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Delay of Treatment among New Smear-Positive Pulmonary Tuberculosis Patients in Thai-Cambodia Border: Cases Study in Surin and Sisaket Province, Thailand

[1]Aree Butsorn, [2]Pornnapa Suggaravetsiri and [3]Nongluck Tesana
[1]Public Health, Graduate School, Khon Kaen University, Thailand
[2]Department of Epidemiology, Faculty of Public Health, Khon Kaen University, Thailand
[3]Sixth Office of Disease Prevention and Control, Khon Kaen Province, Thailand

Abstract: Delay treatment of Pulmonary Tuberculosis (PTB) caused severe disease and higher mortality. It also leads to an increased period of infectivity and transmission in the community. The objectives of this study were to, identify time of delays, duration from the appearance of first symptom of the disease until date of initial treatment (Total Delay: TTD), duration from the appearance of first symptom of the disease until first contact health workers (Patient Delay: PTD) and duration of first contact health workers until date of initial treatment (Health System Delay: HSD), identify factors predicting delay of treatment among new-smear positive pulmonary tuberculosis patients in Thai-Cambodia border. A cross-sectional analytical studied new smear-positive pulmonary tuberculosis patients in Thai-Cambodia border over a 2 year period. Patients were interviewed on entry, reporting the duration of symptoms before the start of treatment and start of contact health provider for initial treatment to be collected. Questionnaires were collected by sixteen well-trained assistant researchers by explaining the purposes of study. It was decided that 60 days was an acceptable total delay. Associations were investigated using univariable and multivariable analysis and the population attribute 443 subjects from 8 hospital public health centers in Thai-Cambodia border were estimated. Of 443 patients, 74.04% had a delay of PTD >28 days (med = 51, Q1 = 28, Q3 = 98), 25.51% had a delay of HSD >14 days (median day = 4, Q1 = 0, Q3 = 16) and 53.72% had delay of TTD >56 days (median day = 62, Q1 = 31, Q3 = 112). It found that 7 factors correlated with patient delay. The best predictor was cough with sputum (56.2%), cough with no sputum (15.33%), cough with hemoptysis (5.4%), chest pain (13.5%), fever (8.8%), loss weight >10% (4.1%) and pay for travel (3.1%) correlated with patient delay ($R^2 = 0.64$, $p<0.05$). It found that 6 factors were correlated with health system delay. The best predictor was other first symptom (53.5%), first diagnostic (13.8%), television perception (9.5%), first contact private hospital (10.1%), border travel (7.1%) and doubt of TB and none practice (5.9%), respectively ($R^2 = 0.168$, $p<0.05$).

Key words: Delay, PTB, Surin, Sisaket, Cambodia, Thailand

INTRODUCTION

From 2003-2006, the highest prevalence of Pulmonary Tuberculosis (PTB) in the Northeast of Thailand was steadily high in Sisaket, Surin provinces (125.93, 111.29). At the same time the PTB prevalence in Cambodia was also high in 2004. The people along the border were traveling and trading with one another causing transmission of the disease. In 2006, 300-500 persons per day travel through Chongsangum immigration office of Sisaket province, 1,000-1,200 persons per day travel through Chongchom immigration office of Surin province. The problems related to border passing immigration and traveling caused difficulty in control of tuberculosis. Delay of treatment is a major problem contributing to the high berden and transmission of tuberculosis in most developing countries. It has been recognized that if treatment is ignored, a person with active pulmonary TB will infect on average 10-15 persons a year. There were several studies in delays of treatment, magnitude of duration before initial treatment and risk factors related to delays from many counties which varied in definitions of delays depending on who was identified as first health care providers responding in starting health system delay until having initial treatment.

Several risk factors were verified and tested for significance but there were no predictor models and intervention models to develop for reducing those factors. Delaying factors of border areas were not identified in former studies. The border area is addressed as high risk group by WHO Stop TB committee which required special attention and strategy to control

Corresponding Author: Aree Butsorn, Public Health, Graduate School, Khon Kaen University, Thailand

because of complexity of communities that there are more homeless people, migratory workers, illegal immigrants and cross-border population those who can contribute to delay in diagnosis and treatment. The researcher studied delays in border area for diversifying border factors and identify factors associated to delay in this specific area aimed to identify duration of delays, duration from the appearance of first symptom of the disease until date of initial treatment (total delay), duration from the appearance of first symptom of the disease until first contact health workers (patient delay) and duration of first contact health workers until date of initial treatment (health system delay) and identify factors predicting delay of treatment among new-smear positive pulmonary tuberculosis patients in Thai-Cambodia border.

MATERIALS AND METHODS

The study design was a cross-sectional analytic research. This study examines factors associated with delay treatment among new smear-positive pulmonary tuberculosis patients along Thai-Cambodia border in Surin and Sisaket province. The questionnaire consists of 8 major sections associated with delay of tuberculosis including the background, health behavior factors, stigma factors, traveling factors, factors related to border area, factors related to delay of diagnosis factors and treatment factors. The delays in diagnosis and treatment of tuberculosis divide for 3 items as follow; Patient's Delay (PTD) is usually defined as the time between onset of first symptoms and first utilization of a health care provider not >4 weeks (Aoki and Mori, 1985; Asch *et al*., 1998) based on the suspected symptoms of tuberculosis disease. Doctor's Delay (HSD) is usually defined as the time between first utilization of a health care provider and initial of treatment no >2 weeks (Hooi, 1994) and Total Delay (TTD) is duration from the appearance of first symptom of the diseases until date of initial treatment not >8 weeks.

The population of this study was new-smear-positive PTB patients registration in 8 hospitals in Surin province (Sangkhal, Bauched, Kabchoeng and Dongrug hospitals) and Sisaket province (Khukhan, Phusing, Khunhan and Khantaralak hospitals), a sample size was calculated for accuracy parameter estimated (Demissie *et al*., 2000) based on constructing the equation to predict the outcomes from independent variables (Rosner, 1990; Daniel, 2005; Kleinbaum *et al*., 1998), about smoke and alcohol consumption. The magnitudes of sample size were at least 438 cases plus 10% for missing data, 443 cases were recruited in this study. Inclusion criteria: new smear-positive pulmonary tuberculosis patients ≥15 years old, new TB patients register in 8 hospitals in Thai-Cambodia border in Surin and Sisaket provinces. Exclusion criteria, patients who do not give consent to collected data, physiological and psychological problems affect to ability of interviewing.

Data collection, the questionnaires were collected by sixteen well-trained assistant researchers by explaining the purposes of the study, research procedure and opening opportunity for asking questions. Then they are trained to collect data from the sample in this study under the supervision and control of the researcher until they understand the procedure and can collect data in the same way. Data entry and analysis was conducted with STATA version 8.2. The percentage of patients who delayed seeking treatment and the median delays were calculated and crude 95% confidence intervals were used to measure association between patients demographic, economic, health status, perception and level of TB awareness and prolonged patient delay and health system delay. Multivariate regression analysis was used to estimate the independent effects (Adjusted R^2, 95% confidence intervals) of each factor on prolonged patient delay and health system delay. Variables with p-value ≤0.2 were entered into multivariate regression models (stepwise) and allowing interaction for confounding effect between potential risk factors.

RESULTS AND DISCUSSION

About 443 new smear positive of pulmonary tuberculosis patients were included in the study. Of these, 287 (64.79%) were male, the median age was 54 years (Q1 = 139, Q3 = 66), 286 (64.56%) were farmers, 306 (69.07%) were married, 371 (83.75%) had history of concomitant diseases of which 50.00% were diabetes mellitus. All of subject achieved blood rechecking for HIV about 58.01 and 6.23% found HIV positive, respectively.

The factors related health behavior we found that 64.56% were smoking, 70.20% related with alcohol consumption, 95.00% not active when had symptoms, 37.02% try to self care in initial of symptoms, 94.36% of first contact going to public hospital 45.37% go to health center 15.80% go to private clinic and 11.29% go to drug store, 46.05% to see doctor by advisor and 85.78% of that advice by parents, 67.04% used welfare and 23.48% used 30 baht scheme.

About 76.9% of samples unknown causes of tuberculosis, 58.24% not accept the way of transmission, 53.50% unknown suspect of TB symptoms, 63.21% unknown method to prevention disease, 60.95% not percept severity of TB disease and 79.46% were stigmatization, respectively. Factors related to area base

as shown 98% of subject were Thailand, Thai and Cambodia language is main language (40%), 99% live long in border (med = 50, Q1 = 34, Q2 = 62) but not trade in border, 64% never gone to border and 85% never gone to border about <5 times ((med = 2, Q1 = 1, Q2 = 4)), respectively. About 87% of subjects not referred to secondary health care, the main symptom to go to hospital is cough with sputum. The median time of cough is 30 days (Q1 = 20, Q3 = 90). About 80% of patient was treated by General Practice (GP) and 64% of first diagnostic was tuberculosis. About 82% of subject was check sputum, 54% check sputum about 3 times before diagnosis and 4% of subject was sent sputum for cultured. About 96% was chest X-ray, 67% had cavities on chest radiography and 92% never used antibiotic drug.

The distribution of TB treatment delays was skewed. The median patient's delay, health system delay and total delay were 51 days (Q1 = 28, Q3 = 98), 4 days (Q1 = 0, Q3 = 16) and 62 days (Q1 = 31, Q3 = 112). Of the total patients, 74.04, 25.51 and 53.72% had prolong patient's delay, health system delay and total delay as shown in Table 1. The univariate were analyzed it found that many factors correlated with patient's delay as shown in Table 2. Prolonged patient's delay was significantly associated sex, smoking, alcohol consumption, traveling by motorcycles, cough with sputum, chest pain, anorexia, first contact at private clinic, first contact with traditional healer, contact health provider by advisor, knowing about symptom suspect TB, knowing method to treatment TB, knowing method for preventing TB, perception TB center, perception barriers to contact health provider, perception travel facility, traveling through border, inconvenience to contact health provider, a few of health center, loss of information related TB, referral, heamoptisis, deapnea, check sputum, check sputum >3 time, sent sputum for culture and first treatment with antibiotic drugs, respectively.

Table 3 shows the results of the multivariate analysis of the correlation among risk factors and predicting variables as found that, cough with sputum, cough no sputum, chest pain, fever, hemoptysis and loss weight >10%, pay for travel correlated with patient delay. Theses seven predicting variables accounted 64% for patient's delay (R^2 at 0.64, 95% CI = 0.59-0.69). For health system delay from the univariate analysis of risk factors for prolong health system delay showed that significantly higher among age (r = -0.022, (p<0.001), education (p = 0.042), travel by taxi (p = 0.021), cough (p = 0.006), chest pain (p<0.028), anorexia (p = 0.04), loss weight >10% (p = 0.05), doubt ill with TB but

Table 1: The duration of patient delay, health system delay and total delay (n = 443)

Socio-demographic characteristics	Number	Percent
Patient delay		
≤28 days	115	25.96
>28 days	328	74.04
Median day (Q1, Q3)	51	(28, 98)
Health system delay		
≤14 days	330	74.49
>14 days	113	25.51
Median day (Q1, Q3)	4	(0, 16)
Total delay		
≤56 days	205	46.28
>56 days	238	53.72
Median day (Q1, Q3)	62	(31, 112)

Table 2: Backgrounds variables, health behavior, stigma, traveling factors and factors relate areas border

	Patient's delay		
Variables	>28 days n (%)	≤28 days n (%)	p value
Sex			
Male	208 (63.40)	79 (68.70)	0.019
Female	120 (36.60)	36 (31.30)	-
Smoke	207 (63.10)	79 (68.70)	0.001
Alcohol consumption	273 (72.30)	74 (64.30)	0.002
Travel by motorcycles	194 (59.15)	80 (69.57)	0.005
Cough with sputum	106 (32.40)	42 (36.50)	0.037
Chest pain	138 (42.70)	31 (27.20)	<0.001
Anorexia	140 (43.30)	29 (25.40)	0.005
First contact clinic	60 (18.30)	10 (8.70)	0.039
First contact traditional healer	14 (3.39)	1 (0.87)	0.009
First contact drugstore	44 (13.40)	6 (5.20)	0.017
Contact health provider by advisor	149 (45.40)	55 (47.80)	0.018
Know symptom suspect tuberculosis	113 (75.80)	26 (70.20)	0.027
Know method to treatment tuberculosis	100 (67.10)	26 (70.20)	0.044
Know method prevent tuberculosis	88 (59.10)	21 (56.70)	0.039
Unknown TB center	124 (37.80)	59 (51.30)	0.043
Barrier to contact health facility	117 (35.60)	25 (21.70)	0.001
Barrier of traveling	80 (68.30)	20 (80.00)	0.001
Traveling through border	125 (38.10)	35 (30.40)	0.023
Inconvenience to contact health facility	56 (17.10)	21 (18.20)	0.009
Inadequate of health facility	21 (6.40)	9 (7.80)	0.034
Lack of TB information	280 (83.30)	91 (79.10)	0.013
No referral	283 (86.28)	104 (90.40)	0.002
No hemoptysis	70 (21.40)	25 (21.70)	<0.001
Deapnea	201 (62.20)	88 (77.20)	<0.001
No check sputum	270 (82.30)	94 (81.70)	0.016
Check sputum>3 times	198 (61.30)	63 (57.80)	0.001
Sent sputum culture	316 (96.30)	111 (96.50)	<0.001
No chest X-ray	315 (96.00)	104 (90.40)	0.022
First treatment with biotic drug	301 (91.80)	106 (92.20)	0.014

Table 3: Multiple linear regression analysis of the predictors of patient's delay in new smear positive pulmonary tuberculosis in Thai-Cambodia border, 2008

	Partial regression coefficient				
VAR	B	β	95% CI of β	t	Sig. level
CWS	0.46	0.53	0.34-0.72	5.45	<0.001
CNS	0.28	0.49	0.29-0.68	5.05	<0.001
CP	0.43	0.32	0.09-0.56	2.72	<0.001
FA	0.20	0.22	-0.11-0.56	1.31	<0.001
CH	-0.01	0.44	0.21-0.68	3.75	<0.001
LW	0.14	0.10	-0.21-0.42	0.65	<0.001
PT	0.06	0.06	0.00-0.12	2.15	<0.001

Constant = 15.18, R = 0.80175, R^2 = 0.64 (95% CI = 0.59-0.69), $R^2_{Adjusted}$ = 0.638, F = 27.15, p value<0.05, VAR; Variables, , CWS; Cough With Sputum, CNS; Cough No Sputum, CP; Chest Pain, FA; Fever (after noon), CH; Cough (Hemoptysis), LW; Loss Weight >10%, PT; Pay for Travel

not do anything (p = 0.042), first contact clinic (p<0.001), first contact hospital (p<0.001), first contact other (p<0.001), advisor contact health provider (p = 0.038), percept TB knowledge from health provider (p = 0.05), percept TB knowledge from village heath volunteer (p = 0.045), percept TB knowledge from radio community (p = 0.011), percept TB knowledge from patient (p = 0.001), percept TB knowledge from television (p<0.001), percept causes of TB (p = 0.016), percept transmission of TB (p = 0.002), percept symptom suspect TB (p = 0.005), percept method for protecting TB (p = 0.001), percept severity for of TB (p = 0.004), perception cost of travel (p = 0.024), travel border (p = 0.031), perception travel facility and distant from health center (p = 0.002), loss of information related TB (p = 0.006), unknown TB disease and unawareness about Tb disease (p = 0.015), check sputum (p = 0.001), anorexia (p = 0.04), check sputum >3 time (p = 0.014) and other disease treatment (p<0.001), respectively.

From the multivariate analysis, six predicting factors correlated with prolong health system delay were first other symptoms, first diagnosis as other chest diseases, knowing TB from television, first contact at private hospital, travel through border and no action after having TB suspected symptoms correlated with health system delay. The model could predict this health system delay accounting for 16.8% (R^2 at 0.168, 95% CI = 0.11-0.23) as shown in Table 4. This study is the first of its kind to show the considerable delay of TB treatment among new smear positive TB patients in Thai Cambodia border. We set 28 days for cut off point of patient's delay and 14 days for health system delay.

The present cross-sectional study revealed that approximately one-third of TB patients initiated treatment >4 weeks after symptoms onset. The median delay among patients who live along Thai Cambodia border was 51, 4 and 62 days for patient's delay, health system delay and total delay which longer than previous study in the south of Thailand (31, 20 and 66 days). Rojpibulstit *et al.* (2006) but shorter when comparing with results of a systematic review about TB treatment delay new smear positive TB patients globally between 1987 and 2007 from 37 original articles which shown median length of patient's delay, health system delay and total delay of 24.5, 26.5 and 62 days.

It also demonstrated that predicting variables for longer patient's delay were sputum producing cough (56.2% of variance) and additional by cough with no sputum accounted for 15.33% of variance, chest pain accounted for 13.49%, paying for travel >50 baht accounted for 3.10% as predicter for prolong patient's

Table 4: Multiple linear regression analysis of the predictors of health system delay in new smear positive pulmonary tuberculosis in Thai-Cambodia border, 2008

	Partial regression coefficient				
VAR	B	β	95% CI of (β)	t	Sig. level
FOS	62.76	0.28	43.29-82.22	6.33	<0.001
FD	-10.48	-0.15	-16.18- to 4.78	-3.61	<0.001
TP	13.81	0.15	5.74-21.87	3.36	<0.001
FCPH	20.44	0.13	7.53-33.54	3.06	<0.002
TRB	-6.98	-0.10	-12.68- to 1.28	-2.40	<0.016
DTB	14.80	0.10	2.24-27.36	2.31	<0.021

Constant = 6.811, R = 0.41, R^2 = 0.168 (95% CI = 0.1155-0.2304), $R^2_{Adjusted}$ = 0.157, F = 14.656, p<0.001, FOS: First Other Symptom, FD: First Diagnostic, TP: Television Perception, FCPH: First Contact Private Hospital, TRB: Travel Border, DTB: Doubt of TB and none practice, VAR: Variables

delay. The study in Turkey showed good economic related to shorter patient's delay. In South Africa; larger size of family (>9 members) related to patient's delay as lower income in China. Longer distance from home to health care facilities caused longer patient's delay: 10, 5 and 2 km from the studies in Ethiopia India, China and USA. The predictors for shorter patient's delay were fever at afternoon, cough with hemoptysis and loss weight >10%, of dose and indicate the severity signs percept by the patina. Generally for rural residence, the symptoms that interrupt their career were more considerably to see the doctors. For cough and chest pain, if not interfere their daily activities, they might buy antitussive drugs themselves or seeing the doctors but were diagnostic as father chest diseases.

Lienhardt *et al.* (2001) and Chiang *et al.* (2005) found that haemoptysis were one of the initial symptoms for sorter patient's delay. Secondly, the multivariate analyzed the predictors for longer health system delay were first other symptoms, first diagnosis as other chest diseases, knowing TB from television, first contact at private hospital, travel through border and no action after having TB suspected symptoms. There are several studies shown that non-specific symptoms or absence of cough could suggest other diseases that related to longer health system's delay especially in those who failure to perform sputum examination or CXR-examination. Knowing TB information from television added for 9.52% of variance (B = 13.81; 95% CI = 5.74-21.87), β = 0.15, p<0.05) according to Rao *et al.* (1999) found that the most commonly reported source of information in the media was television. More men than women reported receiving TB information from the TV (71.4 vs. 51.3%, p = 0.0002). The next most common source was the radio (40.7%); however, none signifcant difference was found between men and women (p = 0.75). First contact The recommendations for reducing delay of treatment were base on the results and summarized as follow; Firstly, the

greatest delay of treatment were patient's delay (82.26%). The best way for reducing delay of treatment were reduced a patient's delay. Three strategies for reducing delay of treatment were constructed knowledge in patient, health provider and people in community. Second, perform public intervention could increase public awareness about TB with emphasis on severity of symptoms, suggestion and provide Information, Education and Communication (IEC) on TB could indicate in remote rural areas by advertisement board, spot radio, leaflet, training, performed network and the last performed referral system among community, private center (clinic, private hospital) and public health center. Private hospital accounted for 10.12% of variance (B = 20.44; 95% CI = 7.53-33.54), $\beta = 0.13$, $p<0.05$) related to the study of Huong *et al.* (2007), the study showed the factors associated with health system delay as follows: for long health care delay this was urban setting and initial visit to a communal health post, TB hospital or the private sector and the studies from Myanmar and Vietnam which first contact with private sectors that convenient and better place associated with longer SHD (Huong *et al.*, 2007; Saw *et al*., 2009). Traveling through border accounted for 7.14% of variance according to the study in Indonesia found that rural areas was the predictor for both PTD and HSD, similarly with systematic review that longer PTD, SSD were found in remote areas or special ethnic groups from various countries. The last factor for predicting health system delay was no action after having TB suspected symptoms accounted for 5.96% of variance. Miss perception and knowledge or inexperience in illness related to longer patient's delay as the study in Tanzania and Yemen were the patients with inadequate provided TB knowledge. In Uganda, patients who perceived smoking as cause of TB and believed that TB can be self treatment (Yemen *et al*., 2005).

Index case of TB in the family could gain experience about TB disease for family members that would contribute to shorter delay (Guneylioglu *et al*., 2004) and related with the study of Storla *et al.* (2008), the study found that the main factors associated with diagnostic delay included negative sputum smear; rural residence; low access initial visitation of a government low-level healthcare facility, private practitioner; low educational level and low awareness of TB.

CONCLUSION

In the border area, delays associated with symptoms relate to pulmonary tuberculosis; believe bases and general awareness towards pulmonary tuberculosis illness. Although PTB intensive cares in health care services are organized and delays are not associated with access to care, delay can leads to an increased period of infectivity and transmission in the community.

RECOMMENDATIONS

Other suggestions and further researches were monitoring trend of delay in order to measure the impact of DOTS or DOT by heart implementation and identifying opportunities to further reduce delays in TB, study in delay over a wider range and more extensive/comprehensive, study in relationship between factors identified and poverty to enable the development of interventions and finding out the potential areas for intervention to reduce delay, be setting-specific for the effectiveness and assessment of those intervention.

LIMITATION

Limitation of this study may arise from patient's inability to recall the exact data of onset of symptoms and some factors detail. However, to minimize variations in estimating patient's delay, interviewer used major national and local events or using seasonal and religious to facilitate patients' recall.

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