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Tuberculosis screening in a novel substance abuse treatment center in Malaysia: Implications for a comprehensive approach for integrated care*

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Abstract

People who use drugs (PWUD) represent a key high risk group for tuberculosis (TB). The prevalence of both latent TB infection (LTBI) and active disease in drug treatment centers in Malaysia is unknown. A cross-sectional convenience survey was conducted to assess the prevalence and correlates of LTBI among attendees at a recently created voluntary drug treatment center using a standardized questionnaire and tuberculin skin testing (TST). Participants ($N = 196$) were mostly men (95%), under 40 (median age = 36 years) and reported heroin use immediately before treatment entry (75%). Positive TST prevalence was 86.7%. Nine (4.6%) participants were HIV-infected. Previous arrest/incarcerations (AOR = 1.1 for every entry, $p < 0.05$) and not being HIV-infected (AOR = 6.04, $p = 0.03$) were significantly associated with TST positivity. There is an urgent need to establish TB screening and treatment programs in substance abuse treatment centers and to tailor service delivery to the complex treatment needs of patients with multiple medical and psychiatric co-morbidities.

Keywords

Tuberculosis; Substance use; HIV; Integration; Malaysia

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1. Introduction

Tuberculosis (TB) remains a major cause of morbidity and mortality worldwide, with a global burden of 8.8 million incident cases and 1.4 million TB-attributed deaths in 2010. Almost 80% of these cases were from the African and Asian regions and 13% of incident cases occurred among people living with HIV/AIDS (PLWHA) (World Health Organization (WHO), 2011a). Despite declining incidence since 2002, many countries in these two regions are unlikely to achieve the TB-related United Nations' Millennium Development Goals (MDG) by 2015 (Ooms, Stuckler, Basu, & McKee, 2010; World Health Organization (WHO), 2011a).

Among other marginalized populations, people who use drugs (PWUD) represent a group recognized to be at high risk for TB infection and disease (Centers for Disease Control and Prevention (CDC), 2005; Nava-Aguilera et al., 2009). This is believed to be related to the drug use environment (close proximity at drug use site), prior experiences of incarceration in closed spaces with high-risk individuals, frequent homelessness, poor nutritional status, co-morbid alcohol use disorders, poor access to health services and highly prevalent HIV infection (Centers for Disease Control and Prevention (CDC), 2005; Deiss, Rodwell, & Garfein, 2009). A systematic review of TB transmission studies showed that PWUD were 3-times more likely to be recently infected with TB than non-drug users (Nava-Aguilera et al., 2009). Furthermore, the worldwide prevalence of latent TB infection (LTBI) in PWUDs (reported to be around 10–59% from various settings) is higher than that of the general population (Deiss et al., 2009). In many countries, incidence of active TB disease (estimated at 1–2 per 100 person–year) (Hwang, Grimes, Beasley, & Graviss, 2009) and TB-related mortality, particularly among PLWHA, are markedly higher than overall national rates (Deiss et al., 2009; World Health Organization (WHO), 2008).

Malaysia is a middle-income country with an estimated intermediate TB incidence and mortality of 82 and 8.5 cases per 100,000 population, respectively, with 9% of TB cases being diagnosed among PLWHA (World Health Organization (WHO), 2011a). HIV prevalence (0.4%) nationwide, however, is concentrated among people who inject drugs (PWID), who represent nearly three quarters of PLWHA in Malaysia (Choi et al., 2010). Prior to the HIV/AIDS epidemic in Malaysia, the government responded to growing rates of illicit drug use by forming an anti-drug task force, criminalizing drug possession and instituting compulsory rehabilitation of PWUD, entailing a compulsory period of detention of 2 years. In 2007, over 54,000 individuals were detained in 28 compulsory drug detention centers (CDDCs) throughout the country under the Dangerous Drug Act (1952). Apart from mandatory HIV testing upon arrival, no further systematic medical screening or care is provided and abstinence from drug use is enforced as a form of 'treatment' (Fu, Bazazi, Altice, Mohamed, & Kamarulzaman, 2012; World Health Organization (WHO), 2009). With high relapse rates (70–90%) post-release from CDDCs along with the recognition that these measures are neither clinically effective nor cost-effective and that national HIV control lags behind the MDG, the Malaysian government began to shift its response, starting with establishing the National Strategic Plan on HIV/AIDS in 2006 (Csete et al., 2011; World Health Organization (WHO), 2009). The national HIV/AIDS strategy initiated the development of an HIV/AIDS surveillance system, established voluntary HIV testing and

counseling programs and needle and syringe exchange programs (NSEP), and improved access to methadone maintenance therapy (MMT) and antiretroviral therapy (ART) (Reid, Kamarulzaman, & Sran, 2007). After decades of deploying only punitive approaches to address illicit drug use, the National Anti-Drug Agency (NADA) recently adopted an innovative voluntary model to treat PWUD, which aligns with recent UNAIDS recommendations (World Health Organization (WHO), 2009, 2011b). These newly developed “Cure and Care” (C&C) centers provide free, voluntary access to MMT for opioid-dependent individuals as well as voluntary inpatient treatment for up to 90 days.

Although data suggests a high prevalence of TB in closed settings and among individuals enrolled in substance abuse treatment programs, there is a lack of available data from Malaysia. To address this gap in knowledge, a survey was conducted to assess the prevalence of LTBI among attendees of a C&C center in Kuala Lumpur, Malaysia.

2. Materials and methods

From December 2011 to February 2012, a cross-sectional standardized TB survey was conducted among attendees of the C&C Clinic in Sungai Besi, Kuala Lumpur. Managed by NADA, the facility is one of the eight CDDCs that have recently been converted into voluntary substance abuse treatment centers. With the ability to accommodate up to 200 individuals, the facility offers inpatient care, counseling and methadone therapy (MMT) for a maximum period of 3 months. All C&C clinic services are free of charge. Participants on MMT receive treatment for up to 90 days, and can continue receiving methadone at this clinic or can be referred to another community-based MMT program closer to their homes, operated either by NADA or the Ministry of Health. Unlike CDDCs, where HIV testing is compulsory, voluntary testing is provided but no further HIV or other medical (including TB) services are available onsite. PLWHA and those with other medical or psychiatric co-morbidities are referred to community hospitals for further management.

Inpatient clients and attendees of the outpatient MMT program were approached for study participation, involving a brief health survey and TB screening. After those who agreed to participate underwent informed consent, participants were interviewed face-to-face using a structured questionnaire. Study questionnaires were translated and back translated from English into Bahasa Malaysia and administered by trained research assistants. Questionnaire content included socio-demographic, drug use, drug treatment, previous arrests and incarcerations, and diagnosis and treatment of HIV, TB and other diseases. Prior Bacillus Calmette-Guerin (BCG) vaccination was verified by the examination of a scar on the left deltoid region. Participants were screened clinically for TB using the WHO symptom scoring: cough >2 weeks (2 points), expectoration (2 points), weight loss (1 point), loss of appetite (1 point) and chest pain (1 point) (World Health Organization (WHO), 2000). Subjects suspected of having active TB (5 points or more) were referred to a community hospital for further assessment. A tuberculin skin test (TST) was placed intradermally using 0.1 mL (2 TU) of RT-23 SSI (Statens Serum Institut, Denmark) and read after 48–72 hours for those who were initially symptom-free or whom active TB was excluded. TST reactivity was defined as induration size of 10 mm among HIV-uninfected or those with unknown HIV status, and 5 mm among HIV-infected participants (Center for Disease Control and

Prevention (CDC, 2000). Two-step TST testing was performed 1 week later for initially TST-negative participants and anergy testing was not provided. Individuals with positive TST were referred to a community hospital to be counseled and assessed for eligibility for starting isoniazid preventive therapy (IPT).

Categorical variables were presented using frequencies, while continuous variables were presented with the median and either standard deviation (SD) or interquartile range (IQR) depending on the variable's distribution normality. The primary study outcome was TST reactivity, and covariates associated with TST positivity significant at the $p < 0.1$ level in bivariate regression models were included in the multivariate regression analysis. In multivariate models, associations were considered significant at the $p < 0.05$ level. Income was categorized according to the Malaysian poverty line income of 800 Malaysian ringgit (MYR) (The Economic Planning Unit Prime Minister's Department, 2010) and BCG vaccination was categorized as having been vaccinated either once or twice over one's lifetime (first at infancy and a booster at either 6 or 12 years old) (Rafiza, Rampal, & Tahir, 2011).

The study was reviewed and approved by the ethics committee of University of Malaya Medical Centre.

3. Results

The disposition of participants is depicted in Fig. 1. A total of 219 C&C Clinic attendees agreed to participate in the study. Twenty two (10%) reported having symptoms associated with active TB based on the initial TB symptom screening (WHO TB symptom scores of 5 or more) and were referred to a community hospital for further assessment. Although none of these 22 individuals had active TB, only 15 agreed to subsequent TST, resulting in a total of 212 subjects who underwent final testing. Of this total, 16 (7.5%) defaulted from TST reading, resulting in 196 (89.5%) participants in the final analysis.

Overall, the reactive TST prevalence in this sample was 86.7%, with a median induration size of 15 mm (SD = 5.78; range 0–30 mm). Table 1 describes the characteristics of the study sample and the correlates of being TST-positive. The majority of participants were men (95.9%), under the age of 40-year old (median age 36, SD = 9.28) and of Malay ethnicity (78.6%). Nearly all (93.9%) participants reported being previously incarcerated and having been in jails, prisons and/or CDDCs for a median of 7 times (IQR = 3–11) and for a median duration of incarceration of 114 weeks (IQR = 23.3–271.5). Only nine (4.6%) participants self-reported being HIV-infected, and most (89.3%) participants had been HIV-tested, primarily through mandatory HIV testing programs in prisons, jails and CDDCs.

Essentially all (99%) participants were vaccinated with BCG and three quarters of the participants were vaccinated twice: the first at infancy and the second either at 6 or 12 years old during primary school, in accordance with the Malaysian Ministry of Health policy for TB prevention. This practice was abolished in Malaysia in 2005 and BCG vaccination is currently offered only to newborns (Rafiza et al., 2011). Ten (5%) participants believed that they previously had active TB but medical records were not available for verification.

Only four variables were significantly correlated with being TST positive in the bivariate analysis: number of times of previous entry into a correctional setting, not being HIV-infected, recent use of heroin and receipt of MMT. After adjusting for potential confounders, TST positivity was significantly associated with incarceration (AOR = 1.1 for every entry into a correctional setting, $p < 0.05$) and not being HIV-infected (AOR = 6.04, $p = 0.03$).

4. Discussion

To our knowledge, this is the first structured TB survey conducted among attendees of a drug rehabilitation center in Malaysia. Of note is the higher prevalence (86.7%) of TST positivity in this sample compared to the reported reactive TST prevalence among PWUD elsewhere (ranging from 10 to 59% in various international settings) (Deiss et al., 2009) and provides direct empiric evidence for the role of previous incarceration and detention on facilitating TB infection.

Reports from other settings, though mostly conducted in low TB burden countries, confirm a high LTBI prevalence in this at-risk population (Deiss et al., 2009). TB survey reports from the United States revealed TST positivity prevalence of 14% from an NSEP center in New York (Salomon, Perlman, Friedmann, Ziluck, & Des Jarlais, 2000) and 15.7% in an MMT clinic in New Haven (Durante, Selwyn, & O'Connor, 1998). Increasing age and duration of injection drug use were the main correlates of TST positivity among attendees at these centers. Positive TST prevalence among clients of substance use treatment centers in Canada was higher than reported in the United States. Compared to the LTBI prevalence of 0.4–16.4% in the general population (Rusen, Yuan, & Millson, 1999), a LTBI survey among PWID in Montreal revealed a prevalence of 22% (Brassard, Bruneau, Schwartzman, Senecal, & Menzies, 2004), while a prevalence of 31% was reported among attendees of NSEP in Toronto (Rusen et al., 1999). The reason for higher LTBI prevalence in the Canadian studies might be related to the use of lower TST cut-off of 5 mm, regardless of the HIV status. Utilizing interferon gamma release assay (IGRA), a survey in Estonia reported a very low LTBI prevalence (7.4%) among MMT attendees (Ruutel et al., 2011), while a similar report from the United States showed higher prevalence (34%) of IGRA positivity among crack cocaine smokers in Texas (Grimes, Hwang, Williams, Austin, & Graviss, 2007).

The high prevalence of TST positivity in this sample compared to other studies might be related to several factors. Correctional settings are highly conducive to TB transmission (Restum, 2005) given poor ventilation, lack of routine TB screening, inadequate access to health services and the concentration of people with risk factors for progression to active TB disease (HIV infection, PWUD and low socio-economic background) (Al-Darraj, Kamarulzaman, & Altice, 2012). Taken together, these factors create the “perfect storm” for facilitating TB transmission and causing a high prevalence of TB (estimated to be 100 times higher compared to the general population) in these settings (World Health Organization (WHO), 2000). The majority (93.9%) of our participants had been admitted into a confined setting (jail, prison or drug detention center) at least once in their lifetime and participants with previous entry into these settings had an increased TST positivity risk of 1.1 for each additional entry into a confined setting. This high incarceration rate is largely the result of

the intensive criminalization of drug use in Malaysia (World Health Organization (WHO), 2009). One recent survey among HIV-infected prisoners in the Kuala Lumpur region showed a similarly high (85%) prevalence of reactive TST (Al-Darraj, Kamarulzaman, & Altice, 2011) while another survey among HIV-infected and HIV-uninfected prisoners in the northeastern state of Kelantan showed a TST-reactive prevalence of 87.6%, and similarly showed that prior incarceration was associated with TST positivity (Margolis, Al-Darraj, Wickersham, Kamarulzaman, & Altice, 2013). Taken together, the high TST prevalence in this community drug treatment setting likely represents the trans-institutionalization from prisons to communities of PWUDs, suggesting the need for expanded community-based drug treatment programs, potentially as an alternative to incarceration, coupled with the need to integrate TB screening and preventive measures into these settings.

Drug treatment programs, especially MMT programs where patients congregate for medications and counseling, may be settings in which TB, including multi-drug resistant TB (MDR-TB) transmission, may occur given the congregation of high-risk individuals (Conover et al., 2001). An effective TB control program in Malaysian drug treatment centers would involve establishing routine TB screening and expanding provision of IPT alongside other previously described infection control measures (Friedland, 2010).

Although BCG vaccination may reduce TST specificity if performed after the first year of life (Farhat, Greenaway, Pai, & Menzies, 2006), repeated BCG vaccination did not significantly influence TST reactivity (Al-Darraj et al., 2011; Tan, Kamarulzaman, Liam, & Lee, 2002). This study confirms earlier reports that HIV infection, presumably through its negative influence on the immune system (Robles et al., 1999), is associated with lower rates of TST positivity among PWUD, even if the TST positivity cut-off was lowered to 5 mm (Graham et al., 1992). In this study, PWUDs without HIV infection were at 6-fold more likely to be TST positive ($p = 0.03$) than their HIV-infected counterparts after adjusting for other potential confounders. Although IPT is more effective among people with positive TST (Akolo, Adetifa, Shepperd, & Volmink, 2010), the WHO recommends IPT to all PLWHA regardless of the TST reaction because of the high risk of TB reactivation and reinfection among this particular population (World Health Organization (WHO), 2011c).

TB screening and treatment services may represent an important primary contact point for PLWHA and PWUDs, and co-location of services for multiple morbidities has the potential to improve access to and delivery of care for this at-risk population (Deiss et al., 2009; Sylla, Bruce, Kamarulzaman, & Altice, 2007; World Health Organization (WHO), 2008). TB screening and provision of directly observed preventive therapy (DOPT) using isoniazid has been shown to be effective and cost-saving when coupled with NSEP or MMT programs, irrespective of whether monetary incentives were added to improve adherence to follow up visits (Deiss et al., 2009; Perlman et al., 2001; Scholten et al., 2003; Snyder et al., 1999). Of note, the main reason for IPT non-completion among attendees of an MMT center in the United States was administrative discharge from the program (O'Connor et al., 1999). On the other hand, MMT or any other effective opioid substitution therapy (OST) program provided in voluntary settings is considered central to improving treatment outcomes for other diseases, including HIV (Altice et al., 2011; Berg, Litwin, Li, Heo, & Arnsten, 2011; Lucas et al., 2010) and HCV (Bruce et al., 2012; Litwin, Berg, Li, Hidalgo, & Arnsten,

2011) infections. The added contribution of TB services might ultimately contribute to reduced morbidity and mortality from these overlapping co-morbidities (Pollack, D'Aunno, & Lamar, 2006). In a report from New York, the co-location of HIV prevention and primary care services in drug treatment programs was found to be effective in delivering high-quality HIV services to PWUD. These programs provide a large population of PWUD or PWUD with access to HIV care, utilizing the expertise of drug treatment staff in serving this population (Rothman et al., 2007). Despite the potential synergistic impact of addressing multiple co-morbidities, many countries challenged with the syndemic of HIV, TB and substance use frequently develop uncoordinated vertical programs, which are managed separately at the local and national levels (Ruutel et al., 2011; Sylla et al., 2007). Additionally, the provision of effective management and interventions of multiple co-morbidities for PWUD have been complicated by multi-level barriers to accessing health services and reciprocal mistrust between PWUD and conventional health care providers (Altice, Kamarulzaman, Soriano, Schechter & Friedland, 2010; Rothman et al., 2007).

To increase access to health services for marginalized populations confronting multiple, prevalent morbidities, the WHO has recommended a model of 'one-stop shopping' in which an array of services for PWUDs (e.g., HIV, TB, OST, NSEPs, etc) would be provided free to individuals needing care (Sylla et al., 2007; World Health Organization (WHO), 2008). Importantly, specific adherence support measures, implemented in collaboration with key community partners, are needed to improve low levels of adherence to treatment regimens and clinical follow-up visits (Binford, Kahana, & Altice, 2012; Meyer, Althoff, & Altice, 2013).

The study is limited by the nonavailability of a gold standard diagnostic test for LTBI. TST is neither 100% sensitive nor specific in diagnosing LTBI and is influenced by the immune status of the individual and previous BCG vaccination. The new IGRA assays perform better than TST but its high cost and technical complexity hamper its potential to be immediately expanded in low- to middle-income countries (World Health Organization (WHO), 2011d). There also does not exist a comparative estimate of the TST reactivity in the Malaysian general population, though the prevalence among Malaysian healthcare workers (52.1%) (Tan et al., 2002) and in the general population in the Western Pacific region (36%) (Dye, Scheele, Dolin, Pathania, & Raviglione, 1999) are markedly lower.

5. Conclusions

PWUDs remain at high risk of LTBI and progression to active disease. This marginalized population has poor access to health services due to criminalization, stigma and lack of community support. Drug treatment centers can provide an effective and cost-effective platform to deliver integrated medical and public health services to prevent and treat HIV, TB and substance use disorders in this socially marginalized population. There is an urgent need to expand integration of these healthcare services in countries where HIV, TB and substance use disorders are especially prevalent among PWUDs.

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Fig. 1. Participants' disposition. Legend: TB: tuberculosis; TST: tuberculin skin test.

Table 1

Correlates of tuberculin skin test positivity.

Variable	N (total = 196)	Univariate analysis		Multivariate analysis	
		Unadjusted OR	p value	Adjusted OR (95% confidence interval)	p value
Residence in Malaysia					
Other states	40	Referent			
Klang Valley	156	0.68	0.49		
Age	All	1.03	0.14		
Institutional status					
Outpatient	35	Referent			
Inpatient	161	1.11	0.84		
Gender					
Female	8	Referent			
Male	188	2.28	0.33		
Ethnicity					
Others	42	Referent			
Malay	154	1.11	0.83		
Secondary school completed					
Yes	90	Referent			
No	106	0.58	0.22		
Marital Status					
Married	30	Referent			
Not married	166	0.19	0.11		
Monthly income (MYR) ^a					
>800	112	Referent			
800	84	0.72	0.43		
Duration of engagement in treatment	All	0.99	0.83		
Stable job in the past 12 months					
Yes	82	Referent			
No	114	1.22	0.63		
Ever arrested and/or incarcerated					

Variable	N (total = 196)	Univariate analysis		Multivariate analysis	
		Unadjusted OR	p value	Adjusted OR (95% confidence interval)	p value
No	12	Referent			
Yes	184	2.33	0.22		
Times of being arrested and/or incarcerated	All	1.07	0.08	1.1 (1–1.2)	0.05
Duration of incarceration (weeks)	All	1	0.11		
Drug use duration	All	1.03	0.13		
Recent Drug use					
Heroin use					
No	49	Referent			
Yes	147	2.55	0.03	1.85 (0.71–4.85)	0.21
Methamphetamine use					
No	128	Referent			
Yes	68	1.00	0.99		
Polydrug use (both heroin and methamphetamine)					
No	142	Referent			
Yes	54	1.3	0.58		
Ever injected drugs					
No	65	Referent			
Yes	131	1.57	0.29		
On methadone therapy					
No	52	Referent			
Yes	144	2.31	0.055	2.16 (0.82–5.67)	0.12
HIV infection					
Yes	9	Referent			
No	166	3.45	0.096	6.04 (1.1–32.79)	0.03
BCG ^b 2 doses					
No	48	Referent			
Yes	148	1.78	0.20		

^aMYR: Malaysian Ringgit.^bBCG: Bacillus Calmette-Guerin.