square test or Fisher exact test. Logistic regression was used to identify factors associated with unsuccessful TB treatment outcome. Crude and adjusted odds ratios (OR) with a 95% confidence interval (CI) were calculated. Variables that showed a P-value of crude OR < 0.1 were included in the multiple logistic regression model. The analysis was performed using SPSS version 20, 2014 (SPSS, Chicago, IL).

Ethical approval

This study was approved by the ethics committee of the Faculty of Tropical Medicine, Mahidol University (TMEC 17-002) and the Chiang Rai provincial public health office (No.27/2560).

Results

Characteristics of hill tribe TB patients

There were 4,650 new TB patients registered in Chiang Rai between 2014 and 2017, among which 770 (16.56%) were from hill tribes. About 65% of the hill tribe patients were male. The majority (87.7%) of patients had pulmonary TB; more than half of them had positive sputum smears. Extra pulmonary TB was observed in only 12.3% of the hill tribe TB patients (Table 1.) The most affected age group was 45–64 years old (37.8%). The majority of hill tribe TB patients (80%) lived in rural areas. According to the patient’s occupation, 53.9 % were farmers followed by employed (23.7%) and student (21.1%), respectively (Table 1).

Table 1. Characteristics of hill tribe TB patients in Chiang Rai, 2014–2017.

Characteristics	n (%)
Sex (n = 753)	
Male	492 (65.3)
Female	261 (34.7)
Type of tuberculosis cases (n = 770)	
Pulmonary smear negative	307 (39.9)
Pulmonary smear positive	368 (47.8)
Extra pulmonary	95 (12.3)
Age in years (n = 722)	
< 25	73 (10.1)
25–44	244 (33.8)
45–64	273 (37.8)
≥ 65	132 (18.3)
Living area (n = 770)	
Rural	616 (80.0)
Urban	154 (20.0)
Occupation (n = 764)	
Student	153 (21.2)
Merchant	9 (1.2)
Agriculture	389 (53.9)
Employee	171 (23.7)
Received ARV-drug (n = 713)	
No	670 (94.0)
Yes	43 (6.0)
History of BCG (n = 460)	
No	326 (70.9)
Yes	134 (29.1)
Attended at hospital (n = 766)	
Regional hospital	182 (23.8)
General hospital	584 (76.2)

ARV-drug: Antiretroviral Drug, BCG: Bacilli Calmatte-Guerin.

Only 6% of patients had an HIV infection and received antiretroviral (ARV) treatment. About 70% of the patients had no history of BCG vaccination. Most of the patients (76%) received treatment at general hospitals.

Tuberculosis treatment outcomes among hill tribe patients

The overall TB treatment success rate among hill tribe patients during 2014 to 2017 was 80.39%. The majority of the unsuccessful treatment was due to death; the death rate was 10.26%. There was an increasing trend in the success of TB treatment from 77.68% in

Table 2. Treatment outcomes among the hill tribe TB patients in Chiang Rai province, 2014–2017.

Year	Total patients	Treatment success	Failure	Death	Default	Transfer out
	n	n (%)	n (%)	n (%)	n (%)	n (%)
2014	224	174 (77.68)	4 (1.79)	22 (9.82)	8 (3.57)	16 (7.14)
2015	204	170 (83.33)	6 (2.94)	12 (5.88)	2 (0.98)	14 (6.86)
2016	153	133 (86.93)	1 (0.65)	15 (9.80)	1 (0.65)	3 (1.96)
2017	189	142 (75.13)	1 (0.53)	30 (15.87)	2 (1.06)	14 (7.41)
Total	770	619 (80.39)	12 (1.56)	79 (10.26)	13(1.69)	47 (6.10)

2014 to 86.93% in 2016. Nonetheless, the treatment success rate again decreased to 75.13% in 2017, and the death rate increased to 15.87%. Default or lost to follow-up was observed in 3.57% of hill tribe TB patients in 2014. However, the default rate decreased to approximately 1% in 2015 to 2017 (Table 2).

Factors associated with unsuccessful tuberculosis treatment among the hill tribe patients

According to the univariate analysis, age, living area, occupation, receipt of ARV, and type of tuberculosis were significantly associated with unsuccessful tuberculosis treatment. However, only age and receipt of ARV treatment remained statistically significant in the multivariable analysis. Patients aged 25–64 years were about three times more likely to have unsuccessful treatment than those aged < 25 years. TB treatment was 2.3 times more likely to be unsuccessful in patients who had received ARV treatment, compared

with those who had not received ARV treatment. Factors including gender, history of BCG vaccination, and treatment at different hospitals were not significantly associated with TB treatment success (Table 3).

Discussion

TB patients require long-term treatment, and unsuccessful treatment could have an impact on TB transmission in the community. Minority people have been shown to be at high risk for unsuccessful treatment [15]. In this study, the TB treatment success rate among new hill tribe TB patients showed an increasing trend from 78 % to 87% during 2014 to 2016; however, the success rate decreased to 75% again in 2017. This dramatic decrease in the success rate in 2017 may have been due to a higher death rate. Death among TB patients can be due to a number of reasons, not limited to TB. The WHO and the National Tuberculosis

Table 3. Crude and adjusted odds ratios for unsuccessful tuberculosis treatment outcome among hill tribe TB patients.

Factors	Unsuccessful treatment		Successful treatment		Crude OR (90% CI)	p-value	Adjusted OR* (95% CI)	p-value
	n	(%)	n	(%)				
Gender								
Male	61	68.4	401	31.6	1			
Female	32	12.3	228	87.7	0.93 (0.58–1.46)	0.730		
History of BCG								
No	25	21.6	105	78.4	1			
Yes	52	16.0	274	84.0	0.74 (0.49–1.11)	0.147		
Attended at the hospital								
Regional hospital	22	13.4	142	86.4	1			
General hospital	71	12.7	487	87.3	0.95 (0.61–1.49)	0.564		
Age								
< 25	4	5.5	69	94.5	1		1	
25–44	35	14.3	209	85.7	2.89 (0.99–8.42)	0.052	3.14 (1.03–9.55)	0.044*
45–64	38	13.9	235	86.1	2.79 (0.96–8.09)	0.059	3.02 (1.01–9.03)	0.048*
≥ 65	16	12.1	116	87.9	2.38 (0.76–7.41)	0.135	1.75 (0.17–18.02)	0.638
Living area								
Rural	69	11.8	518	88.2	1		1	
Urban	24	17.8	111	82.2	1.62 (0.97–2.70)	0.061	1.62 (0.88–2.99)	0.123
Received ARV-drug								
No	76	11.4	593	88.6	1		1	
Yes	10	23.3	33	76.7	2.36 (1.12–4.99)	0.020	2.30 (1.02–5.15)	0.044*
Occupation								
Student	18	11.8	135	88.2	1		1	
Merchant	2	22.2	7	77.8	2.14 (0.41–11.12)	0.375	1.32 (0.24–7.32)	0.754
Agriculture	58	14.9	331	85.1	1.31 (1.02–2.31)	0.049	0.86 (0.42–1.75)	0.669
Employee	15	8.8	156	91.2	0.72 (0.35–1.49)	0.198	0.53 (0.23–1.21)	0.131
Type of tuberculosis								
Pulmonary smear negative	44	15.8	234	84.2	1		1	
Pulmonary smear positive	38	10.6	320	89.4	0.63 (0.39–1.01)	0.053	0.65 (0.37–1.14)	0.129
Extra pulmonary	11	12.8	75	87.2	0.78 (0.38–1.59)	0.493	0.83 (0.37–1.84)	0.642

*Adjusted for age, living area, received ARV-drug, occupation, type of tuberculosis; ARV-drug: Antiretroviral Drug, BCG: Bacilli Calmatte-Guerin.

Control Program of Thailand have set a treatment success rate goal of 85% [16]. Although the treatment success rate among the hill tribe patients was lower than the national goal, the success rate of 75% in 2017 was still higher than that among Thai (70%) and non-Thai (49%) patients in the same province. In Thailand, hill tribes are considered to be permanent residents and hill tribe patients have access to free-of-charge health services, under the national health insurance policy, whereas non-Thai patients in the area are mainly immigrants who are not covered by the national health insurance. The default (lost to follow-up) and death rate among hill tribe TB patients were less than for Thai patients [17]. Death among TB patients has been shown to be associated with HIV-coinfection [18], and the overall rate of HIV infection among TB patients in this province was about 14.59% [19], whereas only 6% of hill tribe patients in this study received ARV treatment, presumably because they had a HIV-coinfection.

In this study, we found that middle-aged hill tribe TB patients were more likely to have unsuccessful TB treatment. Middle-aged people are the main working demographic providing income for the family. Many middle-aged hill tribe people move to the cities for employment [20] and return to their home town when they are sick, as hill tribe patients need to seek treatment at the hospital they are registered to under the universal health coverage. These working middle-aged patients usually wait until they get very sick before seeking treatment, as they do not want to lose their job, leading to delayed treatment. Delayed treatment can lead to treatment failure [21-22], indeed, in this study, the failure rate was also highest among middle-aged hill tribe patients. Moreover, many patients lost their jobs during the treatment. Due to limited family incomes, middle-aged patients may need to return to the city to find employment, once the symptoms have subsided. In addition, a previous study found that middle-aged hill tribe populations are vulnerable to drug and alcohol abuse [23], which could also lead to a high treatment default among this age group [24-26].

Another factor associated with unsuccessful TB treatment among hill tribe patients was the use of antiretroviral (ARV) medication, a proxy variable for HIV coinfection. Although ARV is recommended for all HIV-TB patients, providing concurrent anti-TB and ARV medication is a challenge. The ARV therapy should be provided with a correct regimen and timing and with adequate support and monitoring of drug interactions and immune reconstitution events [27-30]. Furthermore, starting ARV therapy when HIV is indicated during TB treatment is important because of

the high death rate among patients with HIV coinfection; even if the appropriate anti-tuberculosis treatment is not overlooked [31-33].

This study has several limitations. Information on patient's HIV status could not be obtained, as we could not access the relevant records in the TB database due to data privacy protection. Although the number of patients receiving ARV could miscalculate the HIV prevalence, as some HIV patients may not have received ARV treatment, this error is estimated to be small as all HIV-TB infected patients must receive ARV treatment under the national policy. In addition, this study was based on the analysis of secondary data, which resulted in the analysis of a limited number of variables. Further prospective study is recommended to provide a more complete analysis of the risk factors associated with unsuccessful TB treatment among this population.

Conclusion

The overall TB treatment success rate among hill tribe patients was about 75%–87%. Although the success rate was lower than the national goal, the success rate among hill tribe patients in this study was higher than Thai and Non-Thai patients in the same province. Age and receipt of ARV treatment were significant risk factors for unsuccessful treatment outcomes. Providing financial support, both for TB treatment and travel costs could increase the treatment success rate among this vulnerable group. Proper case management, particularly among HIV-TB patients, could also help to improve the success rate of TB treatment.

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