Treatment Outcomes of New and Previously-Treated Smear Positive Pulmonary Tuberculosis at Srinagarind Hospital, a Tertiary Care Center in Northeast Thailand

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Objective: *To study treatment outcomes of new and previously-treated smear positive pulmonary TB according to current WHO guideline 2010 and factors related to treatment success at Srinagarind Hospital.*
Material and Method: *Adult patients who had smear-positive pulmonary TB treated at Srinagarind Hospital between January 2005 and December 2010 were enrolled in the present study.*
Results: *Over a 6-years period, 322 patients (272 new and 50 previously-treated cases) were diagnosed smear positive pulmonary TB. The mean age was 48.85 (SD 17.9) years and the male to female ratio was 1.8:1. The mean duration of symptoms in the previously-treated group was longer than the new cases (2.39 vs. 1.99 months, p = 0.38). Symptoms, underlying diseases, HIV status, and organ involvement between these two groups were not different. Two-thirds (72.1% of patients) had cough, 35.4% had fever, and 20.5% weight loss. Twenty-three percent of cases had underlying DM and 7.8% were HIV positive. Disseminated TB was found in 18.9% of cases. The mean duration of treatment in new cases was 6.88 months vs. 11.20 months in previously-treated cases. The common regimens for new cases included 2IRZE/4IR (72.8%) and 2IRE/7IR (19.1%) vs. 2IRZE/4IR (62%), 2IRE/7IR (12%), and other regimens for MDR patients (6%) among the previously-treated cases. However in previously-treated group IRZES/IRZE/IRE (p = 0.001), second-line drugs (p = 0.002), and MDR regimens (p<0.001) were statistically more common treatments than in the new cases group. About 60% of cases were treated at TB clinic. The success rate among new cases who had completed treatment at Srinagarind Hospital was higher than for previously-treated ones (94.8% vs. 86.4%; p = 0.04). Among previously-treated cases (n = 50); 24 were defaulters, 19 were relapses, and seven were failures. For the defaulted and relapsed cases, patients usually received the IRZE/IR or IRZES/IRZE/IRE regimens. On the other hand, for failure cases, patients usually received the second-line drugs or MDR regimens. The overall success rate in defaulted cases was 87.6%, vs. 68.4% who relapsed and 57.1% who failed (p = 0.067). For new cases, the isolations found DR-TB 3.6% and MDR-TB 0%. For previously-treated cases, the isolations found DR-TB 16.67% and MDR-TB 6.25%. The only one factor related to successful outcomes was treatment at TB clinic (adjusted OR 2.01, 95% CI 1.18-3.43).*
Conclusion: *Previously-treated pulmonary TB had less success rate than new cases. Culture and susceptibility for previously-treated group were recommended before starting treatment. Treatment at TB clinic improved treatment outcomes.*

Keywords: *Pulmonary TB, Treatment outcomes, Factors related to success*

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Tuberculosis (TB) remains a major global health problem despite the availability of highly effective treatment for decades. The World Health Organization (WHO) declared TB a global public health emergency in 1993 with an aim to eliminate TB by the year 2050[1]. However, the incidence and mortality rate of TB are still high, especially in low income and developing countries. In 2011, there were 8.7 million of new cases and 1.43 million deaths worldwide[2]. According to the 2012 WHO TB report, Thailand was listed among 22 high burden countries with an estimated incidence of 124 per 100,000 populations[2]. In 2011, local data from the Bureau Epidemiology of TB, Ministry of Public Health (MOPH), Thailand, reported 57,641 new TB cases and half of them (29,733) were smear positive[3]. The smear positive pulmonary tuberculosis patients are considered to be an important group because they have contagious infectious diseases.

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Recent treatment of tuberculosis guidelines released by WHO on the year 2010[4], aims to simplify tuberculosis treatment and achieve the goal of success rate to over 87% by the year 2015. The new guideline, right now, has already been implemented in many countries worldwide. There are no categories (CAT I-IV), as patients are now grouped as either new or previously-treated cases. The rifampicin-containing regimen is recommended for treatment during the intensive and maintenance phases, in order to prevent tuberculosis relapse. For new cases, 2IRZE/4IR is the recommended regimen, with a high success rate especially under directly observed therapy short course (DOTS) because of primary drug resistance worldwide is quite low (3.7%). However, for previously-treated cases, the 2IRZES/1IRZE/5IRE regimen is recommended for treatment after defaulted or relapsed cases, and the multidrug-resistant (MDR) regimen comprising injectable aminoglycoside and oral fluoroquinolone for treatment failure patients. This recommendation due to secondary drug resistance is high (~20%) for re-treatment TB patients. Especially in the treatment failure subgroup, reports of MDR-TB by culture are nearly fifty percent of cases[4].

The objective of the present study was to determine the treatment outcomes of smear positive pulmonary tuberculosis patients as categorized by the WHO 2010 guidelines as new or previously-treated cases and to analyze the factors related to successful treatment outcomes.

Material and Method

This cross-sectional study was conducted between January 2005 and December 2010 at Srinagarind Hospital, Khon Kaen University, a 1,200-bed tertiary care center in northeast Thailand. The patient's age more than 18 years, diagnosed smear-positive pulmonary tuberculosis, and initial treatment with anti-TB drugs at Srinagarind Hospital were included. We excluded smear-negative pulmonary tuberculosis, extrapulmonary tuberculosis, and the patients with sputum culture reported non-tuberculous mycobacterium (NTM).

The data were collected and reviewed for details on age, sex, occupation, duration of symptoms, clinical symptoms and signs, diagnosis, organ involvement, previous history of TB treatment, underlying diseases, HIV status, chest radiographs, sputum acid-fast bacilli (AFB) smear results, and culture and susceptibility results. In cases where patients were registered for treatment at Srinagarind Hospital, they were categorized as new and previously-treated pulmonary tuberculosis. For the previously-treated, we explored the site of receiving treatment (TB clinic vs. non-TB clinic), regimen of anti-tuberculosis drugs, duration of treatment, and adverse events. The anti-TB drugs regimen defined as intensive phase for sputum conversion and maintenance phase for complete treatment. The MDR regimen was the regimen comprised of injectable aminoglycoside, fluoroquinolone, and three to four other anti-TB drugs including second-line drugs. The outcomes of treatment were defined as cure, treatment completed, treatment failure, transfer out, died, and other. The successful outcomes included cure and treatment completed. Factors related to outcome of treatment were also collected such as sex, age, history of previous treatment, site of received treatment, severity of infection (disseminated vs. non-disseminated form), and adverse events.

Descriptive statistics were used to describe the data. Means and standard deviations (SD) were calculated for the continuous data, number and percentages for the categorical data. All variables of demographic data, regimens of treatment, and treatment outcomes between the new and previously-treated group were compared, and considered statistically significant if the *p*-value were less than 0.05. Factors associated with successful treatment were initially analyzed by univariate analysis. Odds Ratios (Crude OR) were then determined using a logistic regression model. An adjusted analysis for confounders was performed with the model constructed by multiple logistic regressions. Adjusted Odds Ratio (Adjusted OR) and 95% confidence intervals (CI) were calculated. Statistical analyses were performed using STATA version 11.0.

The present study was approved by the Ethics Committee of the Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand.

Results

Over six-year period, 348 patients had a diagnosis of smear-positive pulmonary tuberculosis. Of these the chart record data could be retrieved for 322 patients (92.5%). 272 were new patients and 50 were previously-treated patients. In the previously-treated group, 24 were defaulters, 19 relapses, and seven failures. The mean age in the new patient group was 48.59 (SD 18.28) years and in previously-treated group 50.28 (SD 15.79) years. Approximately

two-thirds of cases were males. The common occupations were employee, agriculture, and government service. The common symptoms were chronic cough, fever, and weight loss as shown in Table 1. Some of them had hemoptysis, anorexia, and pleuritic chest pain. The mean duration of symptoms in the previously-treated group was longer than the new patient group but no statistical significance (2.39 vs. 1.99 months; $p = 0.38$). Nearly half of the patients had underlying diseases. The most common medical co-morbidity was diabetes mellitus (~25% of cases). Seventy percent of cases had serology for HIV, and about 13% tested positive. Localized pulmonary involvement, defined as pulmonary tuberculosis, occurred in about 80% of cases. Multi-organ involvement, defined as disseminated tuberculosis, occurred in about 20% of cases.

The details of treatment for smear-positive pulmonary tuberculosis were shown in Table 2. The mean duration of treatment in new cases was 6.88 months and previously-treated cases was 11.20 months. The common regimens for new cases were IRZE/IR (72.8%) and IRE/IR (19.1%), and other regimens for patients who had adverse events from prior regimens. The common regimens for previously-treated cases were IRZE/IR (62%), IRE/IR (12%), and other regimens for patients who infected with drug resistant pathogens. The data showed that the previously-treated group had been statistically significant treated with IRZES/IRZE/IRE ($p = 0.001$), second-line drugs ($p = 0.002$) and MDR regimens ($p<0.001$) more than the new cases group. Approximately 60% of cases received treatment at TB clinic and 10% received treatment at Infectious clinic, while the remaining cases

Table 1. Demographic data of smear-positive pulmonary tuberculosis patients

Characteristic	New cases (n = 272)	Previously-treated cases (n = 50)	*p*-value
Age, years (mean, SD)	48.59 (18.28)	50.28 (15.79)	0.54
Male:female	1.72:1	2.57:1	0.23
Occupation (n, %)			
Agriculture	48 (17.6)	12 (24.0)	0.29
Employee	59 (21.7)	16 (32.0)	0.11
Government service	54 (19.9)	8 (16.0)	0.52
Business	15 (5.5)	1 (2.0)	0.29
Other	96 (35.3)	13 (26.0)	0.20
Duration of symptoms, months (mean, SD)	1.99 (2.31)	2.39 (3.07)	0.38
Symptoms (n, %)*			
Fever	102 (37.5)	12 (24.0)	0.07
Cough	195 (71.7)	37 (74.0)	0.74
Hemoptysis	27 (9.9)	9 (18.0)	0.10
Anorexia	17 (6.3)	2 (4.0)	0.54
Weight loss	54 (19.9)	12 (24.0)	0.50
Pleuritic pain	8 (2.9)	0 (0.0)	0.22
Other	51 (18.8)	7 (14.0)	0.42
Underlying diseases (n, %)*	120 (44.1)	22 (44.0)	0.99
Diabetes mellitus	61 (22.4)	13 (26.0)	0.58
Renal disease	14 (5.1)	2 (4.0)	0.73
Liver disease	17 (6.3)	4 (8.0)	0.64
Other	67 (24.6)	10 (20.0)	0.48
HIV status (n, %)			
Positive	21 (7.7)	4 (8.0)	0.95
Negative	139 (51.1)	31 (62.0)	0.16
Not done	111 (40.8)	14 (28.0)	0.09
Inconclusive	1 (0.4)	1 (2.0)	0.18
Organ involvement			
Pulmonary tuberculosis	220 (80.9)	41 (82.0)	0.85
Disseminated tuberculosis	52 (19.1)	9 (18.0)	0.85

* Some patients had more than one symptom or underlying disease

received treatment at other clinics. Adverse events from anti-tuberculosis drugs occurred in one-fifth of patients; most common were rash, jaundice, and hepatitis. The adverse events of optic neuritis and peripheral neuropathy were reported in the previously-treated group, but not in new cases group.

The treatment outcomes could not be determined among the new cases more than the previously-treated group, because of transfer out (Table 3). The successful treatment outcomes in the new cases group were 74.2% (202/272), comprised of 72.4% cure and 1.8% complete treatment. For the previously-treated group, successful treatment outcomes were 76% (38/50), subgroup to be 87.5% (21/24) for defaulters, 68.42% (13/19) for relapses, and 57.1% (4/7) for failures (p = 0.067). When we compared the IRZE/IR regimen with other regimens, the odds ratio for success in new cases was 2.26 (95% CI, 1.21, 5.51) and odds ratio for success in previously-treated group was 1.22 (95% CI, 0.25, 5.51). Then, we analyzed patients who had regular follow-up until their treatment at Srinagarind Hospital was completed, by excluded transfer out and other outcomes, such that new cases had successful outcomes (94.8%, 202/213) significantly higher than the previously-treated group (86.4%, 38/44) (p-value = 0.04).

Table 2. Treatment for smear-positive pulmonary tuberculosis patients

Treatment	New cases (n = 272)	Previously-treated cases (n = 50)	p-value
Regimens (n, %)			
IRZE + IR	198 (72.8)	31 (62.0)	0.122
IRE + IR	52 (19.1)	6 (12.0)	0.229
EOS + EO	6 (2.2)	1 (2.0)	0.927
IEO + IE	10 (3.7)	1 (2.0)	0.549
IRZES + IRZE + IRE	1 (0.4)	3 (6.0)	0.001*
MDR regimen	0 (0.0)	3 (6.0)	<0.001*
Other	5 (1.8)	5 (10.0)	0.002*
Duration of treatment, months (mean, SD)	6.88 (4.03)	11.20 (9.69)	0.003*
Site of treatment (n, %)			
TB clinic	160 (58.8)	32 (64.0)	0.493
Infectious clinic	25 (9.2)	4 (8.0)	0.787
Other clinic	87 (32.0)	14 (28.0)	0.577
Adverse event (n, %)**	69 (25.36)	11 (22.0)	0.612
Rash	16 (5.9)	3 (6.0)	0.974
Nausea/vomiting	5 (1.8)	1 (2.0)	0.938
Jaundice	17 (6.3)	0 (0.0)	0.069
Hepatitis	17 (6.3)	2 (4.0)	0.535
Optic neuritis	0 (0.0)	3 (6.0)	<0.001*
Peripheral neuropathy	0 (0.0)	2 (4.0)	0.001
Other	23 (8.5)	2 (4.0)	0.279

MDR = multidrug-resistant; TB = tuberculosis
* Statistical significance if p-value <0.05
** Some patients had more than one adverse event

Table 3. Outcomes of treatment for smear-positive pulmonary tuberculosis

Outcomes of treatment (n, %)	New cases (n = 272)	Previously-treated cases		
		Defaulters (n = 24)	Relapses (n = 19)	Failures (n = 7)
Cure	197 (72.4)	21 (87.5)	13 (68.42)	4 (57.1)
Treatment completed	5 (1.8)	0 (0)	0 (0)	0 (0)
Treatment failure	0 (0)	0 (0)	2 (10.5)	1 (14.3)
Transfer out	43 (15.8)	0 (0)	2 (10.5)	1 (14.3)
Died	11 (4.6)	2 (8.3)	1 (5.3)	0 (0)
Other	16 (5.9)	1 (4.2)	1 (5.3)	1 (14.3)

Table 4 showed the regimens and treatment outcomes from previously-treated patients. More than half of the defaulters and relapses had successful treatment outcomes with IRZE/IR or IRE/IR regimens. However, in the failures needing second line anti-tuberculosis drugs or MDR regimens, the success rate decreased. Fig. 1 showed the percentage of drug resistant (DR) and multidrug resistant TB among new and previously-treated cases that had isolated and tested for drug susceptibility pattern. Among the new cases, isolations revealed 3.6% DR-TB and 0% MDR-TB. Among the previously-treated cases, isolations revealed 16.67% DR-TB and 6.25% MDR-TB. The only one factor related to successful outcomes was treatment at TB clinic (Adjusted OR 2.01, 95% CI 1.18-3.43) as showed in Table 5. History of new cases, sex, age, non-disseminated TB, and no adverse events were not related with successful outcomes.

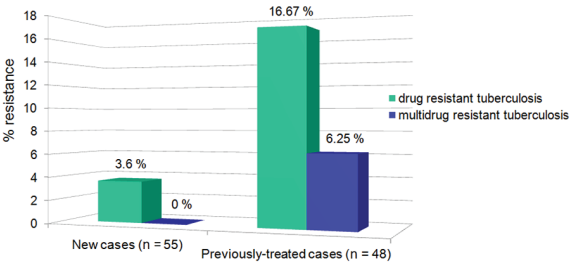

Fig. 1 Percentage of drug resistant and multidrug resistant TB in new and previously-treated cases.

Discussion

According to our data, one-sixth of smear-positive pulmonary tuberculosis was previously-treated cases. Overall demographic data of new and previously-treated cases were similar, except for the duration of symptoms. The common presenting symptoms were cough, fever, and weight loss, occurred predominately in middle-aged men, similar to other developing countries[5]. It is apparent that in high-prevalence countries, TB is greatly affecting the most productive age groups. On the other hand, TB is a serious health issue of the elderly in low-prevalence countries[6].

Table 4. Regimens of treatment and outcomes for previously-treated patients

Regimens of treatment	Outcomes (n = 50)		
	Successful (cure + treatment completed) (n, %)	Unsuccessful (treatment failure + died) (n, %)	Undetermined (transfer out + other) (n, %)
Group: defaulters			
IRZE + IR	14 (58.33)	1 (4.17)	1 (4.17)
IRE + IR	3 (12.50)	0 (0)	0 (0)
EOS + EO	0 (0)	1 (4.17)	0 (0)
IEO + IE	1 (4.17)	0 (0)	0 (0)
IRZES + IRZE + IRE	1 (4.17)	0 (0)	0 (0)
MDR regimen	0 (0)	0 (0)	0 (0)
Other	2 (8.33)	0 (0)	0 (0)
Group: relapses			
IRZE + IR	9 (47.37)	2 (10.53)	3 (15.79)
IRE + IR	3 (15.79)	0 (0)	0 (0)
EOS + EO	0 (0)	0 (0)	0 (0)
IEO + IE	0 (0)	0 (0)	0 (0)
IRZES + IRZE + IRE	0 (0)	0 (0)	0 (0)
MDR regimen	0 (0)	1 (5.26)	0 (0)
Other	1 (5.25)	0 (0)	0 (0)
Group: failures			
IRZE + IR	1 (14.28)	0 (0)	0 (0)
IRE + IR	0 (0)	0 (0)	0 (0)
EOS + EO	0 (0)	0 (0)	0 (0)
IEO + IE	0 (0)	0 (0)	0 (0)
IRZES + IRZE + IRE	1 (14.28)	0 (0)	1 (14.28)
MDR regimen	1 (14.28)	1 (14.28)	0 (0)
Other	1 (14.28)	0 (0)	1 (14.28)

Table 5. Factors associated with successful of treatment in smear-positive pulmonary tuberculosis

Factors associated with successful outcomes	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
New case	0.91 (0.41, 1.91)	0.95 (0.46, 1.95)
Male sex	0.74 (0.42, 1.31)	0.75 (0.43, 1.31)
Age <60 years	1.25 (0.69, 2.22)	1.28 (0.73, 2.27)
Treatment at TB clinic	2.22 (1.29, 3.81)	2.01 (1.18, 3.43)
Non disseminated TB	2.07 (1.08, 3.89)	1.77 (0.93, 3.34)
No adverse events	1.36 (0.74, 2.46)	1.49 (0.83, 2.67)

Diabetes mellitus (DM) was the most common medical co-morbidity among our TB patients, found nearly one-fourth of cases. Patients with DM are at high risk of developing TB, especially among those with poorly controlled DM[7]. Treatment outcomes and regimen of anti-TB drugs were not different between diabetes and non-diabetes patients[7,8]. In reports from Thailand, the three leading co-morbid conditions are HIV infection (40%), diabetes mellitus (6%), and chronic liver disease (2%)[9]. For persons who had serology for HIV, 13% of tests were positive results. These percentage were equal to the data reported by WHO for Thailand in the year 2012[2]. The case fatality rate among patients with TB associated with HIV has been particularly high, especially before the introduction of antiretroviral therapy in the last decade[10]. In Chiang Rai, northern Thailand, the mortality rate of TB/HIV was as high as 50%, but decreased to 28% after early antiretroviral therapy with anti-TB drugs were introduced in the course of treatment[11]. The duration of symptoms in previously-treated cases were a little bit longer than the new cases, but not statistically significant. The long duration of symptoms before diagnosis and treatment will increase transmission of airborne infectious agent to close contact persons[12]. It is dangerous if the pathogen is a drug resistant organism, which occurs more often among previously-treated cases[13]. Worldwide, 3.7% of new cases and 20% of previously-treated cases were estimated to be MDR-TB[2]. Lungs are the major organ involved in tuberculosis infections[14]. In this study, the severity of infection as pulmonary or disseminated form did not differ between new and previously-treated cases. The data showed that 20% had disseminated tuberculosis.

In the present study, the usual regimen for new cases was IRZE/IR (72.8%) for a period of six months treatment as per WHO guidelines recommendation[4]. Most of the remaining cases received IRE/IR for nine months, which was preferred for the elderly or patients with underlying liver diseases. The incidence of adverse events in the elderly is much greater than in younger patients, often resulting in the need to change to better-tolerated medication. This may require changing to regimens that are less effective and have to be taken for longer periods[15]. The principle clinical risk factors of hepatotoxicity are the old age, malnutrition, alcoholism, HIV infection, as well as chronic hepatitis B and C infections[16]. A few cases in the new cases group were treated with EOS/EO or IEO/IE because of adverse events from the standard regimen. These regimens are safe for patients with hepatotoxicity and unable to tolerate standard first line drugs. However, the course of treatment might be 12 to 18 months[4]. One-fourth of cases had adverse events, most of them were jaundice, hepatitis, or rash, which were the minor events and could be challenged with appropriate regimens. The mean duration of treatment for new cases in the present study was 6.88 months, and the success rate was high especially in cases that completed treatment at TB clinic.

According to WHO guidelines, previously-treated cases should be considered drug-resistant organisms[4]. Surveys and surveillance on MDR among TB retreatment cases in 12 countries between 1997 and 2007 found that approximately 30% of defaulters or relapses were MDR-TB and 50% of failures were MDR-TB[17]. Then the recommended regimen for defaulters and relapses was 2IRZES/1IRZE/5IRE, and for treatment failure cases was the MDR regimen including injectable aminoglycoside, oral fluoroquinolone, and oral second line anti-TB drugs[4]. In the present study, most of our patients still received the same regimen as new patients that was IRZE/IR or IRE/IR. Only 6% received IRZES/IRZE/IRE and 6% received MDR regimen. However, when subgroup analysis, we found that IRZE/IR or IRE/IR was frequently prescribed for defaulters or relapses, and 2IRZES/1IRZE/5IRE or the MDR

regimen was frequently prescribed for treatment failure cases.

Drug resistant organisms among previously-treated pulmonary TB were high, so the standard re-treatment regimen appeared inadequate for this group[18]. Success rate in treatment failure group was lower than defaulters and relapses. In order to increase treatment success among previously-treated TB cases, the recommendation is early empiric 2IRZES/1IRZE/5IRE for defaulters and relapses and the MDR regimen for treatment failure patients, after sending sputum for mycobacterium culture and susceptibility test[4].

One-fifth of previously-treated cases had adverse events. The percentage of adverse events among previously-treated cases was not greater than among new cases. Most of them were rash or optic neuritis. In the present study, these two adverse events were found among previously-treated cases more often than among new cases. The reasons for the high rate of optic neuritis were due to high dose and/or long duration of ethambutol, and, in some cases, multiple medical co-morbidities. Then, regular eye examination in indicated cases was recommended[19]. Because of drug resistance in previously-treated cases that needed second line anti-TB drugs, the mean duration of treatment was 11.20 months. Additionally, the success rate was low, especially in failure subgroup of previously-treated cases[4].

Resistant organisms were more often found among previously-treated cases than new cases[2,13,20]. In the current study, drug resistant tuberculosis was found in 3.6% of new cases and in 16.67% of previously-treated cases. No MDR tuberculosis was found in new cases, but found 6.25% in previously-treated cases. Based on surveillance of anti-tuberculosis drug resistance in the world between 2007 and 2010, globally, multidrug resistance was observed in 3.4% (95% CI; 1.9, 5.0) of new TB cases and in 19.8% (95% CI; 14.4, 25.1) of previously-treated TB cases[20]. In Thailand, the estimated MDR-TB burden was 1.7% (95% CI; 1.0, 2.6) of new cases and 35% (95% CI; 28, 42) of previously-treated cases[2]. Current study on drug resistance among new smear positive pulmonary tuberculosis in Thailand reported that the overall rates of pre-treatment isoniazid resistance were 11.8% while multidrug- resistant TB were 2.5%[21]. The emergence of drug resistance is a major problem for TB control. Quality DOTS (directly observe therapy short course) become the cornerstone treatment for new TB cases to achieve cure rate of greater than 95% and prevent MDR-TB[22]. Among previously-treated cases, DOTS-plus is recommended for the drug resistance program. DOTS strategy is using second-line drugs plus drug susceptibility testing (DST)[22]. The present study showed that new TB cases infected with MDR were low but previously-treated TB cases infected with MDR were high when compared with the global data. Therefore, an effective quality DOTS for new diagnosed TB cases will improve the success rate and prevent MDR and XDR-TB in Thailand. When compared with our previous studies[23,24], drug resistant and MDR-TB trended upward especially among previously-treated TB cases. However, the treatment success rate among these groups had improved. The reason for success outcome in this study was probably due to more effective TB control programs. We recommended culture and susceptibility testing for *Mycobacterium tuberculosis* in patients at high risk for drug resistant tuberculosis[23,24].

Factors associated with successful outcomes were evaluated. Only one factor, which was treatment at TB clinic, was statistically significant to improve outcomes in the present study. By contrast age, sex, history of previous treatment, and adverse events did not affect the treatment outcomes. Our results differed from previous studies that reported old age and previously-treated cases as contributing to unfavorable outcomes[25,26]. However, patients receiving directly observed therapy and with high education status were significantly more likely to have favorable outcomes[26]. This means that poor adherence to anti-TB drugs was a predictor for poor treatment outcomes[27]. Disseminated tuberculosis infection usually occurs in immunocompromised hosts or delayed diagnosis, is a severe form of infection that may deteriorate and increase morbidity and mortality[28]. However, in the present study, prognosis of disseminated tuberculosis was not worse because of a high index of suspicion to early diagnosis and treatment. Based on our data, registration and adherence to treatment at TB clinic were the key factors to improve the treatment outcomes.

Conclusion

Smear positive pulmonary tuberculosis patients are contagious, needed early diagnosis and prompt treatment with appropriate regimens. In the present study, the affected patients were predominantly middle aged and male. Clinical features did not differ between new and previously-treated cases, except for longer duration of symptoms in the previously-treated

cases. Approximately 13% of patients testing for anti-HIV were positive, and nearly 20% of cases had severe infections with disseminated form. The average overall successful outcome for TB treatment among previously-treated cases was lower than new cases. According to the high incidence of drug resistant and multidrug resistant organisms in previously-treated cases, culture and susceptibility testing for *Mycobacterium tuberculosis* was needed before starting treatment. The suggested anti-TB drug regimen for new cases was six months short-course therapy with 2IRZE/4IR under directly observation. Alternative regimens should be considered in patients who could not tolerate standard regimens or who had adverse events. The recommendation for previously-treated cases depended on the subgroups of patients. Among defaulters or relapses, treatment should start with 2IRZES/1IRZE/5IRE, and among failures start with MDR regimens. In our study, previously-treated cases delayed to receive second-line anti-TB drugs. Then we recommended that implement early initial appropriate regimens for each group of the patients and adjustment anti-TB drugs after culture susceptibility results. The outcomes of treatment can be improved by adherence to treatment at TB clinic and early detection of disseminated TB infection form for urgent appropriate treatment.

What is already known on this topic?

The fourth edition treatment guidelines of tuberculosis had been written by WHO on 2010. This guideline changed the category of tuberculosis management from previous third edition, 2003 guideline. The old one divided patients to be four category (I-IV), but the new one simplify divided patients to be two groups, new and previously-treated cases. It recommended the same regimen to treat new patients to improve high cure rate, and early treatment of previously-treated cases with second-line or MDR-TB regimen. This based on the global finding of increasing drug resistant-TB in previously-treated group.

National tuberculosis guideline of Thailand in 2008 used the same category of treatment as previous third edition, 2003 WHO guideline. In addition, in 2013, the Ministry of Public Health launched an updated National tuberculosis guideline following the fourth edition, 2010 WHO guideline.

What this study adds?

The present study analyzed the data of treatment outcomes of tuberculosis categorized as the fourth edition, 2010 WHO guideline. Patient characteristics, regimens of treatment, success rate, and drug resistant problems for new and previously-treated cases were presented. Factors associated with successful of treatment were analyzed. All of these data will add on local data of tuberculosis in Thailand for implement a new update National tuberculosis guideline.

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Declarations

The authors have no competing interests. All authors participated in the design, prosecution, data analysis, and composing of the manuscript. This work has neither been published nor submitted elsewhere.

Potential conflicts of interest

None.

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ผลการรักษาผู้ป่วยวัณโรคปอดเสมหะบวกที่รับการรักษาครั้งแรกและที่มีประวัติได้รับการรักษามาก่อนที่โรงพยาบาลศรีนครินทร์

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วัตถุประสงค์: *เพื่อศึกษาผลการรักษาของผู้ป่วยวัณโรคปอดเสมหะบวก โดยใช้เกณฑ์ตามองค์การอนามัยโลก ปี 2010 แบ่งเป็นกลุ่มผู้ป่วยที่รับการรักษาครั้งแรก และกลุ่มผู้ป่วยที่มีประวัติได้รับการรักษามาก่อน และปัจจัยที่มีผลต่อความสำเร็จในการรักษาที่โรงพยาบาลศรีนครินทร์*

วัสดุและวิธีการ: *ผู้ป่วยผู้ใหญ่ที่ได้รับการวินิจฉัยวัณโรคปอดเสมหะบวกที่โรงพยาบาลศรีนครินทร์ ระหว่างเดือนมกราคม พ.ศ. 2548 ถึง เดือนธันวาคม พ.ศ. 2553 นำข้อมูลจากเวชระเบียนการรักษามาวิเคราะห์*

ผลการศึกษา: *ในระยะเวลา 6 ปี มีจำนวนผู้ป่วยทั้งสิ้น 322 ราย เป็นผู้ป่วยที่ให้การรักษาครั้งแรก 272 ราย และผู้ป่วยที่มีประวัติได้รับการรักษามาก่อน 50 ราย อายุเฉลี่ย 48.85 (SD 17.9) ปี เพศชาย:หญิง เท่ากับ 1.8:1 ระยะเวลาเฉลี่ยของอาการในกลุ่มที่มีประวัติได้รับการรักษามาก่อนนานกว่ากลุ่มที่ให้การรักษาครั้งแรก (2.39 และ 1.99 เดือน, p-value = 0.38) อาการแสดงโรคประจำตัว ผลตรวจ HIV และอวัยวะที่มีการติดเชื้อ ไม่แตกต่างกันทั้งสองกลุ่ม ประมาณ 2 ใน 3 ของผู้ป่วย (72.1%) มีอาการไอ 35.4% มีอาการไข้ และ 20.5% มีน้ำหนักลด พบว่า 23% ของผู้ป่วยมีโรคประจำตัวเป็นเบาหวาน และ 7.8% มีผล HIV เป็นบวก พบวัณโรคแพร่กระจาย 18.9% ระยะเวลาในการรักษาในกลุ่มที่ให้การรักษาครั้งแรก 6.88 เดือน และกลุ่มที่มีประวัติได้รับการรักษามาก่อน 11.20 เดือน การรักษาส่วนใหญ่ของกลุ่มที่รับการรักษาครั้งแรก คือ 2IRZE/4IR (72.8%) และ 2IRE/7IR (19.1%) การรักษาส่วนใหญ่ของกลุ่มที่มีประวัติได้รับการรักษามาก่อน คือ 2IRZE/4IR (62%), 2IRE/7IR (12%) และสูตรยารักษาวัณโรคดื้อยา (6%) อย่างไรก็ตามกลุ่มที่มีประวัติได้รับการรักษามาก่อน มีสูตรในการรักษาแตกต่างจากกลุ่มที่ให้การรักษาครั้งแรกอย่างมีนัยสำคัญทางสถิติ คือ IRZES/IRZE/IRE (p = 0.001), second-line drugs (p = 0.002) และ MDR regimens (p<0.001) ประมาณ 60% ของผู้ป่วยได้รับการรักษาที่คลินิกวัณโรค ผลการรักษาที่โรงพยาบาลศรีนครินทร์พบว่า กลุ่มที่ให้การรักษาครั้งแรกได้ผลการรักษาดีกว่ากลุ่มที่มีประวัติได้รับการรักษามาก่อน (94.8% vs. 86.4%; p = 0.04) ในกลุ่มที่มีประวัติได้รับการรักษามาก่อน 50 ราย ประกอบด้วย ผู้ป่วยที่ขาดการรักษา 24 ราย ผู้ป่วยกลับเป็นซ้ำ 19 ราย ผู้ป่วยรักษาล้มเหลว 7 ราย ผู้ป่วยที่ขาดการรักษาและผู้ป่วยกลับเป็นซ้ำส่วนใหญ่จะได้สูตรการรักษาเป็น IRZE/IR or IRZES/IRZE/IRE ส่วนผู้ป่วยรักษาล้มเหลวส่วนใหญ่จะได้สูตรการรักษาเป็น second-line drugs หรือ MDR regimens ผลสำเร็จของการรักษาของกลุ่มผู้ป่วยที่ขาดการรักษา ผู้ป่วยกลับเป็นซ้ำ และผู้ป่วยที่เคยรักษาล้มเหลวมาก่อน เท่ากับ 87.6%, 68.4% และ 57.1% ตามลำดับ (p = 0.067) ผลเพาะเชื้อพบ DR-TB 3.6% และ MDR-TB 0% ในกลุ่มที่รับการรักษาครั้งแรก ส่วนกลุ่มที่มีประวัติได้รับการรักษามาก่อนพบ DR-TB 16.67% และ MDR-TB 6.25% ปัจจัยที่มีผลต่อความสำเร็จในการรักษา คือผู้ป่วยที่ได้รับการรักษาที่คลินิกวัณโรค (adjusted OR 2.01, 95% CI 1.18-3.43)*

สรุป: *ผู้ป่วยวัณโรคปอดเสมหะบวกที่มีประวัติได้รับการรักษามาก่อนมีผลการรักษาสำเร็จน้อยกว่าผู้ป่วยที่รับการรักษาครั้งแรก ก่อนเริ่มให้การรักษาผู้ป่วยวัณโรคที่มีประวัติได้รับการรักษามาก่อน แนะนำให้ส่งเสมหะเพาะเชื้อและทดสอบความไวของเชื้อต่อยาการรักษาที่คลินิกวัณโรคเพิ่มผลสำเร็จในการรักษา*