Prevalence and Factors Associated with Unsuccessful Pulmonary Tuberculosis Treatment in Thai Military Hospitals

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Abstract:

Background: Thailand is one of high TB burden countries. Military hospitals have been providing TB care for both military officers and civilians. However, there has never been studies of TB treatment in these hospitals in large scale.

Objective: This study aimed to report prevalence and associated factors of unsuccessful pulmonary TB treatment outcomes among Thai military hospitals.

Materials and Methods: A cross-sectional study was conducted in nine military hospitals across four regions of Thailand. Data from 2012 to 2021 were collected which included demographic and follow-ups data. Outcomes were successful and unsuccessful treatment. Logistic regression was used for predicting associated factors of unsuccessful pulmonary TB treatment.

Results: Prevalence of unsuccessful TB treatment was 17.72%. Associated factors of unsuccessful treatment included being agriculturist, laborer and household business owner, fever and weight, not investigated sputum culture, abnormal liver function test (LFT) and blood urea nitrogen (BUN) at the start, positive sputum AFB and uninvestigated sputum AFB at second month follow-up, uninvestigated chest radiograph at fifth month and unmonitored weight throughout treatment. Protective factor was having cutaneous adverse reactions during follow-up.

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Conclusion: Several factors associated with unsuccessful pulmonary TB treatment outcomes were system-related or individual factors. Establishing community-based treatment system can be a solution.

Keywords: Pulmonary tuberculosis, Prevalence; Associated factor, Thailand

Introduction

TB has been one of the leading causes of death globally despite advanced and adequate medical care in the past five decades.[1] It was estimated that a quarter of world's population is infected with TB.[2] Although new TB cases are decreasing, but the process was slow.[1]

Regarding Thailand, challenges to TB management strategies in the past years included high mortality, late diagnosis, duplications in monitoring and evaluation systems, under-reported from non-Ministry of Public Health settings, insufficient coverage of multi-drug resistance tuberculosis (MDR-TB) detection and difficulties in accessing TB care for migrant workers.[3]

Military hospitals, as secondary and tertiary care units, have long been providing healthcare services for both military, civilian officers and civilian as well as their families including TB diagnosis, monitoring and treatment. However, military hospitals are not under supervision by Ministry of Public Health and the specific reports of TB treatment in military hospitals were sporadic. In addition, there has never been studies of TB treatment in these hospitals in large scale. To address this problem, this study aimed to report prevalence and associated factors of unsuccessful pulmonary TB treatment outcomes among Thai military hospitals.

Methods

Study design and setting

A cross-sectional study was conducted in nine military hospitals across four regions of Thailand. Data from 2012 to 2021 were collected. Two military hospitals are from each region except for central region which has three hospitals. One hospital in central region located in Bangkok, capital city of Thailand. Eight hospitals are secondary care units and one hospital in Bangkok is tertiary care center as well as being a teaching hospital.

Study population

This study included all patients receiving pulmonary TB treatment. Excluded were patients who has extrapulmonary TB without co-existing pulmonary TB and latent TB.

Data collection

Data stored in TB registration cards, outpatient records and computer-stored information of patients receiving TB treatment at each hospital from 2012 to 2021 were collected with permission from hospitals' directorial boards. Collected data included demographic data (gender, age, occupation, hospital and past medical history), baseline characteristics at start of treatment (registered status, weight, clinical symptoms, chest radiographs, sputum acid-fast bacilli (AFB), sputum gene X-pert, sputum culture, liver function tests, renal function tests and drug regimen) and follow-ups data before 2 months, at second month and at fifth month (sputum AFB, chest radiographs and drug adverse effects). Results of treatment were collected at either sixth month or final month of treatment in case of prolonged treatment regimen. The results included 'cure', 'complete', 'fail', 'transferred out', 'loss to follow-up' and 'death'.

Operational definitions

According to WHO[4] and Thai national tuberculosis control programme guideline[5], pulmonary TB is a case of TB involving the lung parenchyma. Treatment outcomes

included 'cure', 'complete', 'fail', 'transferred out', 'loss to follow-up' and 'death'. Cured is defined as sputum AFB smear or culture is negative at the end of treatment. Completion is considered if the treatment was completed, but without evidence of negative sputum AFB smear or culture results in the last month of treatment, but the latest sputum smear is negative. Failure is defined when the sputum AFB smear or culture is positive at the fifth month or later. Death includes all patients who died from any causes during treatment. Loss to follow-up is characterized by interruption of treatment for two or more consecutive months. Transferred out is considered when a patient was transferred to other treatment facilities without known final treatment result. Cure and complete were categorized into 'successful treatment', while fail, transferred out and loss to follow-up were regarded as 'unsuccessful treatment.

Statistical analysis

Statistical analysis was performed with SPSS 23.0 (Armonk, New York, U.S.). Descriptive statistics was used for describing characteristics of the studied population. Univariate analysis was used for predicting associated factors of unsuccessful pulmonary TB treatment. Factors which had p-value < 0.20 and significant in previous studies were recruited for multivariate analysis using 'Enter' function. Factors with p-value ≤ 0.05 at 95% confidential interval (CI) were considered statistically significant.

Ethical consideration

This study was approved by Institutional Review Board of Royal Thai Army Medical Unit numbering S040h/63_Exp. Data were collected with permission from each hospital's directorial boards.

Results

A total of 2,307 cases were collected from all hospitals. After data cleaning by filtering out incomplete demographics, follow-ups data and final treatment results, 2,003 cases were available for analysis.

Demographic data

Most patients were from hospital in Bangkok Metropolis (74.39%) and male (70.19%). Average age was 48.35 ± 19.44 years with most patients' age range was 21-30 years (22.27%) followed by 51-60 years (20.57%). Approximately 64.35% had HIV co-infection. Around 8.09% had history of TB contact, 4.89% had history of previous TB and 2.08% had co-existing extrapulmonary TB. Most patients presented with chronic cough (59.41%). Around 34.90% had reticulonodular infiltration. Most were smear-negative TB (50.50%). Around 40.84% did not receive DOT (directly observed therapy). Demographic data and baseline characteristics were shown in Table 1.

Table 1 Demographic and baseline characteristics of patients receiving TB treatment in Thai military hospitals

Characteristics	N (%)
Hospital region	
Bangkok Metropolis	1490 (74.39)
Southern region	220 (10.98)
Northern and Northeastern regions	127 (6.34)
Central region	166 (8.29)
Gender	
Male	1406 (70.19)
Female	597 (29.81)
Occupation	
Laborer	602 (30.05)
Military officer	526 (26.26)
Civilian officer	144 (7.19)
Trader/merchant	88 (4.39)
Student	71 (3.54)
Household business	57 (2.85)
Agriculturist	51 (2.55)
Healthcare providers	14 (0.70)
Unemployed	450 (22.47)
Age (years)	
< 20	32 (1.60)
20-29	439 (21.92)
30-39	256 (12.78)
40-49	291 (14.53)
50-59	402 (20.07)
60-69	237 (11.83)
70-79	212 (10.58)
≥ 80	134 (6.69)
Mean (age ± S.D.)	48.35 ± 19.44
Registration status	
New	1905 (95.11)
Relapse	71 (3.54)

Characteristics	N (%)
Treatment after loss to follow-up	23 (1.15)
Treatment after failure	4 (0.20)
TB drug regimen at start	
2 HRZE/4HR	1924 (96.06)
2 HRZES/1HRZE/5HRE	32 (1.60)
MDR regimen	39 (1.95)
Other regimens	8 (0.40)
Medical history and co-morbid illnesses	
HIV infection	
Yes	1289 (64.35)
No	714 (35.65)
Diabetes mellitus	
Yes	906 (45.23)
No	1097 (54.77)
Chronic lung diseases	
Yes	34 (1.70)
No	1969 (98.30)
Kidney diseases	
Yes	21 (1.05)
No	1982 (98.95)
Liver diseases	
Yes	11 (0.55)
No	1992 (99.45)
History of TB contact	
Yes	162 (8.09)
No	1841 (91.91)
Previous history of TB	
Yes	98 (4.89)
No	1905 (95.11)
Presence of extra-pulmonary TB	
Yes	56 (2.80)
No	1947 (97.20)

Characteristics	N (%)
Malnutrition	
Yes	13 (0.65)
No	1990 (99.35)
BCG vaccination	
Yes	1872 (93.46)
No	131 (93.46)
History of imprisonment	
Yes	15 (0.75)
No	1988 (99.25)
Initial clinical presentation	
Chronic cough (> 2 weeks)	
Yes	1190 (59.41)
No	813 (40.59)
Fever	
Yes	577 (28.81)
No	1426 (71.19)
Weight loss	
Yes	575 (28.71)
No	1428 (71.29)
Hemoptysis	
Yes	249 (12.43)
No	1754 (87.57)
Initial chest radiographs	
Reticulonodular infiltration	
Yes	699 (34.90)
No	1304 (65.10)
Miliary shadow	
Yes	57 (2.85)
No	1946 (97.15)
Lung cavity	
Yes	242 (12.08)
No	1761 (87.92)

Characteristics	N (%)
Pleural effusion	
Yes	190 (9.49)
No	1813 (90.51)
Initial sputum AFB	
Positive	985 (42.70)
Negative	1165 (50.50)
Not investigated	157 (6.81)
Initial sputum Gene X-pert	
MTB not detected	221 (11.03)
MTB detected	50 (2.50)
Error	1 (0.05)
Not investigated	1731 (86.42)
Initial sputum Culture	
No growth	463 (23.12)
M.TB detected	549 (27.41)
Contaminated	3 (0.15)
Not investigated	988 (49.33)
Initial AST level	
Normal	824 (35.72)
Abnormal (> 40 U/L)	215 (9.32)
Not investigated	1268 (54.96)
Initial ALT level	
Normal	858 (37.19)
Abnormal (> 40 U/L)	186 (8.06)
Not investigated	1263 (54.75)
Initial BUN level	
Normal	849 (36.80)
Abnormal (> 20 mg/dL)	121 (5.24)
Not investigated	1337 (57.95)
Initial creatinine level	
Normal	909 (39.40)
Abnormal (> 1.2 mg/dL)	93 (4.03)
Not investigated	1305 (56.57)

Characteristics	N (%)
DOT	
By hospital staffs	964 (48.13)
By healthcare volunteers	190 (9.49)
By relatives	8 (0.40)
By unknown personnel	23 (1.15)
Not DOT	818 (40.84)
Vitamin B6 prescription	
Yes	1091 (54.47)
No	912 (45.53)

Follow-ups and results of treatment

Most patients were followed-up before second month (81.13%) with 4.39% had cutaneous adverse drug reactions. At second month follow-up, 30.65% still had cough, 35.45% had reticulonodular infiltration in chest radiographs and 6.59% still had positive sputum AFB. During fifth month follow-up, 14.63% still had reticulonodular infiltration. Most patients had increasing weight compared with weight at the start of treatment (39.59%). At the end, 33.15% completed treatment, 19.87% cured, 9.34% loss to follow-up, 3.99% died, 3.94% transferred out and 0.45% failed the treatment. Follow-up data was displayed in Table 2.

Table 2 Follow-ups of pulmonary TB treatment and results of treatment

Follow-up characteristics	N (%)
Follow-up before 2nd month	
Follow-up	
Yes	1625 (81.13)
No	378 (18.87)
Cutaneous adverse drug reactions	
Yes	88 (4.39)
No	1915 (95.61)
Follow-up 2nd month	
Cough	
Yes	614 (30.65)
No	1389 (69.34)
Chest radiographs	
Reticulonodular infiltration	710 (35.45)

Follow-up characteristics	N (%)
Pleural effusion	95 (4.74)
Lung cavity	45 (2.25)
Miliary shadows	21 (1.05)
Multiple lung lesions	98 (4.89)
Normal	25 (1.25)
Not investigated	1009 (50.37)
Sputum AFB	
Positive	132 (6.59)
Negative	1195 (59.66)
Not investigated	676 (33.75)
Follow-up 5th month	
Chest radiographs	
Reticulonodular infiltration	293 (14.63)
Pleural effusion	48 (2.40)
Lung cavity	24 (1.20)
Miliary shadows	6 (0.30)
Multiple lung lesions	40 (2.00)
Normal	38 (1.90)
Not investigated	1554 (77.58)
Sputum AFB	
Positive	29 (1.45)
Negative	658 (32.85)
Not investigated	1316 (65.70)
Overall weight difference from start	
Increased	793 (39.59)
No change	172 (8.59)
Decreased	597 (29.81)
Not weighed	441 (22.02)
Change of regimen from start	
Yes	253 (12.63)
No	1750 (87.37)

Follow-up characteristics	N (%)
Results of treatment	
Successful	
Completed	984 (49.13)
Cured	664 (33.15)
Unsuccessful	
Loss to follow-up	187 (9.34)
Death	80 (3.99)
Transferred	79 (3.94)
Failed	9 (0.45)

Factors associated with unsuccessful pulmonary TB treatment

Associated factors of unsuccessful treatment included being agriculturist (p = 0.005, 95% CI 1.47-8.56), laborer (p = 0.017, 95% CI 1.13-3.66) and household business (p = 0.041, 95% CI 1.04-6.24), symptoms presented with fever (p = 0.024, 95% CI 1.12-1.81) and weight loss (p = 0.044, 95% CI 1.05-1.91) at the beginning of treatment, sputum culture was not collected for investigation at the start of treatment (p = 0.001, 95% CI 1.28-2.46), having abnormal liver function test (LFT) at the start (p = 0.002, 95% CI 1.25-2.72) and having abnormal blood urea nitrogen (BUN) at the start (p = 0.034, 95% CI 1.11-3.40). During second month follow-up, positive sputum AFB (p = 0.001, 95% CI 1.38-3.79) and sputum AFB not collected for investigated (p < 0.0001, 95% CI 1.32-2.35) were associated with unsuccessful treatment as well as uninvestigated chest radiograph (p = 0.046, 95% CI 1.03-59.31). Patients whose weight was not monitored through the treatment were associated with unsuccessful treatment as well (p < 0.0001, 95% CI 1.56-3.10). On the contrary, protective factors of unsuccessful treatment included having cutaneous adverse reactions during follow-up (p = 0.019, 95% CI 0.15-1.21). The whole results were displayed in Table 3.

Table 3 Univariate and multivariate analysis of associated factors of unsuccessful TB treatment outcomes

Factors	Treatment outcomes		Univariate analysis			Multivariate analysis		
	Successful N (%)	Unsuccessful N (%)	Crude OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
Hospital setting								
Bangkok Metropolis	1204 (80.81)	286 (19.19)	1	-	-	1	-	-
Other provinces	444 (86.55)	69 (13.558)	0.65	0.49-0.87	0.003	0.65	0.40-1.06	0.082
Gender								
Male	1143 (81.29)	263 (18.71)	1	-	-	1	-	-
Female	505 (84.59)	92 (15.41)	0.792	0.61-1.03	0.078	0.87	0.64-1.17	0.353
Occupation								
Civilian officer	127 (88.19)	17 (11.81)	1	-	-	1	-	-
Agriculturist	38 (74.51)	13 (25.49)	2.56	1.14-5.73	0.023	3.54	1.47-8.56	0.005*
Laborer	487 (80.90)	115 (19.10)	1.76	1.02-3.04	0.041	2.04	1.13-3.66	0.017*
Military officer	426 (80.99)	100 (19.01)	1.75	1.01-3.04	0.046	1.81	1.00-3.28	0.051
Traders/merchant	74 (84.09)	14 (15.91)	1.41	0.66-3.03	0.374	1.67	0.73-3.80	0.222
Household business	46 (80.70)	11 (19.30)	1.79	0.78-4.10	0.171	2.55	1.04-6.24	0.041*
Healthcare provider	12 (85.71)	2 (14.29)	1.25	0.26-6.05	0.786	2.23	0.42-11.97	0.348
Students	58 (81.69)	13 (18.31)	1.67	0.76-3.68	0.199	1.87	0.80-4.38	0.150
Unemployed	380 (84.44)	70 (15.56)	1.38	0.78-2.43	0.269	1.51	0.82-2.78	0.189
Age								
< 20	26 (81.25)	6 (18.75)	1	-	-			
20-29	344 (78.36)	95 (21.64)	1.12	0.48-2.99	0.701			
30-39	215 (83.98)	41 (16.02)	0.83	0.32-2.13	0.693			

Factors	Treatment outcomes		Univariate analysis			Multivariate analysis		
	Successful N (%)	Unsuccessful N (%)	Crude OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
40-49	232 (79.73)	59 (20.27)	1.10	0.43-2.80	0.838			
50-59	348 (86.57)	54 (13.43)	0.67	0.27-1.71	0.404			
60-69	204 (86.08)	33 (13.92)	0.70	0.27-1.83	0.469			
70-79	175 (82.55)	37 (17.45)	0.92	0.35-2.38	0.858			
≥ 80	104 (77.61)	30 (22.39)	1.25	0.47-3.32	0.654			
Medical history and co-morbid illnesses								
HIV infection								
No	605 (84.73)	109 (15.27)	1	-	-	1	-	-
Yes	1043 (80.92)	246 (19.08)	1.31	1.02-1.68	0.032	1.06	0.73-1.54	0.763
Diabetes mellitus								
No	902 (82.22)	195 (17.78)	1	-	-			
Yes	746 (82.34)	160 (17.66)	0.992	0.79-1.25	0.946			
Chronic lung diseases								
No	1620 (82.28)	349 (17.72)	1	-	-			
Yes	28 (82.35)	6 (17.65)	0.995	0.41-2.42	0.991			
Liver diseases								
No	1640 (82.23)	352 (17.67)	1	-	-			
Yes	8 (72.73)	3 (27.27)	1.75	0.46-6.62	0.412			
Chronic kidney disease								
No	1629 (82.19)	353 (17.81)	1	-	-			
Yes	19 (90.48)	2 (9.52)	0.49	0.11-2.10	0.333			

Factors	Treatment outcomes		Univariate analysis			Multivariate analysis		
	Successful N (%)	Unsuccessful N (%)	Crude OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
Malnutrition								
No	1636 (82.21)	354 (17.79)	1	-	-			
Yes	12 (92.31)	1 (7.69)	0.39	0.05-2.97	0.360			
History of TB contact	1517 (82.40)	324 (17.60)	1	-	-			
No	131 (80.86)	31 (19.14)	1.11	0.74-1.67	0.624			
Yes								
Previous history of TB								
No	1564 (82.10)	341 (17.90)	1	-	-			
Yes	84 (85.71)	14 (14.29)	0.76	0.43-1.36	0.362			
Presence of extra-pulmonary TB	1601 (82.23)	346 (17.77)	1	-	-			
No	47 (83.93)	9 (16.07)	0.89	0.43-1.83	0.743			
Yes								
History of imprisonment								
No	1647 (82.19)	357 (17.81)	1	-	-			
Yes	12 (80.00)	3 (20.00)	1.15	0.32-4.11	0.826			
BCG vaccination								
Yes	1557 (82.47)	331 (17.53)	1	-	-	1	-	-
No	102 (77.86)	29 (22.14)	1.34	0.87-2.05	0.184	1.18	0.72-1.94	0.500
Initial clinical presentation								
Chronic cough (> 2 weeks)								
No	660 (80.49)	160 (19.51)	1	-	-	1	-	-
Yes	999 (83.32)	200 (16.68)	0.83	0.66-1.04	0.103	0.78	0.58-1.04	0.092

Factors	Treatment outcomes		Univariate analysis			Multivariate analysis		
	Successful N (%)	Unsuccessful N (%)	Crude OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
Hemoptysis								
No	1453 (82.84)	301 (17.16)	1	-	-	1	-	-
Yes	195 (78.31)	54 (21.69)	1.32	0.96-1.83	0.089	1.35	0.93-1.96	0.113
Fever								
No	1187 (83.24)	239 (16.76)	1	-	-	1	-	-
Yes	461 (79.90)	116 (20.10)	1.27	1.00-1.62	0.054	1.35	1.12-1.81	0.024*
Weight loss								
No	1188 (83.19)	240 (16.81)	1	-	-	1	-	-
Yes	460 (80.00)	115 (20.00)	1.26	0.99-1.61	0.061	1.41	1.05-1.91	0.044*
Initial chest radiographs								
Normal	25 (80.65)	6 (19.35)	1	-	-			
Reticulonodular infiltration	927 (82.25)	200 (17.75)	0.90	0.36-2.22	0.817			
Miliary shadows	42 (89.36)	5 (10.64)	0.50	0.14-1.80	0.285			
Lung cavity	86 (85.15)	15 (14.85)	0.73	0.26-2.07	0.550			
Pleural effusion	122 (80.26)	30 (19.74)	1.03	0.39-2.72	0.961			
Multiple lung lesions	155 (85.64)	26 (14.36)	0.70	0.26-1.87	0.475			
Not investigated	291 (79.95)	73 (20.05)	1.05	0.41-2.64	0.925			
Initial sputum AFB								
Negative	831 (82.11)	181 (17.89)	1	-	-			
Positive	718 (82.43)	153 (17.57)	0.98	0.77-1.24	0.856			
Not investigated	99 (82.50)	21 (17.50)	0.97	0.59-1.60	0.917			

Factors	Treatment outcomes		Univariate analysis			Multivariate analysis		
	Successful N (%)	Unsuccessful N (%)	Crude OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
Initial sputum gene X-pert								
M.TB not detected	181 (81.90)	40 (18.10)	1	-	-			
M.TB detected	37 (74.00)	13 (26.00)	1.59	0.78-3.26	0.206			
Error	1 (100.00)	0 (0.00)	-	-	-			
Not investigated	1429 (82.55)	302 (17.45)	0.96	0.66-1.38	0.810			
Initial sputum culture								
No growth	399 (86.18)	64 (13.82)	1	-	-	1	-	-
M.TB detected	481 (87.61)	68 (12.39)	0.88	0.61-1.27	0.499	0.80	0.54-1.20	0.280
Contaminated	3 (100.00)	0 (0.00)	-	-	-	-	-	-
Not investigated	765 (77.43)	223 (22.57)	1.82	1.34-2.46	< 0.0001	1.78	1.28-2.46	0.001*
Initial LFT								
Normal	581 (82.88)	120 (17.12)	1	-	-	1	-	-
Abnormal (AST or ALT > 40 U/L)	169 (72.53)	64 (27.47)	1.83	1.29-2.60	0.001	1.84	1.25-2.72	0.002*
Not investigated	171 (16.00)	0.92	0.71-1.19	0.533	0.75	0.51-1.11	0.148	
Initial BUN level								
Normal	621 (82.14)	135 (17.86)	1	-	-	1	-	-
Abnormal (> 20 mg/dL)	75 (71.43)	30 (28.57)	1.84	1.16-2.92	0.010	1.90	1.04-2.96	0.034*
Not investigated	952 (83.36)	190 (16.64)	0.92	0.72-1.17	0.490	1.29	0.82-1.75	0.350
Initial creatinine level								
Normal	655 (81.77)	146 (18.23)	1	-	-			
Abnormal (> 1.2 mg/dL)	67 (77.91)	19 (22.09)	1.27	0.74-2.18	0.382			
Not investigated	926 (82.97)	190 (17.03)	0.92	0.73-1.17	0.495			

Factors	Treatment outcomes		Univariate analysis			Multivariate analysis		
	Successful N (%)	Unsuccessful N (%)	Crude OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
DOT (directly observed therapy)								
Yes	995 (83.97)	190 (16.03)	1	-	-	1	-	-
No	653 (79.83)	165 (20.17)	1.32	1.05-1.67	0.018	1.15	0.89-1.49	0.299
Vitamin B6 prescription								
Yes	912 (83.59)	179 (16.41)	1	-	-	1	-	-
No	736 (80.70)	176 (19.30)	1.22	0.97-1.53	0.092	1.29	0.91-1.68	0.055
Cutaneous adverse drug reactions after treatment								
No	1566 (81.78)	349 (18.22)	1	-	-	1	-	-
Yes	82 (93.18)	6 (6.82)	0.33	0.14-0.76	0.009	0.35	0.15-0.85	0.019*
Cough at the end of 2nd month								
No	1113 (80.13)	276 (19.87)	1	-	-	1	-	-
Yes	535 (87.13)	79 (12.87)	0.595	0.45-0.78	< 0.0001	0.88	0.64-1.21	0.445
Chest radiographs at the end of 2nd month								
Normal	24 (96.00)	1 (4.00)	1	-	-	1	-	-
Reticulonodular infiltration	619 (87.18)	91 (12.82)	3.53	0.47-26.40	0.219	3.66	0.48-28.19	0.200
Miliary shadows	18 (85.71)	3 (14.29)	4.00	0.38-41.70	0.246	5.54	0.51-60.58	0.161
Lung cavity	40 (88.89)	5 (11.11)	3.00	0.33-27.23	0.329	3.52	0.37-33.53	0.273
Pleural effusion	85 (89.47)	10 (10.53)	2.82	0.34-23.17	0.334	2.14	0.25-18.40	0.488
Multiple lung lesions	80 (81.63)	18 (18.37)	5.40	0.69-42.57	0.109	6.38	0.78-52.47	0.085
Not investigated	782 (77.50)	227 (22.50)	6.97	0.94-51.78	0.058	4.31	0.56-32.92	0.159

Factors	Treatment outcomes		Univariate analysis			Multivariate analysis		
	Successful N (%)	Unsuccessful N (%)	Crude OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
Sputum AFB at the end of 2nd month								
Negative	1047 (87.62)	148 (12.38)	1	-	-	1	-	-
Positive	105 (79.55)	27 (20.45)	1.82	1.15-2.87	0.010	2.29	1.38-3.79	0.001*
Not investigated	496 (73.37)	180 (26.63)	2.57	2.02-3.27	< 0.0001	1.76	1.32-2.35	< 0.0001*
Chest radiographs at the end of 5th month								
Normal	37 (97.37)	1 (2.63)	1	-	-	1	-	-
Reticulonodular infiltration	274 (93.52)	19 (6.48)	2.57	0.33-19.73	0.365	2.23	0.28-17.86	0.450
Miliary shadows	6 (100.00)	0 (0.00)	-	-	-	-	-	-
Lung cavity	23 (95.83)	1 (4.17)	1.61	0.10-27.00	0.741	1.55	0.09-27.72	0.765
Pleural effusion	45 (93.75)	3 (6.25)	2.47	0.25-24.72	0.443	2.00	0.19-21.33	0.566
Multiple lung lesions	38 (95.00)	2 (5.00)	1.95	0.17-22.40	0.593	1.18	0.10-14.56	0.900
Not investigated	1225 (78.83)	329 (21.17)	9.94	1.36-72.70	0.024	7.83	1.03-59.31	0.046*
Overall weight difference from start								
Increased	694 (87.52)	99 (12.48)	1	-	-	1	-	-
No change	150 (87.21)	22 (12.79)	1.03	0.63-1.69	0.912	1.07	0.62-1.86	0.801
Decreased	509 (85.26)	88 (14.74)	1.21	0.89-1.65	0.223	1.30	0.93-1.81	0.119
Not weighed	295 (66.89)	146 (33.11)	3.47	2.60-4.63	< 0.0001	2.20	1.56-3.10	< 0.0001*
Change of regimen from start								
No	1447 (82.69)	303 (17.31)	1	-	-			
Yes	201 (79.45)	52 (20.55)	1.24	0.89-1.72	0.208			

* Significant at 95% CI

Discussion

This study addressed prevalence and associated factors of unfavorable TB treatment outcomes. At 17.72%, the prevalence of unsuccessful pulmonary TB treatment in military settings was comparable to previous studies conducted in other secondary or tertiary care units.[6-8] This number might reflect the universal rate of TB treatment outcomes among all settings, disregarding supervision by Ministry of Public Health. However, most of the unsuccessful treatment cases were attributed to loss to follow-up which contrasted to previous studies in Thailand of which death was the most common cause of unsuccessful treatment.[6-9]

In this study, being agriculturists, laborers and business owner were associated with unsuccessful treatment. Agriculturists and laborers likely to be linked to low socio-economic status, low educational level and rural living.[10,11] Household business, in this context, usually referred to small household business which usually associated with low- and middle-income socioeconomic levels. These factors were addressed to be associated with unsuccessful TB treatment in previous studies.[9,12,13] To cope with unsuccessful treatment, management in community level and to be more exact, individual level, is essential.

Initial clinical presentation also correlated with clinical outcomes. In this study, fever and weight loss were associated with unsuccessful treatment. Fever was reported to be one of the most common clinical features of pulmonary TB, along with chronic cough and weight loss.[14,15] In a previous study, people who were underweight were significantly presented with fever and weight loss.[16] This might be implied that people who were underweight (BMI<18.5) at the diagnosis, which might be initially presented with fever and weight loss, usually had higher risk of treatment failure and death.[16,17] As a result, fever and weight loss were associated with unsuccessful treatment outcome. However, this study did not indicate that underlying malnourishment was associated with unfavorable treatment outcomes as well as decreased weight in the overall treatment course.

This study found that people who was not weighed or monitored throughout the treatment were significantly associated with treatment failure. Patients who were not weighed at the beginning of treatment might be missed for low BMI status, which associated with unsuccessful treatment. Also, patients whose weight were not monitored in the subsequent follow-ups might include those who loss to follow-up, died or transferred out. A study in Vietnam found that weight loss during first two months of treatment might associated with poor treatment response due to drug resistance, malnourishment and HIV co-infection.[18] Weight reduction during TB treatment was also linked to drug-induced hepatotoxicity[18,19] of which the patient usually had lower favorable treatment outcome.[20] As a result, in patients who remain at the treatment facilities, weight monitoring should be done in follow-ups.

People whose sputum culture was not investigated at the beginning of treatment were more likely to have unfavorable treatment outcome. Diagnostic methods of MDR-TB included drug susceptibility test and culture.[21] Sputum culture also plays a major role in monitoring response to treatment in MDR-TB patients.[21,22] In some settings where laboratory resources are limited for sputum culture or gene X-pert, logistic processing is required for sputum transportation to more advanced laboratory of which it usually add additional duration to obtain the result.[21,23] As a result, some facilities decide not to send the sputum for culture or gene X-pert at all. This might lead to the treatment regimen does not match TB strains.

The trend of unsuccessful treatment among patients whose sputum AFB was positive or not performed at the end of intensive phase (2nd month) was observed. According to Thai National Guideline, in new pulmonary TB patients, sputum AFB should be performed at the end of intensive phase and at the fifth month.[5] Sputum AFB follow ups can determine treatment outcomes, especially at the end of intensive phase.[24,25] Previous studies indicated that positive sputum AFB at the end of intensive phase might be due to patients' poor compliance and drug-resistance TB[8,24,26] , while positive sputum AFB at the 5th month was an indicator of treatment failure.[4,5] In a previous study, uninvestigated sputum AFB can be caused by poor treatment compliance, receiving out-of-track management or missing cases follow-up.[8]

This study found that the proportion of unsuccessful treatment among patients whose sputum AFB positive or not investigated at the end of intensive phase were towering. Thai National Guideline had imposed the regulations for patients whose sputum AFB were positive at the end of intensive to have sputum gene X-pert and culture investigated.[5] However, these indicators took several days to weeks to accomplish the result.[21,23] Other rapid diagnostic tests for treatment resistance should be developed to alleviate this problem.

Uninvestigated chest radiograph at the fifth month was associated with unsuccessful treatment. Chest radiograph was usually taken for all patients at the end of intensive phase and at the end of treatment, according to Thai National Guideline.[21] There was no recommendation on chest radiography at the fifth month of treatment. However, unimproved chest radiograph at the fifth month can predict treatment failure.[25] In a previous study, no radiographic improvement on CXR at the fifth month.[25] Thus, monitoring this parameter at fifth month might enhance treatment success.

This study found that abnormal LFT (either elevated AST or ALT or both) was significantly related to unsuccessful TB treatment. Hepatitis was noted to be associated with unsuccessful TB treatment due to various factors such as change in regimen, treatment interruption, liver failure and death.[20,27,28] Thus, it is suggested to examine liver function of every TB patient before initiate treatment.

The unsuccessful treatment was also found in patients with elevated BUN. It cannot be concluded that elevated BUN solely is defined as chronic kidney disease. Elevated BUN can be caused by several factors, not only chronic kidney disease, which is associated with unsuccessful TB treatment.[29,30] However, elevated BUN in the absence of renal disease or high creatinine was previously reported to be associated with death in miliary TB patients due to dehydration tendencies or hypercatabolism.[31]

Cutaneous adverse drug reaction was reported to be a protective factor of unsuccessful treatment. There are limited data on suggestion on patients with severe cutaneous adverse drug reaction are required to interrupt the treatment with most interruptions are based upon the knowledge that treatment should be interrupted if any adverse drug reaction occurred.[32] There is still controversy regarding cutaneous adverse drug reaction and treatment outcomes as well as patients' adherence to therapy following adverse drug reaction.[32] Although treatment interruption might be associated with treatment failure and death[33], it was usually due to patients' own incompliance to treatment than interruption due to adverse drug reaction by physicians.[32] However, non-severe cutaneous adverse drug reaction might not require treatment interruption, but usually require only anti-histamine medication.[34]

This study hypothesized that in this setting, most patients were not affected by serious cutaneous adverse drug reaction and having good adherence to the treatment. Also, having cutaneous drug reaction might provoke concerns of both patients to be adhere to treatment and healthcare providers to be more specifically monitor the patient.

This study discovered several factors associated with unsuccessful pulmonary TB treatment outcomes. Many of these factors were system-related such as patient tracking, patient follow-up visits and monitoring, proper facilities and recording of patient treatment history. Others included individual factors such as individual's compliance and adherence to the treatment system. To enhance treatment success, establishing community-based treatment system can be a solution. Community-based treatment system can deliver fast and efficient TB diagnosis, treatment, monitoring and follow ups better than hospital-based system which patients require several resources to access the treatment and healthcare workers have multiple workloads to deal with than specifically monitoring and exploring each patient's problems. In addition, attaching TB treatment system in military hospitals to the national TB information program established by Ministry of Public Health would make each patient's data regarding TB treatment history be systematically collected, standard and easier to monitor.

There were some limitations in this study. First, some patients' treatment data from some of the studied hospitals, especially the older data, were registered in paper form and was not scanned to the computer system. Thus, some data in the older years were loss. Second, some hospitals in this study did not register to national TB information program. This resulted in difficulty to retrieve patients' data, laboratory results and date of treatment. Third, the database did not include CD4 level of HIV patients.

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