The Outcome of Tuberculosis Control in Special High-risk Populations in Northern Thailand: An Observational Study

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Abstract

Objectives: To evaluate and review the tuberculosis situation in various populations at high risk of contracting tuberculosis, at various periods of time and general tuberculosis control outcomes in northern Thailand.

Methods: Data on various high-risk populations were analyzed from the DOTS database and special project paper-based record systems for various high-risk populations in areas of northern Thailand in various periods of time.

Results: The 2003 and 2004 reports showed 30 and 60 percent of multidrug-resistant tuberculosis respectively with cure rates of less than 60 percent of the registered cases. The 2004 report revealed that tuberculosis was the most common opportunistic infection (38.9%) among the HIV-seropositive/AIDS cases. Reports of isoniazid therapy for tuberculosis prevention among HIV-seropositive/AIDS populations showed that 78 percent of them had not developed tuberculosis at the end of the 24th month since starting therapy. The 2005 report demonstrated that only 3.2 and 37.1 percent of the suspected childhood tuberculosis cases were diagnosed as tuberculosis and latent infection cases, respectively.

There were no statistically significant correlations between the types of the patient observers and the cure rates among the general tuberculosis population analyzed from the 2003 report (Pearson correlation coefficients > 0.01, 2-tailed). There also were no statistically significant changes or improvement in the treatment outcomes (sputum conversion rates, default rates, death rates, and treatment success rates), when comparing the 2003 and 2004 reports ($p > 0.01$).

Conclusions: These findings indicate the DOTS program implementation was not well-developed for various populations at high risk of tuberculosis in these areas. Recording and reporting systems for childhood tuberculosis cases in this area still were not well-developed and this contributed to underreporting of this section of the high-risk population.

Key words: *tuberculosis, high-risk populations, northern Thailand*

บทคัดย่อ

ผลจากการควบคุมวัณโรคในกลุ่มประชากรที่มีความเสี่ยงสูงพิเศษต่อการเป็นวัณโรคในภาคเหนือของประเทศไทย: กรณีศึกษาแบบการสังเกต

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รายงานนี้เสนอข้อมูลจากการทบทวนสถานการณ์วัณโรคในกลุ่มประชากรที่มีความเสี่ยงสูง ต่อการป่วยเป็นวัณโรค และผลของการควบคุมวัณโรคโดยรวมในช่วงเวลาต่างๆ ในพื้นที่ภาคเหนือของประเทศไทย โดยทบทวนและวิเคราะห์

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ข้อมูลจากรายงานรอบปรกติของผู้ป่วยวัณโรค และรายงานพิเศษสำหรับโครงการควบคุมวัณโรคในกลุ่มผู้ที่มีความเสี่ยงสูงที่จะเป็นวัณโรค. จากการศึกษาพบการดื้อยาหลายขนานร้อยละ ๓๐ และ ๖๐ ใน พ.ศ. ๒๕๔๖ และ พ.ศ. ๒๕๔๗ ตามลำดับ; อัตราการรักษาหายในผู้ป่วยกลุ่มนี้น้อยกว่าร้อยละ ๖๐. จากรายงานใน พ.ศ. ๒๕๔๗ พบวัณโรคเป็นโรคฉวยโอกาสบ่อยที่สุดในกลุ่มผู้ติดเชื้อเอชไอวีถึงร้อยละ ๓๘.๙. ไอโซไนอะซิดป้องกันไม่ให้เป็นวัณโรคได้ร้อยละ ๗๘ ในกลุ่มผู้ติดเชื้อเอชไอวี เมื่อครบ ๒๔ เดือนนับจากเริ่มกินยา. จากรายงาน พ.ศ. ๒๕๓๗-๒๕๓๙ มีเด็กที่สัมผัสผู้ป่วยวัณโรคถูกวินิจฉัยว่าป่วยเป็นวัณโรคและติดเชื้อวัณโรคร้อยละ ๓.๒ และ ๓๗.๑ ตามลำดับ. จากรายงาน พ.ศ. ๒๕๔๘ มีการตรวจพบเชื้อวัณโรคจากการย้อมเชื้อเพียงร้อยละ ๒๐-๒๕ และพบว่าประเภทของผู้สังเกตการณ์กินยารักษาวัณโรคของผู้ป่วยและอัตราการหายป่วยจากวัณโรคในพื้นที่จังหวัดต่างๆ ในรายงาน พ.ศ. ๒๕๔๖ ไม่มีความสัมพันธ์กันโดยนัยสำคัญทางสถิติ. ผลจากการควบคุมวัณโรคในพื้นที่นี้เปรียบเทียบกันระหว่าง พ.ศ. ๒๕๔๖ กับ พ.ศ. ๒๕๔๗ ยังไม่มีการเปลี่ยนแปลงหรือดีขึ้นอย่างมีนัยสำคัญทางสถิติ (ค่าพี > ๐.๐๑).

สรุป จากการวิเคราะห์ผลการควบคุมวัณโรคในกลุ่มประชากรที่ทำการศึกษาแสดงว่าแผนกำหนดการควบคุมวัณโรคในพื้นที่นี้ยังไม่มีประสิทธิภาพเพียงพอ อัตราร้อยละการพบผู้ป่วยวัณโรคชนิดที่ดื้อยาหลายขนานและอัตราร้อยละการเป็นวัณโรคในกลุ่มผู้ติดเชื้อเอชไอวียังสูงอยู่. ส่วนการตรวจพบวัณโรคในเด็กยังต่ำกว่าที่ควรจะเป็นอยู่มากเนื่องจากการวินิจฉัยทางเวชกรรมและทางห้องปฏิบัติการรวมทั้งอัตราความสำเร็จของการรักษาที่ยังต่ำกว่าเป้าหมายสากลอยู่มาก. การเน้นใช้บุคลากรทางสาธารณสุขเพื่อสังเกตการกินยาต้านวัณโรคของผู้ป่วยนั้น ถ้าสถานพยาบาลไม่สามารถทำได้และจำเป็นต้องใช้บุคคลอื่นแทนจะต้องมีระบบการติดตามและประเมินการกินยาต้านวัณโรคของผู้ป่วยอย่างสม่ำเสมอและมีประสิทธิภาพ

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Background and Rationale

The World Health Organization (WHO) has assessed the status of the tuberculosis (TB) epidemic and the progress made in controling the disease every year since 1997, following the start of reliable recording and reporting in 1995.[1] The first part defines the global targets and indicators for TB control set for 2005 (at least 70% of people with sputum smear-positive TB will be diagnosed) under the directly observed treatment, short course (DOTS), a case detection rate of at least 70 percent (in Thailand, it reached 70% in 2006[2] and 72% in 2007[1]), and a treatment success rate of at least 85 percent. These goals were targeted first in 1991 (in Thailand, it improved to 77% in 2006). By 2015, the global burden of TB (per capita prevalence and death rates) will be reduced by 50 percent relative to 1990 levels and by 2050, the global incidence of active TB will be less than 1 case per million population per year.[1]

The present authors' objectives are to evaluate and review the TB situation among various populations at high risk of contracting TB in various periods of time, including the general TB control outcomes in northern Thailand.

Methodology

Study population

The 10th Zonal TB and Chest Disease Center, Chiang Mai, 10th Office of Disease Prevention and Control, Thailand currently is responsible for TB control in the northern provinces of Thailand. Registered adult and childhood cases of new pulmonary TB, extrapulmonary TB, and relapsed TB among various populations at high risk of contracting TB in various periods of time (described above) who were diagnosed by clinical manifestations, chest

roentgenographs, and bacteriological examinations (AFB smears and cultures) according to the WHO guidelines were analyzed. A HIV-seropositive population on using isoniazid for TB prevention was also studied.

Collection of data

All patients attending the healthcare facilities mentioned above in 2003 and 2004 were retrospectively tracked through two data sources. The first was a paper-based TB patient registration and recording system recommended by WHO, including the number of cases, ages and sexes of the patients, percentages (rates) of sputum conversion, cure, completion treatment, treatment success, failure, default, transfer out, death, and the laboratory results. The second was the DOTS database (DMIS-TB online, established by the office of National Health Security, Thailand), a computerized database containing data on registration, treatment progress, and outcomes, all of which were prospectively recorded. Data on HIV-seropositive persons under using isoniazid for TB prophylaxis were prospectively recorded at 33 selected hospitals between 1994 and 1996, data on TB-high-risk populations in 2004, data on DOTS observers in 2003, data on MDR-TB in 2003 and 2004, data on HIV-infected/AIDS TB control outcomes in 2003 and 2004, data on childhood TB control outcomes between 2002 and 2005, and data on TB control among healthcare staff in 2005 and data on MDR-TB control in 2003 and 2004 were tracked through special project paper-based record systems independent of DOTS. Some patient data for some periods of time were not available for analyses in this study because of the incompletenen of the records.

Statistical analysis

The demographic and clinical variables were analyzed descriptively retrospectively and cross-sectionally as percentages or mean with standard deviation (SD) or median values with interquartile range (IQR) as appropriate to their distribution. Pearson correlation coefficients were used to measure the degree of association between two variables. Correlation coefficients that exceeded the 0.01 level (2-tailed) were considered not statistically significant. Values of $p< 0.05$ were considered statistically significant by using the paired-t test. The SPSS program for Windows® (SPSS® Inc., Chicago, IL, USA) version 16.0 was employed for analysis.

Results

Table 1 Classification of registered TB patients: 2004

Type	%
Positive-AFB smear pulmonary TB	48.9
Negative-AFB smear pulmonary TB	29.5
Extrapulmonary TB	18.7
Relapsed TB	2.9

Table 2 The average treatment outcomes of the MDR-TB patients: 2003 and 2004

Outcome	%
Cure	< 60
Failure	24
Death	12

Discussion

The WHO[1,2] TB annual report of Thailand in 2007 demonstrated that only 67 and 32 percent of new HIV-infected TB cases received co-trimoxazole for *Pneumocystis jiroveci (carinii)* pneumonia prophylaxis[2,3] and anti-retroviral therapy (ART), respectively.[2] A study in Thailand, conducted by JK Varma et al. revealed that death among HIV-infected TB cases occurred in 17 percent of patients during TB treat-

Table 3 Outcomes of HIV-seropositive/AIDS TB control: 2003 and 2004

Outcome	Year (%)	
	2003	2004
HIV-seropositive/AIDS-related deaths among HIV-seropositive/AIDS cases	22.74	50.32
Opportunistic infection		
Tuberculosis	Not available	38.9
Pneumocystis jiroveci (carinii) pneumonia	Not available	25.5
Cryptococcosis	Not available	16.2
Penicillosis	Not available	10.0
Toxoplasmosis	Not available	9.4
Receiving HIV-blood testing among new TB cases	92.4	91.6
HIV-seropositivity among new TB cases	38.9	42.4
New TB cases with HIV-seropositive/AIDS receiving anti-retroviral therapy (stavudine +lamivudine +evavirenz or stavudine +lamivudine +nevirapine or Stavudine+lamivudine+indinavir/ritonavir)	Not available	48.0

Table 4 Outcomes of isoniazid using for prophylaxis (300 milligrams per day) among HIV-seropositive persons: 1994-1996

Outcome	%
Completion of the 9 months period	70
Still had not developed TB disease at the 24 the month period	78
Developed TB disease at the 9 the month period	0.24
Developed TB disease at the 12 the month period	0.24

Table 5 Outcomes of childhood TB control: 2002-2005

Outcome	Year				
	2002	2003	2004	2005	
Estimated number of cases	> 205	> 150	50-100	> 300	
Percentage of AFB-smear positivity among suspected cases	Not available	Not available	Not available	20-25	
Number with diagnosis of close contact with TB cases	Not available	Not available	Not available	>400	37.1% of latent TB infection 3.2% of TB disease
treatment success rate	not available	60%-70%		Not available	

ment; factors strongly associated with risk reduction were ART use, fluconazole use, and co-trimoxazole use.[4] The single most important determinant of survival during TB treatment among HIV-infected/AIDS patients was ART use.[4] The deaths occurring among all forms of new TB cases during TB treatment in northern Thailand were 22.7 and 20.2 percent in 2003 and 2004, respectively (target <10%), whereas TB mortality in England and Wales was only 8.9 percent.[5] Most of the deaths occurred among HIV-infected/AIDS and elderly patients. Scientific proof of these causes of deaths is urgently needed. Factors significantly correlated with death were age,[6,7] sputum culture not performed/unknown,[6,7] and comorbidity with respiratory disease,[6,7] infectious disease,[6] renal disease[6] or malignancy,[6] compared with other patients.[6] One of the limitations of the present study was the search for the number of deaths in which TB was the principal cause, not computing the cases in which TB was present as a comorbid condition. Isoniazid and rifampicin resistance and advancing age were the strongest predictors of death.[8] TB was the primary cause of death in 23.19 percent of all natural causes of death[9] and was the most common opportunistic infection among the HIV-infected/AIDS population in northern Thailand (38.9%, Table 3) and the most frequent cause of death among this population (28%)[10] compared with a mortality rate of 35 percent among the new smear-positive cases with HIV-infection/AIDS registered at the 10th Zonal TB and Chest Disease Center, Chiang Mai, between 1997 and 1999.[11]

The most common extrapulmonary site (18.7%, Table 1) compared with 12.12 percent in 2001[12] of the new TB patients was TB of the jugular nodes compared with 42.6 percent,[13] 56.3 percent[14] and 37.3 percent,[15] which had been studied in Nepal, Turkey and Afghanistan, respectively. The results revealed that 92.4 percent and 91.6 percent of the new TB patients with HIV-infection in 2003 and 2004 received HIV-blood testing (target=75%) whereas only 48.0 percent of them in 2003 received ART (target=100%, Table 3). The outcomes of a special project of using isoniazid for prevention among 415 HIV-seropositive persons in northern Thailand between 1994 and 1996 revealed that 70 percent completed nine months of using isoniazid (Table 4) compared with 61.05 percent in a study conducted at the 10th Zonal TB and Chest Disease Center, Chiang Mai, Thailand between 1992 and 1997,[16] 73.9-84.5 percent in a study conducted in Bangkok,[17] 66 percent[18] in a study in Uganda, and 85 percent in a study in South Africa.[19] The effectiveness of prophylaxis against TB was 78 percent (Table 4) compared with 98.88 percent[16] and 80 percent[20] in two studies at the 10th Zonal TB and Chest Disease Center, Chiang Mai, and in Columbia, respectively. The lower effectiveness of the prophylaxis in a special project in northern Thailand compared with other studies could be due to isoniazid monoresistance among the subjects and a not well-developed DOTS program that was being implemented in this area. The prophylaxis was effective in HIV-seropositive persons, independently of the viral load, immune status, and highly-active ART.[20] The treatment outcomes in northern Thailand and northern Vietnam[21] in 2003 were 6.4 and 1.4 percent of default rates, and 22.7 and 2.6 percent of death rates, respectively. Defaulting resulted in a high death rate among TB patients.[21,22] Overall, more than 90 percent of the deaths among TB patients were recorded as being caused by TB in healthcare facilities in northern Thailand compared with 96 percent of these deaths demonstrated in a study of MDR-TB in Uzbekistan.[23]

The average outcomes of the treatment of MDR cases registered at the 10th Zonal TB and Chest Disease Center, Chiang Mai in 2003 and 2004, which

recorded more fatal treatment outcomes[24] in northern Thailand, was less than 60 percent of the cure rate, 24 percent of the failure rate, and 12 percent of death rate (Table 2), which might make it difficult to reach the WHO target,[1] whereas a cure rate of only 52.2 percent and MDR-TB prevalence of 3.9 percent in the area of northern Thailand surveyed in 2006 were noted. Recent results of antituberculous-drug susceptibility testing in 2008 in these areas in 2008 revealed that multidrug-resisitant TB cases were 3.13 percent of the total, whereas 11.07 percent demonstrated isoniazid monoresistance. These results indicated a "hot spot" of MDR-TB in these areas; thus, implementation of DOTS-Plus projects and programs is needed.[25]

In 2005, only 3.2 percent of childhood cases from nine selected regional and general hospital in northern Thailand were confirmed TB compared with 2 percent in a study in Thailand between 2005 and 2006,[26] whereas only 20-25 percent of childhood cases between 2001 and 2004 in this area were smear-positive (Table 5) compared with 28 percent of cases in the above study[26] with reporting of a very small number of cases and low treatment success rates (Table 5) according to the difficulty of making diagnosis. The reporting and recording system for this population is still under development in these areas. A study in the United Kingdom and the Republic of Ireland showed that 51 and 43 percent of the cases presented clinically and at contact tracing, whereas 40 percent presented pulmonary TB, which is a higher percen-tage than the cases reported in Thailand and northern Thailand.[27]

A 2003 survey among 84 hospitals in northern Thailand revealed that 40 percent utilize the national TB control programme (NTP), 13 percent have a TB-infection control committee, 52 percent have a TB screening service, 43 percent have a TB clinic, and 51 percent have an in-patient isolation room,[28] which percentages were lower than those in a survey of TB services in hospitals in Asia and north Africa.[29] A 2005 survey in a northern Thailand university hospi-

Table 6 Outcomes of TB control among healthcare staff: 2005

Type of healthcare staff	Percentage of TB disease development
Physician-in-training and clinical-year medical students	1.46
Nurse	2.52
Other paramedical staff	1.54

Table 7 Types of the observers who directly observed patients taking the prescribed antituberculous drugs throughout the treatment course: 2003

Province	Type of observer			
	Healthcare officer	Community leader	Family member	Drug-self administration
Chiang Rai	57.1	18.9	13.6	10.4
Mae Hong Son	49.3	0	27.1	23.6
Phayao	10.9	0.6	43.5	45.0
Chiang Mai	8.9	0.1	54.0	37.1
Lamphun	2.6	6.6	40.0	50.8
Lampang	1.2	0	0	98.8

Table 8 General outcomes of TB control: 2003 and 2004

TB control indicator	Year (%)		Mean ± SD	p
	2003	2004		
New case finding coverage	85	84	84.5+/-0.707	> 0.01
Sputum conversion rate	72.2	71.2	71.7+/-0.707	> 0.01
Default rate	6.4	6.5	6.45+/-0.0707	> 0.01
Death rate	22.7	20.2	21.45+/-1.7675	> 0.01
Treatment success rate	64.4	63.7	64.05+/-0.4949	> 0.01

Table 9 Cure rates and default rates by provinces: 2003

Province	Cure rate (%)	Default rate (%)	Mean ± SD/Median/IQR		Association between type of DOTS observer and cure rate
			Cure rate	Default rate	
Phayao	69.47	6.32	60.6950	3.9883	p > 0.01
Lamphun	69.44	1.39	+/-8.27455	+/-3.25568	
Mae Hong Son	62.5	0.60	/59.985/	/3.18/	
Chiang Mai	57.47	9.26	57.42-69.45	1.19-7.06	
Chiang Rai	57.42	3.52			
Lampang	47.87	2.84			

tal showed that 1.46 percent of doctors and 2.52 percent of nursing staff were diagnosed with TB (Table 6) compared with 16 and 12 percent, respectively in a study in Brazil.[30] A recent study in Thailand suggested that indoor ventilation in high-risk-nosocomial TB areas in public hospitals in Thailand was inadequate due to the installation of central air-conditioning systems in the modern hospital buildings.[31] Healthcare facilities should improve TB-infection control practices, and provide good quality occupational health services to address the TB burden among hospital staff.

There are a number of limitations to the data available for analysis in this observational study of a functioning DOTS program and a number of special projects. Some patient data for some periods of time were not available for analyses in this study because of the incompleteness of the records. The poor success rates of treatment in northern Thailand may be due to a lack of treatment adherence that was demonstrated by high default, low sputum conversion, and high death rates. Successfully treated patients classified under the descriptor "completion of treatment" (not shown) may comprise a study limitation to accurately determine higher treatment success rates. The above data did not accurately reflect the true situation; therefore, they were not used in the present analysis to assess treatment adherence. Poor treatment adherence may be considered a principal study limitation. It is therefore not possible to

determine the exact contribution to mortality, including disease recurrence, in this study. Percentage of DOTS observed by the healthcare officers was highest in Chiang Rai, whereas the highest cure rate was found in Phayao, with 45 percent of drug self-administration (Table 7). No statistically significant correlation was noted between the type of DOTS observer and cure rate in 2003 (2-tailed Pearson correlation coefficient, Tables 7,8,9). There was also no statistically significant changes in the TB control indicators compared between 7,601 patients in 2003 and 7,487 patients in 2004 (Table 10, $p > 0.01$). This finding indicates that high community participation in the DOTS strategy in Phayao, where there was a high prevalence of HIV-infection/AIDS, is highly empowering for a high TB cure rate. Community participation in DOTS is one of the five TB control strategies in Thailand.

The major challenges and constraints in TB control of the northern region and the country are addressing human resource constraints at the central and regional levels, ensuring systematic MDR-TB care with good recording and reporting on these cases, further strengthening TB/HIV integrated activities, better managing systematic and regular supervision of program activities, obtaining adequate commitment for implementing TB control activities in Bangkok and big cities, improving the quality of DOTS in a decentralized situation and in big cities, and involving private hospitals in TB control. In conclusion, despite reductions in the global burden of TB, the death rates in the northern areas and of Thailand will remain high if the DOTS program is not well developed.

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