

CHARACTERISTICS OF HIV-INFECTED TUBERCULOSIS PATIENTS IN THAILAND

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Abstract. To improve understanding about the epidemiology and clinical features of HIV-associated tuberculosis (TB) infection we conducted a prospective, multi-center observational study of HIV-infected TB patients in Thailand. We enrolled HIV-infected patients diagnosed with TB at public health facilities from three provinces and the national infectious diseases referral hospital in Thailand. Patients underwent standardized interviews, evaluations, and laboratory testing at the beginning of TB treatment. We analyzed demographic and clinical characteristics of patients and stratified our findings by level of immune-suppression and whether antiretroviral therapy (ART) was used before TB diagnosis. Of 769 patients analyzed, pulmonary TB was diagnosed in 461 (60%). The median CD4+ T-lymphocyte (CD4) count was 63 cells/ μ l [interquartile range (IQR), 23-163.5] and the median HIV RNA viral load was 308,000 copies/ml (IQR, 51,900-759,000) at the time of TB diagnosis. Methamphetamine use was reported by 304 patients (40%), marijuana by 267 patients (35%), and injection drug use by 199 patients (26%). Three hundred three patients (40%) reported having been previously incarcerated. Among sexually active patients, 142 (42%) reported never using condoms at all. Patients with CD4 counts <200 cells/ μ l were significantly more likely than patients with CD4 counts \geq 200 cells/ μ l to have extra-pulmonary TB, fever, fatigue, muscle weakness, no hemoptysis, tachycardia, low body mass index, jaundice, or no pleural effusion. Of the 94 patients that received ART before TB diagnosis, the median time from ART initiation to TB diagnosis was 105 days (IQR, 31-468). HIV-infected patients who developed TB after ART initiation were more likely than other HIV-infected TB patients to have extra-pulmonary TB, a normal chest radiograph, low HIV RNA viral load, or a history of previous TB treatment.

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INTRODUCTION

HIV-associated tuberculosis (TB) is an important global public health problem. Of the over nine million TB cases that occur around the world annually, an estimated 11% of them are HIV-associated (World Health Organization, 2007). Due to various

epidemiological factors, HIV-infected patients are uniquely susceptible to acquiring TB infection, and because of immunological factors, they are at high risk for developing TB disease after infection (Corbett *et al*, 2006). The case-fatality rate for TB is substantially higher in HIV-infected patients compared with HIV-uninfected patients, but anti-retroviral therapy (ART) can reduce this rate substantially (Mukadi *et al*, 2001; Akksilp *et al*, 2007). From the perspective of physicians, one of the greatest challenges is to know when to suspect HIV-associated TB in a person seeking care. Clinicians require a good understanding of the epidemiology and clinical features of HIV-associated TB, particularly how those features vary depending on the extent of HIV disease and the use of ART (Burman and Jones, 2003).

Expanded access to ART in the developing world has presented clinicians with an additional diagnostic and therapeutic dilemma. HIV-infected patients that receive ART are frequently diagnosed with TB soon after initiation of ART (Hirsch *et al*, 2004; Colebunders *et al*, 2006). Such cases are commonly grouped together as cases of "immune reconstitution inflammatory syndrome" (IRIS), although the cases arise from at least three different pathways: (a) patients with underlying (*ie*, latent) TB infection that progress to TB disease after ART initiation; (b) patients with underlying TB disease that was sub-clinical, but becomes clinically apparent after ART initiation; or (c) patients with underlying TB disease and clinical symptoms of TB disease that is only diagnosed after ART is initiated and TB symptoms increase in severity (Hirsch *et al*, 2004; Colebunders *et al*, 2006).

Thailand is one of 22 countries with the highest burden of TB in the world (World Health Organization, 2007). An estimated 15% of TB cases are HIV-associated, and mortality from HIV-associated TB is high

(Akksilp *et al*, 2007; Varma *et al*, 2007; Nateniyom *et al*, 2008). Two previous studies have described the clinical features of HIV-associated TB, but both were done retrospectively at one tertiary care referral center and before widespread availability of ART in Thailand (Tansuphasawadikul *et al*, 1998; Putong *et al*, 2002). To improve understanding about the epidemiology and clinical features of HIV-associated TB, we conducted a prospective, multi-center observational study of HIV-infected TB patients in Thailand. We studied the demographic and clinical characteristics of patients, and stratify our findings by level of immune-suppression and by use of ART before TB diagnosis.

MATERIALS AND METHODS

Study population and setting

We enrolled HIV-infected TB patients from public TB treatment facilities in Bangkok, Phuket, and Ubon Ratchathani Provinces and at the national infectious diseases referral hospital (Bamrasnaradura Infectious Diseases Institute) in Nonthaburi Province. The study population included adults aged ≥ 18 years with documented HIV infection who were clinically diagnosed with active TB disease according to national TB program guidelines (TB Cluster Bureau of AIDS, TB and STIs, 2005), registered for TB treatment at one of the participating facilities, and receiving anti-TB therapy for < 4 weeks before study enrollment. All enrolled patients received anti-TB treatment. We excluded prisoners and pregnant women. Patients who consenting to study enrollment were followed for three study visits: at TB treatment initiation, at the end of the intensive phase and at the end of TB treatment. For this study, patients received usual care for TB, HIV, and other diseases, and no health-related interventions were per-

formed. This study was approved by the ethical review committees of the Bangkok Metropolitan Administration, the Thailand Ministry of Public Health, and the US Centers for Disease Control and Prevention.

Data collection and laboratory studies

At the beginning of TB treatment, patients received a physical examination and answered questions about demographic characteristics, past and present medical history, knowledge and attitudes related to TB and HIV, and sex and drug use history. Patients underwent a chest radiograph that was interpreted by the attending physician caring for the patient. Blood samples were tested for aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, complete blood count, CD4+ T-lymphocyte (CD4) count, hepatitis B surface antigen, and hepatitis C antibody at local facilities. Plasma specimens from selected patients were frozen and shipped to the national infectious diseases referral hospital in Nonthaburi for measurement of HIV RNA using polymerase chain reaction (Amplicor HIV Monitor Test, version 1.5, Roche Molecular Systems, Branchburg, NJ). We encouraged, but did not require, physicians to send patients' sputum and specimens from extra-pulmonary sites for acid-fast bacilli (AFB) smear, mycobacterial culture, identification, and drug-susceptibility testing.

Statistical analysis

Although patients could initially be enrolled in the study based on a clinical diagnosis of TB, we excluded from the analysis patients who subsequently had their diagnosis changed (eg, non-tuberculous mycobacterial infection or other lung disease). We calculated proportions for the description of demographic characteristics and clinical features of the patients and stratified them into groups based on a CD4 count of <200 or \geq 200 cells/ μ l and based on the use of ART before

TB diagnosis. A wealth index was created using principal components analysis of household ownership items (methodology available upon request); patients were defined as not wealthy if their index was in the 4th or 5th quintile of the study population. We used the chi-square or Fisher's exact test to determine characteristics significantly associated with CD4 levels and with ART use before TB diagnosis. Patients with unavailable CD4 counts were excluded from the study. A two-sided *p*-value of \leq 0.05 was used to indicate statistical significance. All analyses were performed using Stata software version 8.0 (StataCorp LP, College Station, TX).

RESULTS

Enrollment

From May 2005 to September 2006, 1,096 HIV-infected TB patients were eligible for the study; of these, 849 (77%) enrolled. Reasons for not enrolling were refusal (125; 51%), death before enrollment (21; 9%), visiting during non-operation hours or after completion of enrollment (84; 34%), self-reported to be too ill (14; 6%), and communication problems (4; 2%). After excluding 80 patients who subsequently were diagnosed as not having TB, we analyzed data for 769 patients.

Demographic characteristics

The median age was 34 years [interquartile (IQR), 30-41], and 538 (70%) were male (Table 1). Four hundred fifty-two (59%) patients were employed; the majority were un-skilled workers (eg, laborer, farmer, street vendor) or semi-skilled workers (eg, clerk, sales person). Of the 769 patients in the study, 26 (3%) had never attended school. Among patients with some education, 436 (57%) finished primary school. The lowest and highest levels of education were grade two and post-graduate study, respectively.

Table 1
Selected characteristics of 769 HIV-infected TB patients in Thailand.

Characteristics	Number (%)	Median (interquartile range)
Male	538 (70)	
Median age in years		34 (30-41)
Never previously treated for TB	667 (87)	
History of injection drug use	199 (26)	
History of incarceration	303 (40)	
History of alcohol use	538 (70)	
Received anti-retroviral therapy before TB diagnosis	94 (27)	
Previous opportunistic infection		
Pneumonia from any causes	87 (11)	
Cryptococcal meningitis	20 (3)	
Other meningitis	18 (2)	
CD4+ T-lymphocyte count, cells/ μ l		63 (23-163.5)
WBC count, cells/ μ l		5,450 (3,870-7,630)
Total lymphocyte count, cells/ μ l		1,000 (567-1,620)
Hemoglobin, g/dl		10.1 (8.7-11.7)
Platelets, cells/ μ l ($\times 10^3$)		296 (218 -391)
Creatinine, mg/dl		0.8 (0.8-1.0)
Albumin, g/dl		3.1 (2.6-3.6)
Aspartate aminotransferase, mEq/l		42 (29-71.5)
Alanine aminotransferase, mEq/l		32 (20-53)
Total bilirubin, mg/dl		0.6 (0.3-0.9)
HIV RNA viral load, copies/ml ($\times 10^3$)		308 (51.9-759)

HIV, human immunodeficiency virus; TB, tuberculosis.

Fifty-one patients (7%) were illiterate.

Most patients lived in a house located within ten minutes of the nearest dispensary or health center (435 patients; 57%) and of public transportation (496 patients; 65%), and lived within 10-40 minutes from the hospital (543 patients; 71%). The availability of electricity, radio, television, refrigerator, and telephone in the household were reported to be 751 (98%), 619 (80%), 688 (89%), 582 (76%), and 564 (73%) patients, respectively. One hundred forty patients (18%) owned a motorcycle and a car; 467 (61%) owned only a motorcycle. The median number of individuals in the household was two (IQR, 1-2.5).

The most common place patients sought care when they first became sick with HIV or TB was the public health facility where they eventually registered for TB treatment (reported by 45% of patients), followed by other public health facilities (30%), a private facility (12%), a pharmacy (11%), or a traditional healer (0.7%).

Smoking was reported by 205 patients (27%). Alcohol use was common; 538 (70%) patients reported ever using alcohol. Of the 180 patients that drank alcohol within the past three months, the median number of times they drank more than five glasses in one evening was three (IQR, 1-10). Methamphetamine use was reported by 304 patients

(40%), followed by marijuana (267; 35%), sleeping pills (138; 18%), and inhalants (130; 17%). The use of other drugs, particularly ecstasy, ketamine and "poppers" (ie, alkyl nitrites), was uncommon, reported by 32 (4%), 26 (3%), and 11 (1%) patients, respectively. Injection drug use was reported by 199 patients (26%); of these, 181 (91%) said that they did not inject during the previous three months, while 6 (3%) reported injecting daily. Three hundred three (40%) patients reported having been previously incarcerated. However, only 36 (12%) were incarcerated during the previous six months.

Of the total of 769 patients, 755 (99%) reported ever having had sexual intercourse; 336 (45%) had been sexually active during the previous six months. Among the sexually active patients, the median number of partners during the previous six months was one (IQR, 1-1). Condom use was uncommon: 142 (42%) reported never using condoms at all, while 88 (26%) said they always used condoms. Of the 336 who had sex in the previous six months, 29 (9%) had it with a sex worker, and 12 (4%) received money, gifts or favors to have sex. Patients were asked to report the mode or modes by which they thought they acquired HIV infection: 569 (74%) believed they were infected with HIV by sexual transmission, 164 (21%) by sharing needles with an HIV-infected person, 9 (1%) by blood transfusion or a medical procedure, and 35 (5%) thought they were infected by other routes.

Signs, symptoms, and laboratory studies

In the four weeks before TB diagnosis, patients reported an array of physical symptoms including fever (reported by 80% of patients), loss of body weight (80%), fatigue (78%), coughing (72%), loss of appetite (67%), severe night sweats (54%), shaking chills (53%), muscle pain (53%), difficulty sleeping (53%), and diarrhea (25%). Of the

554 patients who reported duration of cough, 333 (60%) and 254 (46%) had cough lasting longer than two and three weeks, respectively. Physical examination on enrollment revealed that 706 (92%) had a respiratory rate greater than 20 times/minute, 443 (58%) had a body mass index less than 18.5 kg/m², and 514 (67%) had a Bacillus Calmette-Guerin (BCG) scar. Peripheral lymphadenopathy was palpable in 233 (31%). One hundred nineteen (15%) patients complained of one or more symptoms of a urinary tract or sexually transmitted infection, eg, burning with urination, blood in the urine, or sores on the penis or in the vagina. Of the total of 769 patients, 297 (39%) complained of pain with swallowing or pain in their mouth or throat. One hundred sixty-two (21%) had visible oral thrush on examination. Table 1 shows the hematology and blood chemistry studies performed on patients at the beginning of TB treatment.

Characteristics of TB disease

Thirteen percent of patients had previously been treated for TB. Pulmonary TB was diagnosed in 461 (60%) (Fig 1). Extra-pulmonary TB was diagnosed in 308 (40%); of these 230 (75%) had extra-pulmonary TB only and the rest (35%) had both extra-pulmonary and pulmonary TB. The most common forms of extra-pulmonary TB were lymphatic (139; 60%), meningeal (29; 13%), and intra-abdominal (29; 13%). Sputum smear results were recorded for 680 patients (94% of patients with any pulmonary disease; 74% of patients with only extra-pulmonary TB). Of these, 358 (53%) were smear-positive (61% of patients with any pulmonary TB, and 13% of patients with extra-pulmonary TB only). In total, 413 (54%) had at least one specimen culture-positive for *Mycobacterium tuberculosis*; 270 of these specimens were from sputum, 135 from both sputum and other sources; and 8 from other sources alone.

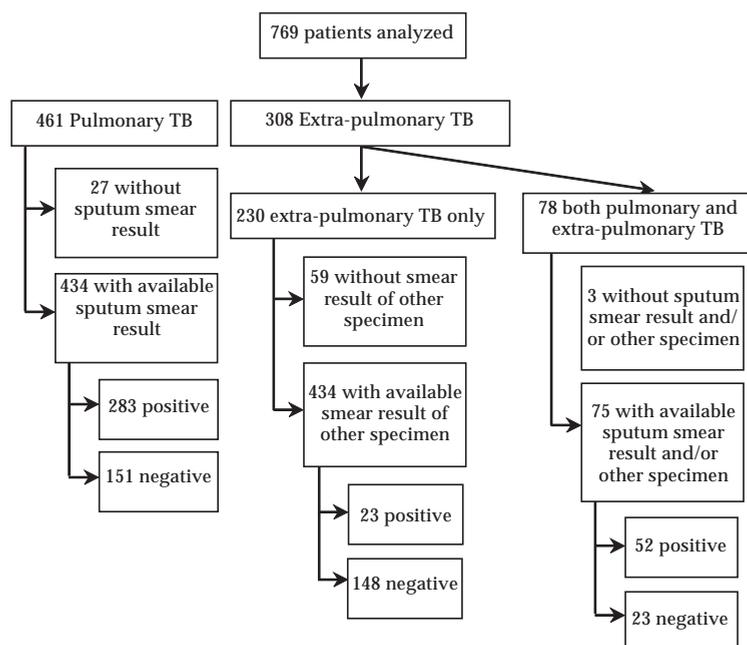


Fig 1–Disease classification and result of smear microscopy examination among 769 HIV-infected TB patients.

Of the 686 patients that had chest radiography results recorded, 552 (80%) had an abnormal film. Of these, 78 (14%) had a cavity, and 59 (11%) a pleural effusion. Chest radiographic patterns showed that 154 (28%) and 176 (32%) patients had more than 1/3 of left and right lung fields abnormal, respectively. Abnormalities in both lungs were seen in 291 patients (53%).

HIV-related disease and treatment

Five hundred twelve (67%) patients knew they were HIV-infected before they were diagnosed with TB. Among the 752 patients with an available CD4 count and 87 patients with an HIV RNA viral load result, the median CD4 was 63 cells/ μ l (IQR, 23-163.5) and the median HIV RNA viral load was 308,000 copies/ml (IQR, 51,900-759,000) at the time of TB diagnosis. *Pneumocystis jiroveci* pneumonia had previously been diagnosed in 87 (11%), and cryptococcal meningitis in 20 (3%). Before TB

diagnosis, 94 (12%) patients received ART, 257 (38%) co-trimoxazole, and 143 (30%) fluconazole.

Clinical characteristics stratified by CD4 count

Table 2 shows the clinical characteristics of patients stratified by CD4 count. Patients with a low CD4 count were significantly more likely to have extra-pulmonary TB only, fever, fatigue, muscle weakness, no hemoptysis, tachycardia, low body mass index, jaundice, and no pleural effusion.

Characteristics of patients who developed TB after ART use

Of the 94 patients that received ART before TB diagnosis, the median time from HIV diagnosis to ART initiation was 68 days (IQR, 24-423), and from ART initiation to TB diagnosis was 105 days (IQR, 31-468). Results were not significantly different within the subset of 37 culture-confirmed cases of

Table 2
Clinical features associated with CD4+ T-lymphocyte levels among 752 HIV-infected TB patients with available CD4+ T-lymphocyte counts in Thailand.

Clinical features	All	CD4 <200 cells/ μ l	CD4 \ge 200 cells/ μ l	p-value
	(n=752) Number (%)	(n=608) Number (%)	(n=144) Number (%)	
Site of disease				
Pulmonary TB	448 (60)	345 (57)	103 (72)	<0.01
Extra-pulmonary TB	227 (30)	192 (32)	35 (24)	
Pulmonary and extra-pulmonary TB	77 (10)	71 (12)	6 (4)	
Symptoms within 4 weeks				
Fever	598 (80)	496 (82)	102 (71)	<0.01
Cough	544 (72)	441 (73)	103 (72)	0.81
Weight loss	601 (80)	504 (83)	97 (67)	0.81
Fatigue	583 (78)	485 (80)	98 (68)	<0.01
Muscle weakness	366 (49)	315 (52)	51 (35)	<0.01
Hemoptysis	76 (10)	54 (9)	22 (15)	0.02
Physical examination				
Pulse >100/minute	212 (28)	185 (30)	27 (19)	0.01
Respiratory rate >20/minute	690 (92)	560 (92)	130 (90)	0.47
Body mass index <18.5	434 (58)	365 (60)	69 (48)	0.01
Jaundice	39 (5)	34 (6)	5 (4)	0.04
Cervical lymphadenopathy	228 (30)	188 (31)	40 (28)	0.47
Chest film abnormality				
Cavity	75 (10)	53 (14)	22 (21)	0.09
Effusion	40 (5)	26 (7)	14 (13)	0.03
>1/3 of left lung abnormality	135 (18)	106 (28)	29 (27)	0.88
>1/3 of right lung abnormality	158 (21)	128 (34)	30 (28)	0.27
>1/3 of both lungs abnormality	259 (34)	195 (51)	64 (60)	0.12
Sputum smear AFB positive	325 (43)	267 (68)	58 (58)	0.07

HIV, human immunodeficiency virus; TB, tuberculosis; CD4, CD4+ T-lymphocytes; AFB, acid-fast bacilli

TB. The time from HIV diagnosis to ART initiation was on average 36.5 days (IQR, 11.5-112), and from ART initiation to TB diagnosis was on average 118.5 days (IQR, 19.5-435). Table 3 shows the characteristics that were more frequent among HIV-infected patients who developed TB after ART initiation compared with other TB patients: being a skilled worker; finishing more than 6th grade being wealthy; not a new case of TB; extra-pulmonary TB only; no alcohol or drug use; no oral ulceration, thrush, or oral

hairy leukoplakia; a normal chest radiograph, hemoglobin, and albumin; no hepatitis C infection, and an HIV RNA viral load of <50,000 copies/ml. Of the 56 patients with extra-pulmonary TB involvement only, the most common sites were peripheral lymphatic (31; 55%), meningeal (13; 23%), and intra-abdominal (4; 7%).

DISCUSSION

We found that HIV-infected TB patients

Table 3
 Characteristics of HIV-infected TB patients in Thailand, stratified by use of anti-retroviral therapy.

Characteristics	All TB				Culture-confirmed TB			
	Took ART (n=94)		Did not take ART (n=675)		Took ART (n=37)		Did not take ART (n=376)	
	n	%	n	%	n	%	n	%
Characteristics								
Age >34 years	43	46	337	50	14	38	179	48
Male	59	63	479	71	24	65	266	71
Skilled and semi-skilled worker	25 ^a	27 ^a	87 ^a	13 ^a	7	19	48	13
Finished >6 th grade education	48 ^a	51 ^a	252 ^a	37 ^a	21 ^a	57 ^a	154 ^a	41 ^a
Single	33	35	204	30	19 ^a	51 ^a	121 ^a	32 ^a
Wealthy	48 ^a	51 ^a	247 ^a	37 ^a	21 ^a	57 ^a	151 ^a	40 ^a
Registered as new case	74 ^a	79 ^a	593 ^a	88 ^a	29	78	323	86
TB disease classification								
Pulmonary TB	38 ^a	40 ^a	423 ^a	63 ^a	23	62	260	69
Extra-pulmonary TB	52 ^a	55 ^a	178 ^a	26 ^a	12	32	68	18
Both pulmonary and extra-pulmonary TB	4 ^a	4 ^a	74 ^a	11 ^a	2	5	48	13
Drug and alcohol use and incarceration history								
Ever drank alcohol	57 ^a	61 ^a	481 ^a	71 ^a	26	70	259	69
Ever used methamphetamine	27 ^a	29 ^a	277 ^a	41 ^a	12	32	163	43
Ever injected drug	14 ^a	15 ^a	185 ^a	27 ^a	7	19	110	29
Ever been in jail	22 ^a	23 ^a	281 ^a	42 ^a	10 ^a	27 ^a	171 ^a	45 ^a
Ever been in prison	14 ^a	15 ^a	204 ^a	30 ^a	8	22	130	35
Physical examination								
Oral ulceration	3 ^a	3 ^a	110 ^a	16 ^a	2	5	57	15
Thrush	9 ^a	10 ^a	153 ^a	23 ^a	4	11	85	23
Oral hairy leukoplakia	1 ^a	1 ^a	65 ^a	10 ^a	0 ^a	0 ^a	33 ^a	9 ^a
Laboratory findings								
Abnormal chest x-ray	42 ^a	58 ^a	510 ^a	83 ^a	26	79	313	89
Cavity	1 ^a	2 ^a	77 ^a	15 ^a	0 ^a	0 ^a	51 ^a	16 ^a
Abnormal hemoglobin	32 ^a	34 ^a	323 ^a	48 ^a	15	41	185	49
Abnormal albumin	12 ^a	13 ^a	152 ^a	23 ^a	4 ^a	11 ^a	98 ^a	26 ^a
Abnormal liver enzyme	15	16	108	16	7	19	71	19
CD4+ T-lymphocyte <100 cells/ μ l ^b	54	57	429	65	23	62	234	63
Anti-HCV reactive ^b	10 ^a	11 ^a	227 ^a	34 ^a	4 ^a	11 ^a	135 ^a	37 ^a
Viral load \geq 50,000 copies/ml ^b	3 ^a	21 ^a	63 ^a	86 ^a	1	33	35	88

HIV, human immunodeficiency virus; TB, tuberculosis; ART, anti-retroviral therapy; CD4, CD4+ T lymphocytes; anti-HCV, antibody to hepatitis C virus; n, number.

^aStatistical significance at $p \leq 0.05$; ^bThose with available results only.

in Thailand had significant clinical and immunological evidence of advanced HIV disease, that the clinical presentation of TB was

altered by CD4 count and ART use, and that drug use and high risk sexual practices were common.

As has been shown in studies from other countries, we found that CD4 count dramatically altered the clinical presentation of TB, because cell-mediated immunity is essential to host defense against mycobacterial infection (Batungwanayo *et al*, 1992; Jones *et al*, 1993; Keiper *et al*, 1995). We found that TB in patients with low CD4 counts was associated with less classical TB symptoms (*eg*, hemoptysis), more systemic symptoms (*eg*, fever, weakness, fatigue), and increased extra-pulmonary involvement. Because the vast majority of HIV-infected TB patients had low CD4 counts, clinicians should be aware that the classical form of TB disease (*eg*, pulmonary disease with cavities and hemoptysis) is actually quite uncommon in HIV-infected patients in Thailand. We found that slightly more than 10% of patients were taking ART before their TB diagnosis. Half of these patients developed TB within three to four months of initiating ART and many had it in extra-pulmonary sites, suggesting that they may be cases of IRIS (Hirsch *et al*, 2004; Colebunders *et al*, 2006). Our study shows that clinicians in Thailand should carefully monitor patients for any signs or symptoms of TB in the first few months after ART initiation, with a particularly high suspicion for investigating TB in extra-pulmonary sites.

The predominance of low CD4 counts and high HIV viral loads suggests that TB is a late presentation of HIV disease in Thailand. In our study, HIV patients reported living in close proximity to health services, favorable indices of wealth, high literacy rates, and willingness to seek care in the public sector when they became ill. In Thailand, access to HIV treatment greatly exceeds that of most developing countries (Chasombat *et al*, 2006). Nevertheless, more than two-thirds of patients knew they were HIV-infected before their TB diagnosis, but only a minority were prescribed ART. We can speculate

that these HIV-infected TB patients represent the subset of HIV patients in Thailand who still do not receive optimum HIV treatment or, alternatively, that TB disease led to dramatic reductions in CD4 counts and increases in HIV viral loads. Thailand has begun initiatives focused on improving the quality of HIV care, not just access. As both access to care and quality of care improve, public health officials should consider using the burden of HIV-associated TB in a given locale as a composite measure of high-quality, accessible HIV care and TB prevention services.

Our study shows that clinicians in TB treatment clinics need to be able to address important health and lifestyle issues beyond TB. Rates of previous incarceration and of recreational drug use, particularly methamphetamines, were strikingly high. It is likely that drug use was primarily a marker of previous incarceration, which is a potent risk factor for both HIV and TB disease in Thailand (Kitayaporn *et al*, 1998; Punnotok *et al*, 2000; Pleumpanupat *et al*, 2003). TB clinics in Thailand should consider asking patients about previous drug use and, among drug users, providing appropriate counseling and referral to drug treatment services. We also found that rates of condom use were strikingly low among sexually active patients. Since TB treatment clinics have close contact with HIV-infected patients for at least six months, they should consider providing HIV prevention messages to their clients to reduce community-wide HIV transmission.

Although our study was limited to only a few provinces, we believe that our findings are generalizable to all of Thailand. One study of HIV-infected TB patients at 15 large hospitals throughout Thailand found similarly low CD4 counts and high rates of pre-existing HIV diagnoses (Nateniyom *et al*, 2008). The high rates of drug use and incarceration, in contrast, may be skewed by the

inclusion of the country's largest urban center (Bangkok).

In conclusion, clinicians in Thailand should maintain a high index of suspicion for extra-pulmonary or atypical manifestations of TB among HIV-infected patients with low CD4 counts or with a recent history of initiating ART. TB clinics should consider incorporating HIV and illicit drug prevention messages into routine services.

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