



RESEARCH ARTICLE

Detection and factors associated with tuberculosis and rifampicin resistance among presumptive patients at the Thailand-Myanmar border

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ARTICLE HISTORY

Received: 8 August 2022

Revised: 19 September 2022

Accepted: 20 September 2022

Published: 30 November 2022

ABSTRACT

Tuberculosis (TB) continues to be a major public health problem in Thailand and many countries. Endemic TB and outbreaks of TB drug resistance in the borderlands are particularly important. The Thailand-Myanmar border has extensive cross-border travel that may accelerate TB's spread. This cross-sectional study aimed to determine the frequency and factors associated with TB, and rifampicin-resistant TB (RR-TB) among presumptive tuberculosis patients in Mae Sot Hospital. Sputum was processed by microscopic examination and Xpert MTB/RIF assay. Laboratory results and socio-demographic characteristics were collected and analyzed. Univariate and multivariate analyses were performed to assess the association of the risk factors with TB and RR-TB. The significant variables at p -values < 0.05 in univariate analysis were selected for multivariate analysis. Of 365 presumptive patients enrolled, 244 (66.85%) were males and 199 (54.52%) were Burmese. Of these, 314 (86.03%) were registered as new cases and 183 (50.14%) worked as laborers. Sputum microscopy was positive in 132 (36.16%) cases. Based on Xpert MTB/RIF, the frequency of TB was 136 (37.26%) and RR-TB was 15 (11.03%). TB was more common in males than females. The majority of the cases belonged to the 26-50-year-old age group and migrant workers. In RR-TB detection, the *rpoB* mutations covered by probe E were the most frequently observed. Sequencing showed that the most highly mutated codon was codon 531 and Ser531Thr was the most common mutation. For risk factor analysis, working as laborers was significantly (p -value < 0.05) associated with TB (aOR 2.83; 95% CI 1.43-5.63) and previously treated cases were significantly associated with RR-TB (aOR 12.33; 95% CI 2.29-66.49). The high frequency of TB and RR-TB in migrants highlights the problem and factors associated with TB at the border and the need for efforts in TB control programs in this setting.

Keywords: Tuberculosis; rifampicin-resistant tuberculosis; associated factors; Thailand-Myanmar border.

INTRODUCTION

Extensive cross-border travel has accelerated the spread of infectious diseases including tuberculosis (TB) (Stop TB partnership, 2016) which remains the major health problem in both Thailand and Myanmar. According to World Health Organization (WHO) report in 2019 (WHO, 2019), both have been categorized in the 14 high-burden countries list for TB and multidrug-resistant TB (MDR-TB) since 2016. The total estimated TB incidences were 106 000 cases or 153 per 100 000 population for Thailand and 181 000 cases or 338 per 100 000 population for Myanmar in 2018. For MDR-TB or rifampicin-resistant TB (RR-TB; MDR-TB is a subset of RR-TB), the estimated incidences were 4 000 cases or 5.7 per 100 000 population and 11 000 cases or 21 per 100 000 population for Thailand and Myanmar, respectively.

Tak Province, Western Thailand, is one of the Thailand-Myanmar borders which is around 500 kilometers in length. Especially in

Mae Sot District of Tak (Figure 1), there is extensive cross-border travel among Thai who live in Thailand but come to Myanmar temporarily for working and Burmese who live in Myanmar but come to Thailand temporarily to work or access essential services, including healthcare. Even though there is a bridge which is the official border crossing between Mae Sot and Myawaddy District, Kayin State, Southeastern Myanmar, many people cross the Moei river, a narrow body of water that separates between two countries unofficially. In a previous study in Tak published in 2008 (Hemhongs et al., 2008), the collected data between September 2006 to August 2007 showed that 1 087 (65%) of 1 662 TB patients and 19 (70%) of 27 MDR-TB patients were Burmese. According to TB diagnosis, bacteriologically confirmed TB is an important part to support a clinical diagnosis of presumptive TB patients. It is defined as a case whose biological specimen is positive for *Mycobacterium tuberculosis* complex (MTB) by laboratory diagnostic tests (WHO, 2013). A microbiological laboratory of Mae Sot Hospital, a general

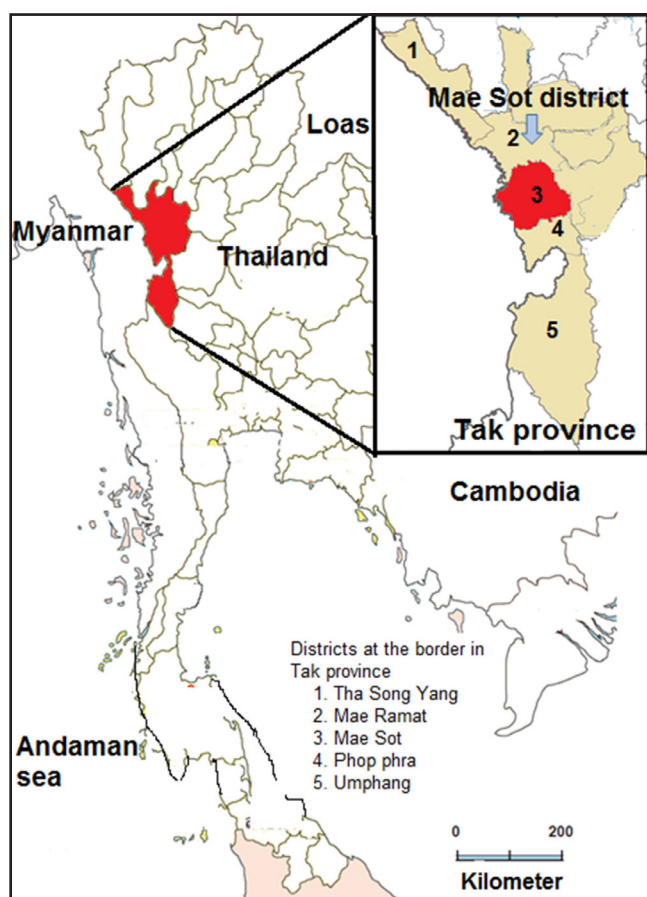


Figure 1. Map of the Thailand-Myanmar borders, Tak province.

hospital located in Mae Sot District achieves WHO-recommended methods as a part of routine service. The molecular testing, Xpert MTB/RIF (Cepheid, Sunnyvale, CA) is highly sensitive and specific comparable to gold standard culture, and simultaneously detects MTB and rifampicin resistance in less than 2 hours (WHO, 2011). There were available reports using Xpert MTB/RIF for TB and RR-TB diagnosis in Thailand (Pinyopornpanish *et al.*, 2015; Reechaipichitkul *et al.*, 2016; Kawkitinarong *et al.*, 2017; Thuncharoon, 2019) which showed good sensitivity and specificity compared to the gold standard culture methods and using Xpert MTB/RIF in the initial TB diagnosis in adult patients presumed to have TB can shorten the time to achieve a correct diagnosis (Khumsri *et al.*, 2020). Since the medical services of Mae Sot Hospital support either Thai or Burmese, we aimed to determine the frequency of TB and RR-TB by Xpert MTB/RIF and associated risk factors for TB and RR-TB among presumptive patients in this study setting. Mutation characteristics associated with RR-TB were also analyzed. The data generated from this study can serve as a basis to help policymakers and implementers to plan and design proper interventions for the border areas to achieve the “End TB” strategy in Thailand (Division of Tuberculosis, 2017) and in similar settings.

MATERIALS AND METHODS

Study setting

A cross-sectional study was conducted between October 2017 to July 2018 at Mae Sot Hospital, a general hospital locates in Mae Sot, Tak Province, Thailand which has a capacity of 365 beds. The data were collected from presumptive TB patients who gave sputum samples for TB diagnosis by microscopy and Xpert MTB/RIF according to a routine mycobacteria laboratory procedure. Individuals’ socio-

demographic characteristics (gender, age, nationality, district, and occupation), clinical-related data, and laboratory results (patient registration group, microscopy and Xpert MTB/RIF results) were recorded, whereas those with any missing information were excluded from the study. All work was approved by the Ethics Committee of Mae Sot Hospital (Approval number MSHP 005/2560).

Sputum microscopy and Xpert MTB/RIF assay

Microscopic examination for acid-fast bacilli (AFB) from sputum was done by Ziehl–Neelsen method based on the national TB diagnostic guidelines. A single sputum sample per patient was then subjected to TB diagnosis by Xpert MTB/RIF according to the manufacturer’s instructions. Briefly, Xpert MTB/RIF sample reagent was added to a collection tube containing an unprocessed sputum sample in a 2:1 ratio. The tube was manually agitated twice during a 15-min incubation at room temperature. Two milliliters of the liquefied sample were transferred to an Xpert MTB/RIF cartridge and loaded into a module of the GeneXpert machine. The instrument reports whether MTB and rifampicin resistance is detected or not. Bacteriologically confirmed TB case was defined by the “MTB DETECTED” result of Xpert MTB/RIF. The results of the Xpert MTB/RIF assay for MTB and RR-TB detection were analyzed.

DNA sequencing of the *rpoB* gene

Polymerase chain reactions (PCRs) were performed in a 20 μ l mixture containing 0.25 mM (each) deoxynucleoside triphosphates, 0.5 M betaine, 1.5 mM magnesium chloride, 0.5 μ M of each primer, 1 U of GoTaq DNA polymerase (Promega, WI, USA), 1 μ l of DNA template. The 278-bp of the *rpoB* fragment was amplified using a primer pair; *rpoB*-F (5-CAGGACGTGGAGGCGATCAC-3) and *rpoB*-R (5-GAGCCGATCAGACCGATGTTGG-3). The reactions were carried out in a thermal cycler (Eppendorf, AG, Germany) as described previously (Rudeeaneksin *et al.*, 2021). DNA fragments recovered from the agarose gel analysis were used for sequencing using primers *rpoB*-F with BigDye™ Terminator V3.1 Cycle Sequencing kit (Life Technologies Corp., CA, USA), and an ABI Prism 3130xl Genetic Analyzer (Life Technologies). The sequences were compared to those of *M. tuberculosis* H37Rv and analyzed using Bio-Edit software version 7.0.

Data analysis

Frequencies were used to summarize data. Stata/IC 14.2 for Windows (StataCorp LLC, College Station, TX, USA) was used for statistical analyses. Univariate and multivariate logistic regressions were analyzed to identify variables associated with bacteriologically confirmed TB and RR-TB. The variables considered being selected in the multivariate logistic regression model were *p*-values < 0.05 by univariate analysis. All reported *p*-values were two-tailed and calculated with statistical significance at a *p*-value < 0.05.

RESULTS

Socio-demographic, clinical characteristics and bacteriologically confirmed TB

A total of 365 presumptive TB patients who provided sputum samples for TB diagnosis and had complete data were enrolled (Table 1). Greater than half, 244 (66.85%), were males and the median age was 46 (interquartile range 33-61) years. More than half, 199 (54.52%), were Burmese and 252 (69.04%) were located in Mae Sot. One hundred and eighty-three (50.14%) worked as laborers. Of all, 314 (86.03%), were registered as new TB cases. One-hundred and thirty-two (36.16%; 95% confidence interval [CI] 31.21-41.12%) were positive for AFB. By Xpert MTB/RIF 136 (37.26%; 95% CI 32.28-42.24%) were detected for MTB and defined as bacteriologically confirmed TB cases. Of these, 125/136 (91.91%) were AFB-positive, while the remaining 11 samples were AFB-negative.

Table 1. Frequency of TB detected by Xpert MTB/RIF, socio-demographic and clinical characteristics among presumptive patients in Mae Sot Hospital, October 2017 to July 2018 ($n = 365$), and univariate and multivariate logistic regressions

Variables	MTB detected	MTB not detected	Crude odds ratio (95% CI)	<i>p</i> -value	Adjusted odds ratio (95% CI)	<i>p</i> -value
Gender						
Female	43 (35.54%)	78	Reference			
Male	93 (38.11%)	151	1.12 (0.69-1.81)	0.6316	–	–
Age (years)						
≤ 25	18 (35.29%)	33	Reference			
26-50	74 (41.81%)	103	1.32 (0.66-2.68)	0.4035	–	–
> 50	44 (32.12%)	93	0.87 (0.42-1.83)	0.6803	–	–
Nationality						
Thai	54 (32.53%)	112	Reference			
Burmese	82 (41.21%)	117	1.45 (0.92-2.29)	0.0878	–	–
District						
Mae Sot	91 (36.11%)	161	Reference			
Other districts ¹	31 (34.44%)	59	0.93 (0.54-1.58)	0.7769	1.32 (0.74-2.4)	0.343
In Myanmar	14 (60.87%)	9	2.75 (1.06-7.48)	0.0193*	5.23 (1.96-14.0)	0.001*
Occupation						
Unemployed	21 (29.17%)	51	Reference			
Laborer ²	87 (47.54%)	96	2.2 (1.18-4.17)	0.0075*	2.6 (1.39-4.84)	0.003*
Farmer ³	14 (35.0%)	26	1.31 (0.52-3.21)	0.5234	1.73 (0.7-4.24)	0.235
Other ⁴	14 (20.0%)	56	0.61 (0.26-1.41)	0.2051	0.63 (0.28-1.43)	0.269
Registration group						
New	129 (41.08%)	185	Reference			
Previously treated ⁵	7 (13.73%)	44	0.23 (0.08-0.53)	0.0002*	0.23 (0.1-0.56)	0.001*

CI = confidence interval; MTB = *Mycobacterium tuberculosis* complex; TB = tuberculosis.

¹Other districts in Tak that are also in the Thailand-Myanmar borders; Mae Ramat, Phop Phra, Tha Song Yang and Umphang.

²Laborer is employed by and receives a wage from an employer or works in a company e.g., housemaids, machine operators in a factory or laborers in the industrial and manufacturing sector.

³Farmer cultivates crops, working on rice, vegetable and fruit farms among others.

⁴Other occupations; merchant, priest, student, prisoner, government officer and unknown.

⁵Previously treated; relapse, treatment after failure, treatment after loss to follow-up and other previously treated patients.

*Statistical significance (p -value < 0.05).

RR-TB and *rpoB* mutation characteristics

Among 136 TB patients positive by Xpert MTB/RIF, 15 (11.03%; 95% CI 5.7-16.36%) were RR-TB and 2 were RIF resistance indeterminate. In RR detection, Xpert MTB/RIF showed four missing probes of A, B, D, and E which covered regions of 507-511, 512-517, 523-527 and 528-533 codons, respectively (Table 2). The frequency of missing probes detected and the codon coverage by each probe were summarized in Table 2. Regardless of missing data (N/A = not available), missing probe E spanning codons 528-533 was the most frequently observed. The available data from sequencing identified the most frequently mutated codon in this region was 531 and the most common mutation was the Ser531Leu in which the nucleotide had a substitution from TCG to TTG. Missing probe D was the second most frequently detected. The sequencing further identified the His526Tyr substitution in the missing probe D region.

Factors associated with TB and RR-TB

The univariate and multivariate odds ratio (OR) of MTB detected and RR-TB with different variables of associated factors were analyzed (Table 1 and 3, respectively). It was shown that presumptive TB patients who lived in Myanmar and worked as laborers were significantly more likely to be bacteriologically confirmed TB. These characteristics persisted in the multivariate analysis (adjusted odds ratio [aOR] 5.23; 95% CI 1.96-14.0 and aOR 2.6; 95% CI 1.39-4.84, respectively; p -value < 0.05). For RR-TB, TB patients who lived in other districts in Tak that are also along the Thailand-Myanmar borders (Mae Ramat, Phop Phra, Tha Song Yang, and Umphang) and were registered as previously treated cases were significantly more likely to be bacteriologically confirmed RR-TB (aOR 3.65; 95% CI 1.04-12.78 and aOR 12.33; 95% CI 2.29-66.49, respectively; p -value < 0.05).

Table 2. Mutations associated with RR detected by missing probe in Xpert MTB/RIF assay and sequencing

Code no.	Missing probe ¹	Codon coverage ²	Sequencing of <i>rpoB</i> gene
0537, 0087 ³	D	523-527	CAC IAC (His526Tyr)
0567	N/A	N/A	TCG TTG (Ser531Leu)
0003	N/A	N/A	TCG TTG (Ser531Leu)
0011	B	512-517	N/A
0023	E	528-533	N/A
0041	E	528-533	TCG TTG (Ser531Leu)
0064	D	523-527	N/A
0081	D	523-527	N/A
0088	A	507-511	N/A
0106, 0276 ³	E	528-533	TCG TTG (Ser531Leu)
0239	N/A	N/A	N/A
0240	N/A	N/A	N/A
0294	E	528-533	N/A
0404	N/A	N/A	N/A
0491	N/A	N/A	N/A

RR = rifampicin-resistance; N/A = data not available.

¹Probes of Xpert MTB/RIF for detection of *rpoB* gene mutations at 81-bp rifampin resistance-determining region (RRDR) between codon 507-533: **probe A**, **probe B**, **probe C**, **probe D** and **probe E**

5'- gGC ACC AGC CAG CTG AGC CAA TTC ATG GAC CAG AAC AAC CCG CTG TCG GGG TTG ACC CAC AAG CGC CGA CTG TCG GCG CTG -3'

3'- cCG TGG TCG GTC GAC TCG GTT AAG TAC CTG GTC TTG TTG GGC GAC AGC CCC AAC TGG GTG TTC GCG GCT GAC AGC CGC GAC -5'

²Codon coverage of *rpoB* gene for each probe of Xpert MTB/RIF.

³Samples from the same patients.

Table 3. Frequency of RR-TB detected by Xpert MTB/RIF, socio-demographic and clinical characteristics among TB patients in Mae Sot Hospital, October 2017 to July 2018 (n = 136), and univariate and multivariate logistic regressions

Variables	RR-TB detected	RR-TB not detected	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value
Gender						
Female	4 (9.3%)	39	Reference			
Male	11 (11.83%)	82	1.31 (0.36-5.98)	0.6620	–	–
Age (years)						
≤ 25	2 (11.11%)	16	Reference			
26-50	11 (14.86%)	63	1.4 (0.26-14.17)	0.6818	–	–
> 50	2 (4.55%)	42	0.38 (0.03-5.77)	0.3395	–	–
Nationality						
Thai	6 (11.11%)	48	Reference			
Burmese	9 (10.98%)	73	0.99 (0.29-3.6)	0.9803	–	–
District						
Mae Sot	6 (6.59%)	85	Reference			
Other districts ¹	7 (22.58%)	24	4.13 (1.06-16.21)	0.0127*	3.65 (1.04-12.78)	0.043*
In Myanmar	2 (14.29%)	12	2.36 (0.21-15.19)	0.3125	2.11 (0.34-13.04)	0.420
Occupation						
Unemployed	1 (4.76%)	20	Reference			
Laborer ²	11 (12.64%)	76	2.89 (0.37-130.72)	0.3023	–	–
Farmer ³	1 (7.14%)	13	1.54 (0.02-126.71)	0.7662	–	–
Other ⁴	2 (14.29%)	12	3.33 (0.15-206.27)	0.3241	–	–
Registration group						
New	11 (8.53%)	118	Reference			
Previously treated ⁵	4 (57.14%)	3	14.3 (2.05-106.12)	0.0001*	12.33 (2.29-66.49)	0.003*

CI = confidence interval; MTB = *Mycobacterium tuberculosis* complex; RR-TB = rifampicin-resistant tuberculosis; TB = tuberculosis.

¹Other districts in Tak that are also in the Thailand-Myanmar borders; Mae Ramat, Phop Phra, Tha Song Yang and Umphang.

²Laborer is employed by and receives a wage from an employer or works in a company e.g., housemaids, machine operators in a factory or laborers in the industrial and manufacturing sector.

³Farmer cultivates crops, working on rice, vegetable and fruit farms among others.

⁴Other occupations; merchant, priest, prisoner, government officer and unknown.

⁵Previously treated; relapse, treatment after failure, treatment after loss to follow-up and other previously treated patients.

*Statistical significance (p-value < 0.05).

DISCUSSION

Early and accurate detection of MTB is targeted to support the end TB Program and identification of potentially associated factors is valuable to design appropriate intervention strategies to control TB. TB in the border areas where humans and pathogens can move across the geographic borderlines is particularly critical for TB control. Here, we reported the frequency of 37.26% bacteriologically confirmed TB in tuberculosis presumptive patients from the border of Thailand-Myanmar, and among these, 11.03% were RR-TB as detected by Xpert MTB/RIF. The prevalence of positive microscopy for AFB in this study population was 36.16% and at the high rate of 91.91% (125/136) among confirmed TB patients. By Xpert MTB/RIF, it could enhance TB case detection by 8.09% among AFB-negative patients. The additional case detection of Xpert MTB/RIF from the presumptive patients was not very high compared to the initial diagnosis by sputum microscopy since most confirmed TB cases were AFB-positive. The greater number of AFB-positive cases might be due to the delay in visiting hospitals. As a result, TB has been detected mostly at the late stages with high bacterial loads detectable by AFB microscopy. However, Xpert MTB/RIF seemed to be useful for the rapid detection of MTB, and RR-TB. It could enhance case detection yield resulting in preventing greater transmission. Although the close positive detection rates of microscopy and Xpert MTB/RIF were observed by 36.16% and 37.26%, respectively, the difference would be of immense value. Of 11 AFB - negative TB patients were cases that would be missed diagnosis if the microscopic examination had

been done alone. This is critical because undetected or untreated cases are likely to progress to the advanced disease with more risk for death and widespread transmission, especially in poor crowded communities. Using Xpert MTB/RIF, a fairly rapid and sensitive diagnostic assay, therefore, would be of great value to reduce morbidity and mortality through early detection and treatment.

For RR-TB, our frequency data compared to the previous report from the same area in 2006-2007 (Hemhongsra *et al.*, 2008) was similar (11.03% vs 11.18%), while the number of registered TB cases in 2014 in Tak (Division of Tuberculosis, 2017) was increased but not remarkably (136 vs 110 +). It may indicate the need for additional powerful TB interventions in the borderlands. The frequency of TB in the current study was higher than 25.8% in a study done in 2016 at Taksin Hospital, Bangkok, Thailand (Thuncharoon, 2019). In contrast, the frequency of TB in this study was less than those of the previous studies reported at 47.37% in 2012-2013 at Chiang Mai University Hospital, Chiang Mai Province, Northern Thailand (Pinyopornpanish *et al.*, 2015) and 53.24% reported in 2017 at 2 tertiary hospitals in Bangkok and 1 tertiary hospital in Nonthaburi Province, Thailand (Kawkitinarong *et al.*, 2017). The variations could be due to differences in the study period, study participants, sample size, geographical variation, the prevalence of TB and detection techniques (culture vs Xpert MTB/RIF). In the present study, locating in Myanmar and working as laborers were significantly associated with TB. Locating in Myanmar meant Burmese who temporarily traveled to Thailand for obtaining medical treatment, seeking employment, or other socio-economic activities. A study in 2014

(Tschirhart *et al.*, 2016) reported that there were Burmese traveled exclusively to seek medical treatment because they could not afford appropriate and effective care locally. Since incidence rates in Myanmar were about 2.2 times for TB and 3.7 times higher for RR-TB compared to those of Thailand in 2018 (WHO, 2019), residing in Myanmar could be a risk factor associated with TB. It should be noted that among 87 TB patients who worked as laborers, most of them were Burmese compared to Thai (75.86% vs 24.14%), and there was a study published in 2017 (Rakprasit *et al.*, 2017) supporting our finding in that for migrant workers, the relative risks for TB were high among laborers. Indeed, migrant workers typically live with others in crowded and poorly ventilated rooms which increase the risk of TB exposure and transmission (Aung & Panza, 2014; Wongkongdech *et al.*, 2015; Luksamijarulkul *et al.*, 2017). A low level of knowledge and a negative attitude toward TB prevention and care were also the problems among migrant workers (Aung & Panza, 2014; Charoensook *et al.*, 2018). Concerning migrants, it should be noted that we had no data on the seasonal migration of Burmese workers, therefore, we could not present information on seasonal changes in TB incidence in the migrant population. It would impact the study results and it should be studied further.

According to rifampicin resistance in the current study, the frequency was higher than those reported in the previous studies in Thailand (Pinyopornpanish *et al.*, 2015; Kawkitinarong *et al.*, 2017; Thuncharoon, 2019) (11.03% vs 3.7% [RR-TB], 5.3% [MDR-TB] and 7.86% [RR-TB], respectively). Based on data from the 4th national anti-tuberculosis drug resistance survey in Thailand reported in 2008 (WHO, 2008) and data from a recent publication in 2020 of the 5th national survey (Kamolwat *et al.*, 2021), RR in new TB cases was 8.53% vs 1.4% compared to 57.14% vs 20.0% in previously treated TB cases, respectively. In the present study, the frequency of RR-TB in previously treated cases was nearly 7 times higher than that of new cases (57.14% vs 8.53%), and a statistically significant association was found similar to that of many reports (Ti *et al.*, 2006; Mohd Shariff *et al.*, 2016; Pradipta *et al.*, 2018; Kamolwat *et al.*, 2021). Another RR-TB-associated factor was living in other districts near the Thailand-Myanmar borders which included Mae Ramat, Phop Phra, Tha Song Yang, and Umphang. To our knowledge, there is only another hospital in Umphang District that can perform RR-TB testing, so other hospitals transfer their presumptive RR-TB patients to Mae Sot Hospital. This might explain the reason why RR-TB patients were found in a high percentage of TB patients who live in other districts than Mae Sot (22.58% vs 6.59%). Nevertheless, our data showed that gender and age were not associated with TB or RR-TB which contrasted with reports described elsewhere (Faustini *et al.*, 2006; Horton *et al.*, 2016; Kamolwat *et al.*, 2021).

Using GeneXpert in this setting enhanced the yield of bacterial confirmation compared to microscopy and revealed a high incidence of RR. Regarding RR, there is limited data on mutations conferring resistance to rifampicin at the district level. Additionally, we analyzed the frequency of mutations associated with RR. Basically, Xpert MTB/RIF can identify RR based on probes for the detection of mutations covering the 81-bp rifampicin resistance-determining region (RRDR), the core region of the *rpoB* gene. Five probes, A, B, C, D, and E were used in the Xpert MTB/RIF assay to detect RR and the missing detection of the probe identified the specific locus of mutations in the RRDR (Chang *et al.*, 2021). In this study, most of the rifampicin resistance mutations were detected by the drop out of probe E which covers the *rpoB* nucleotide sequences encoding codons 523-527, followed by the mutations detected by probe D missing. Further sequencing using a standard technique could identify the Ser531Leu substitution as the most frequently detected mutation followed by the His526Tyr substitution. This finding was similar to an American study reporting that the main probes missing in the detection of RR were probes E and D (Berhanu *et al.*, 2019). In Thailand, Ser531Leu and His526Tyr substitution were

reported in many studies as the most common mutations found in RR-TB (Anukool *et al.*, 2020; Suthum *et al.*, 2020; Rudeeaneksin *et al.*, 2021). These should be detected by the Xpert MTB/RIF assay based on the missing of probes E and D. To our knowledge, little information is available in publications regarding missing probes in RR-TB detection by Xpert MTB/RIF. Meanwhile, it was proposed that the distribution of mutations conferring resistance to RR might vary based on the MTB population and the geographic location. The mutations associated with RR identified in present study will contribute to the database on the MTB drug resistance profile. Regarding indeterminate results of RR detection through the Xpert MTB/RIF assay, repeating or drug susceptibility testing (DST) might be helpful to find out the resolution.

Our study had some limitations. First, some important variables of risk factors associated with TB, such as HIV testing were missing. Second, we could not perform mycobacterial culture and phenotypic drug susceptibility testing to confirm the Xpert MTB/RIF results. Therefore, limited methods were utilized in this study. Third, the prevalence and risk factors for TB and RR-TB were determined based on the Xpert/MTB/ RIF assay without culture results. The obtained data might be different according to the techniques used. In this study, we assumed that positive results of Xpert MTB/RIF were true positives according to several studies on the sensitivity and specificity of Xpert MTB/RIF. Finally, since there was a smaller number of RR-TB patients for some variables, data at some points might not be sufficient to confirm associations between some variables and patients. In addition to this, we could focus only on RR-TB due to the limitation of the detection technique. Despite the limitations of this study, these data could draw a conclusion on the prevalence and factors associated with TB and RR-TB at the targeted site even though the population sampled showed the majority of migrants (41.21%) and laborers (47.54%) and not a population survey. All were recruited into the study consecutively to avoid inclusion bias.

CONCLUSION

In summary, the frequency of TB (37.26%) and RR-TB (11.03%) among presumptive patients was high which highlights the problem of TB at the border and the need for more efforts in TB monitoring programs in the study setting. The risk factors associated with TB included being migrants and working as laborers. The previously treated TB is significantly associated with developing RR-TB. Scaled up of Xpert MTB/RIF in the borderlands and across the country could be useful for rapid diagnosis, proper management, and expanded surveillance of drug-resistant TB.

ACKNOWLEDGEMENTS

This work was supported by the Health Systems Research Institute (HSRI), Thailand [grant number 60-086]. We thank the staff of Mae Sot Hospital and the National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Thailand for their providing support and cooperation to do this research.

Conflict of interest

The author declares that they have no conflict of interest.

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