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Demographic, socio-economic and behavior as risk factors of tuberculosis in Malaysia: a systematic review of the literature

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Abstract

Background: Tuberculosis (TB) is making a comeback and has remained one of the main causes of mortality among the list of infectious diseases in Malaysia.

Objective: To evaluate the burden and demographic, socio-economic and behavior as risk factors of TB among communities in Malaysia.

Method: A comprehensive search of Scopus, Sciencedirect, PubMed, DOAJ, CINAHL Plus, MyJournal, BIREME, BMC Public Health, Medline, CAB, EMBASE (Excerpta Medica dataBASE), and Web of Science (WoS) was undertaken from the articles published from 1st January 2008 to 31st December 2017 using medical subject heading (MeSH) key terms.

Results: Of 717 papers screened, 31 eligible studies met our inclusion criteria. Gender, age, marriage status, ethnicity, area of living, being in prison and immigrant were evaluated as demographic factors, while educational level, occupation and household income were evaluated as socio-economic factors. For behavioral factors, smoking, drug abuse, alcohol consumption and other lifestyle were evaluat-

ed. However, not all the studies were statistically significantly associated with these risk factors. Studies on household income were few and too small to permit a conclusion. We also did not find any study that investigated TB infection among sex workers.

Conclusion: Immigrant in high density settings may increase the progression of disease infection in Malaysia. The risk factors for the development of TB, specifically in a high-risk population, should be targeted through the implementation of specialized interventions. Further research into the role of indoor and outdoor physical environments is required to better understand the association between the physical environment and the social environment with TB infection.

Keywords: behavioral; demographic; risk factors; socio-economic; tuberculosis.

Introduction

Tuberculosis (TB) is the ninth leading cause of mortality worldwide. It remains the most deadly infectious disease, ranking above HIV/AIDS infection (1). In 2016, the World Health Organization (WHO) reported 10.4 million new TB cases and 1.7 million deaths globally. In Malaysia, there were 1945 deaths from 25,739 cases in 2017 with increase of 14.7% over 1696 deaths from 24,220 cases in 2015 compared to dengue (237 deaths) and leptospirosis (52 deaths) (2). It was reported that between 1960 to the mid-1980s, Malaysia managed to reduce TB cases from more than 30,000 to fewer than 6000 cases but the cases gradually increased again from the mid-1990s. In 2017, the highest number of cases was found in Sabah, followed by Selangor.

It is crucial to understand the risk of acquiring tuberculous infection and its risk of progression from infection to the disease to adopt a strategic plan for TB control. Developing active TB and the probability of reactivation of latent TB infection depends primarily on the balance

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between exogenous and endogenous factors. An exogenous factor is determined by an intrinsic combination of the infectiousness and clinical onset of a source case, duration and proximity to contact and behavioral risk factors including smoking, alcohol and drug abuse (3). In high density settings such as prisons and hospitals where people are socially closer and there is overcrowding, people will be frequently be exposed to pathogens. Endogenous factors lead to the development of the disease and increase the severity from infection to active disease (4).

Immigration of foreign workers enhances the high TB prevalence in Malaysia. Although the number of TB patients was higher among the local population, it is believed that the trend in TB transmission among those of different nationalities from endemic countries likely impacted the prevalence of TB in Malaysia (5). The movement of persons across the region is common as people seek employment opportunities, do religious pilgrimage or for trading purposes (6). Based on molecular tests (7, 8), the high number of TB cases among immigrant is thought to be largely due to reactivation of latent infection acquired in their country of origin.

Thus, conducting a systematic review will provide a comprehensive assessment of the TB which might be useful for stakeholders, such as policy makers, health experts and researchers to implement appropriate strategies for high-risk populations. We sought to identify, summarize and quantify existing evidence to evaluate the burden of TB for an association between demographic, socio-economic and behavioral risk factors and TB infection conducted in Malaysia.

Methods

Search strategy

We created a strategy to search all published studies with the aim of identifying TB cases among communities in Malaysia. The search was limited to articles published from 31st January 2008 to 31st December 2017. The search was done in Scopus, Scencedirect, PubMed, DOAJ, CINAHL Plus, MyJournal, BIREME, BMC Public Health, Medline, CAB, EMBASE, and WoS databases. The search terms combined medical subject heading (MeSH) terms and text words including “tuberculosis”, “TB”, and “Malaysia”. The details of the search terms are outlined in the Table 1. The articles identified by the search strategy were entered into the reference management software library, Mendeley Desktop, version 1.17.3 (9). Reference lists of included studies were screened for relevant citations.

We screened all titles and abstracts such as [1] which were duplicated [2] which were not published in a peer-review journal, not published in English, were conference abstracts, notes and book studies

Table 1: The search strategies.

Database	Search terms
Scopus	[tuberculosis] or [tb] AND [Malaysia]
Science direct	#1 [tuberculosis] or AND [Malaysia] #2 [tb] AND [Malaysia]
PubMed	[tuberculosis] or [tb] AND [Malaysia]
DOAJ	#1 [tuberculosis Malaysia] #1 [tb Malaysia]
CINAHL Plus	[tuberculosis] or [tb] AND [Malaysia]
MyJournal	[tuberculosis]
BIREME (Virtual Health Library)	#1 [tuberculosis] or AND [Malaysia] articles #2 [tb] AND [Malaysia]
BMC Public Health	[tuberculosis] or [tb] AND [Malaysia]
Medline	[tuberculosis] or [tb] AND [Malaysia]
CAB	[tuberculosis] or [tb] AND [Malaysia]
EMBASE OVID	[tuberculosis] or [tb] AND [Malaysia]
WoS	[tuberculosis] or [tb] AND [Malaysia]

and these were therefore excluded. The remaining full-text articles such as [3] non-original research/review, non-human studies, conducted outside of the Malaysia, irrelevant to demographic, socio-economic and behavioral risk factors of TB infection were excluded to determine the eligibility. Further screening and review of the titles/ abstracts/full texts articles were filtered reveal 31 articles that met the inclusion criteria (Figure 1).

Selection criteria

The article consists of various study designs that were methodologically diverse and comparative between ecological studies, descriptive studies, correlational, etiological, analytical studies, ecological studies, case-control studies, cohort studies, and cross-sectional study.

The inclusion criteria being applied were as follows: 1) demographic, socio-economic, and behavioral risk factors of TB cases; 2) tuberculous infection and/or TB disease diagnoses were confirmed by laboratory diagnosis [acid-fast bacilli (AFB), culture and/or molecular tests], tuberculin skin test (TST), radiograph, clinical diagnosis or a combination of these; 3) the epidemiological study of primary or secondary data analysis.

Data extraction

The first author (Nur Adibah Mohidem) independently extracted the data from all included studies. Four reviewers, Zailina Hashim, Malina Osman, Rafiza Shaharudin, and Farrah Melissa Muharam cross-checked the findings. Common themes were identified and collated. Any discrepancies were discussed and resolved by the reviewers.

The data and information extracted included: 1) authors, 2) journal, 3) year of publication, 4) study design, 5) setting and 6) key

findings from publications that were eligible for inclusion in the final systematic review. Data were extracted to a standardized Microsoft Excel 2018 spreadsheet.

Data synthesis

A summary of the information extracted from the included studies were presented in tabular form (Table 2). These findings were compared narratively and suggestions for the identified gaps in previous studies in terms of associated risk factors of TB were discussed.

Ethical approval

The study did not involve either the use of human or animal subjects.

Results

Literature search and selection of eligible articles

Our search strategy yielded a total of 717 studies of which 353 references remained after eliminating any duplicates. After screening the titles and abstracts, 314 references continued to the next stage for re-evaluation of the articles according to the full texts. Ultimately, 32 articles fulfilled the inclusion criteria and were included in this systematic review. Additionally, one record was excluded due to an ambiguous year. The flow diagram of the study selection process is shown in Figure 1. The remaining 31 publications were eligible for more detailed review in the final analysis (Table 2).

Association measures

All 31 articles reported an association between demographic, socio-economic and behavior as risk factors for TB. Twenty-eight studies reported demographic risk factors while 11 and 19 studies reported socio-economic and behavioral risk factors, respectively.

Demographic risk factor of TB

Several studies considered differential cases of TB with an association of demographic risk factors and their potential reasons. Most of the studies found TB cases were statistically significantly higher among men compared to women. However, there is a difference between Kurniawati et al. (10)

and the other studies which found no statistically significant association between gender and drug resistant TB ($p = 0.05$).

The majority of the studies proved that TB affects the younger age group (below 40 years). In contrast, Liew et al. (11) found that the older age group was more vulnerable to TB (40 above) with a mean age of 42.36 ± 17.77 years. The statement was supported by Dujaili et al. (12). However, Khan et al. (13) reported a slightly lower mean age of 36.4 ± 12.87 years. Of the 109 TB lymphadenitis patients, 35 (33.0%), 37 (34.0%) and 36 (33.0%) were examined for 2006, 2007 and 2008, respectively. The incidence of TB lymphadenitis was significantly higher among the young-est age group 21–30 years, followed by 51–60, 31–40 and 41–50 years. This finding did not synchronize according to the categories of age group from youngest to oldest. This proposes that higher TB infection is not wholly dependent on younger age. There was no available study, or available but not eligible study based on the inclusion/exclusion criteria among children and babies.

Not sufficient studies included marriage status as a risk factor. Mohd Shariff et al. (14) found that TB was more prevalent among single TB patients compared to those who are married. Single [odds ratio (OR): 2.58, 95% (CI): 1.09–6.09] is associated with the multidrug-resistant (MDR-TB) occurrence. Mohd Shariff et al. (14) found that three times the possibility of developing MDR-TB among single patients compared to those who are married [odds ratio (OR): 2.58, 95% confidence interval (CI): 1.09–6.09]. However, Aung et al. (15) found that being divorced ($p = 0.128$) was reported to be statistically significant, unadjusted and to have a higher association than being single ($p = 0.073$) for the recurrence of TB. In contrast, Rafiza et al. (16) highlighted that TB prevalence had a significantly higher risk among married people (OR: 1.69, 95% CI: 1.04–2.74) on overall the prevalence rate of latent TB infection among health care workers. Contrary to these findings, Aung et al. (15) were unable to prove any significant association between sex and marriage status and sputum smear conversion at the end of intensive anti-TB treatment.

By considering ethnicity, most of the studies found that those who were Malay had the most statistically significant association with the TB morbidity rate, drug-resistant TB, TB lymphadenitis and the TB trend. Surprisingly, this finding contradicts Syed Suleiman et al. (17) who found a higher prevalence of pulmonary TB cases among Chinese (48.8%) and Indians (40.8%) than Malays (32.9%) ($p < 0.05$). Yet, according to the result by Kurniawati et al. (18) there was no statistically significant correlation between race and drug resistant TB (CI: 0.597, $p < 0.05$).

Two studies found a statistically significant relationship between TB infection and immigrants from

Table 2: Studies included in the systematic review.

Authors	Journal	Year of publication	Study design	Study period	Setting	Key findings
Ong et al.	International Journal of Pharmacy and Technology	2016	Ecological study of surveillance data	2013–2014	All states and Federal Territories in Malaysia	Highest risk of TB-HIV co-infection morbidity rate according to sex, ethnicity and age was in Kelantan while the lowest was in Federal Territory of Labuan
Al-Darraj et al.	Tropical Medicine and International Health	2016	Ecological study of clinical data	2012–2013	Kajang	64.7% of previously undiagnosed active pulmonary TB patients were not able to complete their treatment in prison due to insufficient time (<6 months) remaining in prison. It was associated with older age groups (age \leq 50 and age 40–49) years among HIV-infected prisoners. It may be due to the lack of performance of internationally recommended case-finding strategies and inadequate of TB screening and treatment program in the systematic approach for the Malaysian correctional system
Elmi et al.	Malaysian Journal of Medical Sciences	2016	Retrospective cohort	2010–2014	Kuala Lumpur, Kelantan, Perak, Penang, Johor Baharu, and Kuala Lumpur Federal Territory	Immigrant status and homeless status were potential associated ($p < 0.001$) with poor treatment outcomes of MDR-TB and non-MDR- TB. However, alcohol or drug addictions were not significantly associated with the poor treatment outcomes
Mohd Shariff et al.	International Journal of Mycobacteriology	2016	Case-control	2013–2014	Institute of Respiratory Medicine, Kuala Lumpur	Indian ethnicity, unmarried, living in suburban areas, living in suburban areas are factors that independently contribute to MDR-TB occurrence
Mohd Shariff et al.	Journal of Global Antimicrobial Resistance	2016	Retrospective cohort	2009–2013	Kuala Lumpur	Factors predicting for poor survival in MDR-TB, patients are of local ethnicity and had a history of drug abuse. Malays have the highest risk of death, followed by Chinese and Indian
Abdul Rassam et al.	ISPRS – International Archives of the Photogrammetry, Remote Sensing and Spatial Information Sciences	2016	Retrospective	2015	Shah Alam, Selangor	Number of population and concentration of high-risk group are categorized as population driven factor contribute 46% of the overall risk factors. It is followed by socio-economic status that includes the type of house factors, distance of factory from the house location, type of land use or urban level, distance of healthcare facilities from housing location and household income or socio-economic status
Liew et al.	International Journal Tuberculosis Lung Disease	2015	Retrospective cohort	2012	Malaysia	Predictors of unfavorable TB treatment outcomes were older age, male sex, foreign citizenship, lower education, treatment in tertiary settings and smoking
William et al.	BMC Infectious Diseases	2015	Observation clinical study	2012–2014	Kota Kinabalu	Patients had high smoking rates among males, and migrants may be over-represented for pulmonary TB infection
Elmi et al.	Journal of Infection in Developing Countries	2015	Case control	2010–2014	peninsular Malaysia	Patients who had received previous treatment for MDR-TB and non-MDR were age range (45–64), gender, immigrants status, lifestyle and contact between HIV-infected patients
Aung et al.	International Journal of Pharmaceutical Research	2015	Retrospective review record	2003–2009	Kelantan	Alcoholism was more likely to have recurrent TB

Table 2 (continued)

Authors	Journal	Year of publication	Study design	Study period	Setting	Key findings
Al-Darraj et al.	Occupational and Environmental Medicine	2015	Cross-sectional	2011	Kajang	Prison employees were mostly young (median = 30.0 years), men (88.8%), and who had only worked at this prison for a median total employment period of 60 months. The majority were correctional officers, while civilian employees represented only 7.6% of the respondents. Prevalence of tuberculosis skin test (TST) positivity was 81% and was independently associated with longer (≥ 12 months) prison employment and current tobacco smoking for latent TB infection
Shanmuganathan et al.	Global Journal of Health Science	2015	Descriptive study	2012–2013	Community clinic	Patients in the age group ranging from 41 to 50 years and male had the highest incidence of the infection. Smoking appears to be the most important risk factor of TB followed by drug abuse
Ariffin et al.	Malaysian Family Physician	2015	Ecological surveillance study	2012–2013	Gombak	The mean age of patients was 40.4 ± 14.4 SD. The majority were men. Out of 117 patients, 82.1% were Malaysian citizens and 17.9% were foreigners. Malays were the majority (65%), followed by 7.7% Chinese, 10.3% Indian and 17.1% others. Drug use and smoking are associated with higher risk of developing pulmonary TB and were identified in this audit
Atif et al.	BMC Infectious Diseases	2014		2010–2011	Penang	Being a smoker is a significant predictor of longer treatment duration of pulmonary TB. Risk factors for unsuccessful treatment outcome were foreign nationality, male and being illiterate. Similarly, risk factor for mortality due was higher among the alcoholic and the elderly
Atif et al.	Health and Quality of Life Outcomes	2014	Cohort	2010–2011	Penang	Age ≥ 45 years and being a smoker were predictive of differences in the physical component summary (PCS) scores. Similarly, monthly income more than 1000MYR and being a smoker at the start of the treatment were predictive of differences in the mental component summary (MCS) scores of TB
Al-Darraj et al.	BMC Public Health	2014	Cross-sectional study	2010	Kajang	Most (82.5%) of the latent TB patient had been previously incarcerated and more than half (53.1%) reported sharing needles just prior to their incarceration. Most of them were men, less than 40 years old (median age 36.0) and Malaysians. TST was positive in 88.8% and was independently associated with frequent previous treatment
Elmi et al.	World Journal of Medical Sciences	2014	Cross-sectional study	2012–2013	Kelantan, Perak, Pulau Pinang, Johor Baru and Kuala Lumpur Federal Territory	Gender difference was associated with MDR-LTBI infection among the household contacts, of which female is the highest. The mean age of the participants was 36.12. Low socio-economic status including the low-level of education, unemployment and low family income are not statistically significantly associated with LTBI transmission. Persons per room as a measure of overcrowding also found that it was not a significant risk factor for MDR-LTBI among the household contacts

Table 2 (continued)

Authors	Journal	Year of publication	Study design	Study period	Setting	Key findings
Elmi et al.	International Medical Journal	2014	Retrospective record review	2010–2012	Peninsular Malaysia	The significant factors associated with previously treated MDR-TB cases were being an immigrant and history of intravenous or subcutaneous drug use. The mean age of previously treated MDR-TB group was 39.03 years old and the majority were male (75.7%) while the mean age for the new MDR-TB group was 43.11 years old and 59.0% were male
Al-Darraj et al.	Journal of Substance Abuse Treatment	2014	Cross-sectional convenience survey	2011–2012	Sungai Besi, Kuala Lumpur	The majority (93.9%) of the active TB patients 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. The high TST prevalence in this community drug treatment setting could represent the trans-institutionalization from prisons to communities of people who use drugs for latent and active TB. The respondents were higher among men (95%) and under 40 (median age = 36 years)
Al-Darraj et al.	PLoS ONE	2013	Clinical trial	2012	Kajang	The prevalence (12%) of undiagnosed active pulmonary TB (15 of 125 prisoners) was high and associated with longer duration of drug use that increased vulnerability to TB infection. The majority of patients with were men and age <40 years
Ismail et al.	Preventive Medicine	2013	Ecological study of clinical data	2010		The default testament rate observed could be contributed by the high prevalence of intravenous drug use. HIV-infected TB patients that have social problems including unemployment, incarceration and homelessness may affect their access to health care
Syed Suleiman	International Journal of Endocrinology	2012	Ross-sectional and cohort study	2005–2008	Pulau Pinang, Kelantan, Kuala Lumpur	A higher prevalence of pulmonary TB cases among Chinese and Indians, which could be related to the increased prevalence of smokers, alcoholics and diabetics in these populations. Higher pulmonary involvement was also observed in males, which was could be due to socio- demographic factors. Males has higher tendency to be smokers and drug and alcohol abusers compared to females
Azura et al.	Pakistan Journal of Medical Sciences	2011	Clinical study	2008–2009	University Kebangsaan Malaysia Medical Centre., Bangi	Positive <i>Mycobacterium</i> TB found it was highest among Malays (52%), Chinese (29%), Indians (13%) and others (6%). The ranges of ages of the patients were from 2 to 78 year-old with mean age was 47.61 years old. No clear association was found between MDR-TB and sex. Unemployment, alcohol abuse, low education and low socioeconomic status also not found to be associated with MDR-TB. MDR-TB patients were more likely to be foreign born out of Europe, but the relative risk was not as strong as being previously treated. This may be due to higher risk of transmission of MDR strains for immigrant and confounded by previous treatment among immigrants

Table 2 (continued)

Authors	Journal	Year of publication	Study design	Study period	Setting	Key findings
Awaisu et al.	Substance Abuse Treatment, Prevention, and Policy	2011	Prospective non-randomized controlled intervention study	2008	Penang and Wilayah Persekutuan Kuala Lumpur	A linear effect on both 7-day point prevalence abstinence and continuous abstinence was observed over time in the intervention group. At the end of 6 months, patients who received the integrated intervention had significantly higher rate of success in quitting smoking when compared with those who received the conventional TB treatment alone
Dujaili et al.	Journal of Public Health	2011	Retrospective cohort	2006–2008	Penang	Ever smokers had increased likelihood of TB treatment failure (OR: 7.48), default (OR: 7.17) and were less likely to be cured (OR: 0.34). Smoking was significantly associated with male gender, alcohol use and intravenous drug use. Treatment failure was more common among current and ex-smokers (ever smokers) compared to non-smokers. A greater risk of mortality in ever-smoking TB patients was not found which may be partly assumed due to the ease of access to healthcare facilities in Malaysia
Ronaidi et al.	Malaysian Journal of Public Health Medicine	2011	Retrospective cohort study	2006–2007	Kelantan	Age, gender, educational level, employment status, family income and smoking were all found to have significant relationship with unsuccessful pulmonary TB treatment outcome. In the current study, gender was not a significant predictor for the treatment outcome. Among the respondents, 71% had lower family income (<RM1000) and 41% were smoking, of which 35% were unmarried or divorcee and 21% had low education level
Rafiza	BMC Infectious Diseases	2011	Cross sectional study	2008–2009	Klang Valley	Being male, worked as a nurse, aged 35 years and older, ever married, had history of living in the same house with close family members or friends who had active TB and who had TB, worked as a nurse and being male were significantly associated with LTBI infection. However, duration of employment was not significantly associated with LTBI infection
Rundi et al.	Journal of Health, Population and Nutrition	2010	Qualitative study	2006	Sabah Kuala Lumpur Federal Territory	Patients who were farmers complained that they did not recover fully from TB, and thus were unable to continue their previous work. Patients changed their life style practices including not sharing their utensils, had a separate sleeping are, and practiced social distancing. Most health workers were not aware of the effects of TB on their patients and knowledge of their patients on TB was not adequate. This might explain the reason why some people did not want to marry those persons who had TB
Khan et al.	Medical Principles and Practice	2010	Retrospective study	2006–2008	Penang	Mean age for patients that infected with for Tuberculous lymphadenitis was 36.48 ± 12.87 years. Ethnically, 41.3% of the patients were Malay, followed by Chinese (33.9%)

Table 2 (continued)

Authors	Publication Year of Study design	Study period	Setting
Awais et al.	2010	Cross-sectional survey	Penang
	2010	Retrospective	University Malaya Medical Centre, Kuala Lumpur
	2000–2007		

Mean total score on knowledge of tobacco use was 4.23 (equivalent to of 5%) tobacco use. Patients in the stage of preparation for behavior change were

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Significance: significantly more knowledgeable than the counterparts who were all uneducated and/or illiterate. The mean score was significantly higher than the counterparts who were all uneducated and/or illiterate. The mean score was significantly higher than the counterparts who were all uneducated and/or illiterate.

Most of the patients were unemployed (39%), followed by housewives (10%), laborers (10%), students (8%), shop assistants (7%) and other occupations (27%),

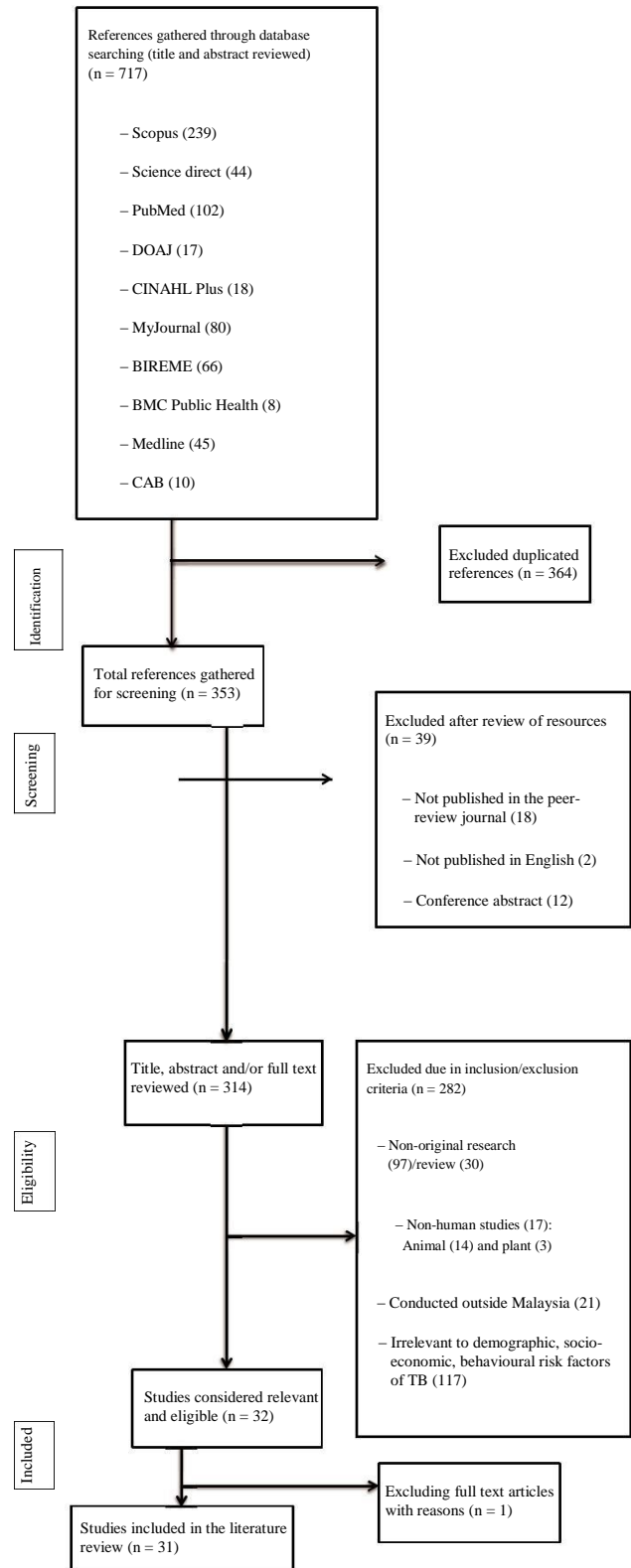


Figure 1: Flow diagram for the study.

Indonesia, Myanmar and Bangladesh. Unsuccessful treatment outcome for new smear positive pulmonary TB was identified among foreign nationalities from South East

Asian countries [adjusted odds ratio (aOR): 21.24, 95% CI: 4.61–97.94]. Similarly, Liew et al. (11) noted a statistically significant association among immigrants (aOR: 76, 95% CI: 7.27–1.77, $p < 0.004$) for the development of a reoccurrence of previously treated MDRTB cases. Elmi et al. (19) found that immigrants had a 21 times higher tendency of unsuccessful treatment outcome compared to Malaysians. Jetan et al. (20) assessed the spatiotemporal distribution of TB and found that there was an increase trend in TB from 2000 to 2007. The study found that the increasing trend was probably due to the massive influx of Indonesian and Myanmar foreign workers to Malaysia.

Only one study, Elmi et al. (21) highlighted found that homeless status was statistically significantly associated with treatment success rate between MDR-TB and non-MDR TB patients ($p < 0.001$). Hence, the majority of studies were unable to investigate if homeless population was the cause of ongoing transmission in shelters.

Socio-economic risk factors of TB

All the selected studies showed an increase of TB infection among patients who have a lower education level. To prove this statement, Ronaidi et al. (22) found that the number of TB patients is higher among the lower education group compared to the higher education group (OR: 3.44, 95% CI: 1.67–7.11, $p < 0.001$). In contrast, Ronaidi et al. (22) reported a higher unsuccessful treatment outcome of pulmonary TB for patients (79.4%) who have a secondary school education and above. Although there is a plausible association between lower education and TB cases, the strength and extent of this association remains uncertain.

All the selected studies found that unemployment was associated with TB infection. The prevalence of TB screening (TST) positivity of latent TB among the unemployed was associated with longer (≥ 12 months out of work) than those who were employed or in a correctional facility (OR: 4.9, 95% CI: 1.5–15.9) (22). However, the study also found that unemployment (aOR: 0.39, 95% CI: 0.18, 0.84) could be a predictor of prolonged treatment duration of new smear-positive pulmonary TB patients. Similarly, Ronaidi et al. (22) showed that TB treatment outcome was significantly associated with being successful and an overall unemployment rate at 45.6% (OR: 2.61, 95% CI: 1.21–5.63, p -value < 0.014) not much difference between the percent of employment (51.5%) and unemployment (48.5%) for unsuccessful pulmonary TB treatment outcome. In contrast, Rafiza et al. (16) also showed that the duration of employment of 11 years or more was the only occupational factor that was statistically significantly associated with a

higher prevalence of infection for latent TB (OR: 3.48, 95% CI: 1.57–7.72). However, the study also showed that the duration of employment was not significantly associated with the infection of latent TB infection.

All the selected studies assessed whether TB infection occurred among low income family. Elmi et al. (23) showed that 47.88% of the household contacts of MDR-TB patients had an income that less than RM675 per month. Another study, (19) shared the same findings for previously treated MDR-TB cases and with newly diagnosed MDR-TB cases, with 80% and 78% of the patients having a family income of less than RM675, respectively. This suggests people in the lower income group have a higher tendency to develop TB.

However, most of the studies were unable to prove any statistically significant association between educational level, occupation and income with sputum smear conversion at the end of intensive anti-TB treatment.

Behavioral risk factor of TB

Smoking is another observed association with TB disease, and studies have been carried out to examine this relationship. For ex-smokers, the median time of cessation was 3.5 months prior to the commencement of pulmonary TB treatment (24). This finding was in line with Dujaili et al. (12) who reported an increase in the likelihood of treatment failure (OR: 7.48), default (OR: 7.17), and smokers were less likely to be cured (OR: 0.34). Meanwhile, TB patients that have ever smoked were approximately 7 times more likely to fail or default from their initial treatment (OR: 7.489, 95% CI: 0.93–60.30) and (OR: 7–176, 95% CI: 2.76–18.62), respectively, compared to those who never smoked. Dujaili et al. (12) discovered that current and ex-smokers were less likely to be cured of TB compared to those who never smoked (OR: 0.342, 95% CI: 21–0.49). Aung et al. (12) estimated that the rate of prevalence for current- and ex-smokers among the TB patients were 40.27% and 13.95%, respectively. That study found that smoking was statistically significantly associated with TB recurrence (crude hazard ratio: 0.76–1.66, 95% CI: 1.32–1.13, p -value: 0.548).

Drug consumption is another behavioral risk factor associated with TB infection. Mohd Shariff et al. (14) found drug abuse as an independent predictor for death among drug-resistant TB patients (aHR: 1.81, 95% CI: 1.01–3.27). The study also showed that patients involved in drug abuse have a nearly 4 times higher risk of dying (aHR: 3.79, 95% CI: 2.07–6.93). Those who have a history of intravenous or subcutaneous drug use were more likely to become infected with MDR-TB disease (OR: 21.34, 2.28–199.71) (23).

Atif et al. (25) also proved this association but in terms of patients' mortality for treatment outcome among new smear positive pulmonary TB patients (OR: 2.54, 95% CI: 1.17–5.51). However, Mohd Shariff et al. (14) failed to prove a statistically significant association between drug consumption and MDR-TB occurrence.

Alcohol consumption also influences TB infection. As shown by Aung et al. (15), the results at the initial diagnosis of previous occurrence of TB (aHR: 4.09, 95% CI: 1.52–11.02) was more likely to have recurrent TB among alcoholics. The treatment regimen with twice weekly doses of streptomycin (S), isoniazid (H) and rifampicin (R) drugs (S2H2R2) during the continuation phase (aHR: 0.11, 95% CI: 0.02, $p < 0.54$) was found to be a statistically significant protective factor for recurrent TB. Elmi et al. (15) also showed the statistically significant association between alcohol consumption and the development of previously treated MDR-TB (OR: 21.34, 95% CI: 2.280199.71, $p < 0.003$). However, Mohd Shariff et al. (14) failed to prove any statistically significant associations between alcoholic status and MDR-TB occurrence.

However, two studies (10, 15) were unable to prove any statistically significant association between smoking status and sputum smear conversion at the end of intensive phase of anti-TB treatment and drug-resistant TB occurrence, respectively.

Discussion

We evaluated the associated risk factor in communities in Malaysia. To the best of our knowledge, this study is the first systematic review that has evaluated the risk of developing TB infection in Malaysia on the basis of demographic, socio-economic and behavioral risk factors.

Demographic risk factors of TB

In this review, we found that men are more at risk to be infected with TB. One possible reason for this is that men predominantly drink alcohol, smoke, consume drug and are more likely to be incarcerated than women. Despite of these behavioral factors, biological factors could also be postulated as causes for the higher incidence and unsuccessful treatment outcome of TB among men (26). However, it is necessary to bear in mind that low notification of cases of TB among women was probably due to them not revealing their infection or seeking treatment. Fear of stigma and discrimination attached to the disease may be the reasons

for not seeking treatment (27). In comparison, women were found to be 2.18 times more compliant than men regarding the probability of adherence to TB treatment (19). While there has been a steep increase in women engaging in risk behavior, it is still predominantly seen more in men supporting difference of TB between the genders.

Age seems to be associated with TB infection, however, the exact age range is unclear. Different behavior may be the factor. Young people are more likely to be exposed to TB because they are more likely to work and are more mobile (28), thus they have less time for treatment. A higher smoking rate among younger people weakens the immune system, putting them at risk of developing TB diseases and related conditions caused by the *Mycobacterium* TB. Although younger TB patients spend more time on social activities such as drinking alcohol, taking drugs and smoking, yet the infection can still occur among older people. This could be due a tendency for the older adult to develop active TB by reactivation of past infections with new and/or latent resistant *Mycobacterium* strains (29). The mean age is an ongoing object of confusion and dispute as different studies categorize different age ranges according to the design of a particular study.

We found that TB patients who are single and unmarried are more likely to have the disease than those who are married. Single people are believed to be more vulnerable to anti-TB drug resistance (30). The potential reason for this is probably due to the lack of emotional support from their spouse, families and friends to monitor and motivate them to seek treatment. Another explanation may be that close contact with patients infected with *Mycobacterium* TB enhances the transmission of TB.

Malay people were found to be the most vulnerable group, followed by Chinese and Indian. However, there could be a bias in the finding due to smoking status and alcohol consumption. This was proven in a study (31) assessing Chinese's and Indian's smokers and alcoholics who are more susceptible to TB infection and which encouraged infectious individuals to cough. The low incidence of alcohol drinkers among Malays may be because it is forbidden by their religion and cultural norms. This suggests that TB infection among different ethnic groups could depend on their behavioral activities. Development of natural resistance (32), also contributes to different susceptibility of TB among different racial groups.

Our study indicates the association between patients' housing area and TB infection. The population may be surrounded by the integration of foreign migrants that act as carriers between workplace environments and communities. Although only a small percentage of the migrant population has been reported to have TB compared to the

number of Malaysian patients, this phenomenon is still a worrying issue. Admitting such an influx of foreign workers from South East Asian countries, specifically from Indonesia, Bangladesh and Myanmar had increased the exposure of infection to the disease. These low-income countries may not have proper health inspections (33) and screening or adequate immunization for the disease as stated by the participants in one study (34). Compared to Malaysia, the WHO has classified that these countries have higher percentages of previously treated MDR-TB cases in the South East Asian region (14). Interestingly, Azura et al. (35) found that TB prevalence does not depend on the number of immigrants. Although transmission of the TB strain may be brought from immigrants' homelands into Malaysia, some of them had undergone treatment from their homeland. It may also be confounded by previous treatment among immigrants. Furthermore, prevention strategies for foreigners by screening them for HIV infection and substance abuse support the fact that there is a small proportion of MDR-TB with HIV co-infection cases (21). Homelessness (36), lack of housing and healthcare services (37) and inappropriate/poor working environment (38) are expected to be major factors contributing to an increase in the prevalence of drug resistance among immigrants and supports the need to improve the living conditions of the immigrant population.

We found that prison has created a conducive environment for the spread of TB. There may be common factors that can cause TB and detection of TB remains passive and failure to complete TB medication among post-release prisoners can create the risk of spreading the disease to communities (39). First, there is a lack of performance for internationally recommended TB case-finding strategies. Second, TB screening policies have not been implemented upon entry into the prisons in Malaysia. Third, there are no national policies on TB screening or infection control policies in Malaysian prisons. Fourth, inadequate policies by the Ministry of Health (MOH) to collaborate between the prison department and the civilian health departments has been organized. Foreign workers should undergo TB screening thoroughly before they can enter Malaysia. Employers should be responsible for having them screened.

Emergence of TB strains contribute to ongoing occupational risk, especially for prison workers in the criminal justice system such as wardens, corporals, sergeants, correctional officers and cell guards. A mean prolonged duration of 60 months' employment in the prison system increased their risk of exposure to TB in this high-congregate setting. The prevalence of TST positivity was independently associated with longer (≥ 12 months) employment in the prison system and current tobacco

smoking. Additionally, failed efforts to detain people who inject drugs (PWID) rather than provide rehabilitation in community settings could contribute to repeated incarcerations that enhance the transmission of TB. Findings from these studies suggest the need to consider alternative approaches to incarceration that reduce placing individuals at high risk for TB in populated settings.

Close contact between a prisoner diagnosed with active TB disease and other prison populations was higher inside the prison. However, not many of the patients reported close contact with a known active TB case outside the prison by released inmates. There is an urgent need to prioritize the implementation of TB control protocols for prison workers, mainly in low to middle income countries. This should also include finding cases of TB by screening upon admission to prison and providing TB preventive therapy with isoniazid or short-term preventive therapy along with evidence-based treatments for HIV and opioid dependence (40). This also involves the exploration of multiple diagnostic approaches using the Xpert technology and potentially combining it with other diagnostic screening modalities in correctional institutions with high HIV prevalence (41).

As there are higher cases of TB among Malaysian prisoners, this indicates the need for further examination on the size of the problem regarding the TB in other populated settings including hospitals. Prison usually creates a conducive environment that facilitates transmission of TB to other inmates because of the lack of proper ventilation, nutritional support and health care services. This particularly occurs in settings that have no routine TB screening procedures before admission into the prison or release into the general society (42).

However, the limitations of the previous studies are on unavailable data on immigrants' treatment outcome. Normally, the clinicians encourage returning them to their country of origin to continue treatment. Sometimes treatment was defaulted on, probably due to the fear of compulsory expulsion from Malaysia. Certain patients failed to complete their diagnosis of active TB in prison due to inadequate time (<6 months) remaining in prison. They are also those previously undiagnosed TB patients serving a prison punishment of less than 6 months (43). This lack of follow-up for post-transferred patients was unfortunate because these patients could conceal their illness for the sake of living and securing employment in Malaysia. There are also patients who spent less than 3 months in prison during the time of diagnosis. This highlights that strengthening TB control programs in targeted high-risk populations and establishing ICF programs for inmates entering prisons is crucial (44). Released prisoners face major challenges when integrating into the community

and may prioritize other transitional issues that can arise during seeking continuity of health care.

Jetan et al. (20) analyzed the trend of TB from 2000 to 2007. Instead of the increasing number of immigrants, the trend could be due to rapid urbanization and overcrowding, which bring about poor sanitation and various health problems. Unpleasant environments can make a person more vulnerable to infection. The increasing number of people and increased mobility can enhance the burden of active TB cases. With these findings, we suggest that immigrant patients can be the carriers that spread the infective *Mycobacterium* to local communities.

Combining the findings of the current review with these studies provides a body of evidence that highlights the important gap in an awareness-raising program for TB care in high transmission closed settings and hard-to-reach populations.

Socio-economic risk factors of TB

Although most of the selected studies found that TB infection occurs among the low educational group, it has not been proved that those who have a higher education understand the importance of seeking treatment for TB. It is not necessary for TB patients to only obtain TB-related information through formal health education. Some of the information can be obtained through educational programs. There is a misconception that having little knowledge in relation to TB results in stopping taking anti-TB treatment once the TB-related signs and symptoms have been resolved (45). Patients need to detect the symptoms of TB early so that immediate treatment can be initiated.

The education/training programs can have an impact on TB control and prevention, poor treatment outcome, relapse, recurrence and poor prognosis. Awaisu et al. (46) found that mass media campaigns to reduce smoking among TB patients under the “Tak Nak” or “Don’t Want” program did not gain positive support in communities against the use of tobacco. In relation to this, this study found that TB patients in the preparation stage for changing their lifestyle were most knowledgeable compared to their counterparts who were still in the pre-action stages (contemplation and pre-contemplation) (5.38 vs. 3.73, respectively).

Healthcare workers could likely to be exposed of TB at their workplace. However, they have different attitudes and beliefs about TB. Most of them were not aware of the effects of TB from their patients, thus knowledge about the possibility of becoming infect from their patients was crucial.

Unemployed TB patients have better performance of completing TB treatment, which was 2.56 times higher

within 6 months (25). One possible reason for this finding might more frequent seek assistance from health carers when they are depressed as a result of being unemployed, thus clinicians can monitor the progression of the treatment. Interestingly, this finding contradicts another study (19) which showed that unemployed people could have social problems such as incarceration and homelessness that inhibit their access to health care and services. Their low immune status and income status prevent them complying with their follow-up appointments scheduling at hospitals or clinics due to the cost of transportation (47). That unemployed TB patients are more exposed to TB transmission compared to those who are employed could be a plausible explanation for the findings of the selected studies.

Nik et al. (14) found that among respondents, 71% had lower family income between January 2006 and December 2007 which added weight to this argument (<RM1000). People with a low socio-economic status tend to have a higher infection rate compared to those of high socio-economic status. High family income can provide the opportunity to buy medicine and undergo treatment.

Behavioral risk factors of TB

Smokers were observed to more susceptible to TB infection. This was proved when Mohd Shariff et al. (48) found that passive smokers have less than a 76% chance of developing active disease upon infection compared to non-passive smokers. With an increase of 1 year of smoking, it will increase the odds of developing MDR-TB by one unit. Smoking has been shown to be the important risk factor for developing TB among local residents. Impaired clearance of mucosal secretion and reduced phagocytic activities of the alveolar macrophages are some of the reasons for smokers being at high risk for TB infection. Furthermore, it can adversely weaken the immune system. Hence, delayed sputum conversion time and prolonged the treatment duration. In relation to the findings of the selected studies, preventing people from smoking could be an appropriate mitigation measure to developing TB disease across communities.

Some of the patients may quit smoking slightly before the onset of TB symptoms of pulmonary irritability such as cough (12). However, the evidence of respiratory symptoms from smoking cessation that are assumed to be early detection of TB in a high-burden setting is unclear and questionable.

Even so, smokers appear to be 3 times more likely to have default on their treatment than those who never

smoked. Dujaili et al. (49) examined the higher rate of treatment failure in both current and ex-smokers (ever smokers) compared to non-smokers (2.9%; 8/274 vs. 0.4%; 1/250). The study did not find a higher mortality risk among former-smoking TB patients. This may be partly described by ease of geographical accessibility to healthcare facilities in Malaysia. Hence, there is greater availability for all patients to register for TB treatment in subsidized health services implemented by the government. It is hypothetical that, if smoking accelerates TB deterioration, it may constrain communities having access to the healthcare system. The lives of smoking TB patients would possibly be at high risk. The results also support the hypothesis of an increased susceptibility of smokers to poor treatment outcomes and prognosis. If smoking increases the risk of rapid disease deterioration, there is undoubtedly an immunopathological basis for the association, which calls for an integrated TB-tobacco intervention.

The changing behavior for the TB patients of quitting smoking reduced over time when they are being treated and after the course of treatment (14). The intensive nature of a smoking cessation intervention plays a significant role in encouraging and maintaining quitting with lower risk of relapse. The most important point is, that although the quit rates reported by the two other group of researchers were more likely to have been over-estimated, quitting was counted on the basis of self-reports from ex-TB patients. This finding shows the high propensity of social desirability bias in reported issues.

From the perspective of drug abusers, Mohd Shariff et al. (25) examined that drug-resistant TB patients who are also drug abusers are at 4 times higher of risk of death compared to those who are not drug abusers. Based on this outcome, this phenomenon not only adversely affects patient survival but it also enhances their probability of TB transmission. On the other hand, longer duration of drug use and substance misuse also increased vulnerability to TB infection. An imbalanced immune system, both natural and cell mediated, seems to be one of the causes for drug use being a risk factor especially in latent TB cases.

The probability of developing TB is not much different between alcoholics and non-alcoholics. Atif et al. (50) found that there was a 2.54 times higher probability of having TB among alcoholics compared to non-alcoholics, suggesting an increased risk of progression from the infection to the disease. Alcohol users are also highly exposed to a high risk of developing TB. This was proved in an audit report by Ariffin et al. (50) that assessed the structure, processes and outcome of the pulmonary TB management among adults.

Patients usually changed their behavior practices, such as not sharing the same utensils, sleeping in separate

areas, and practiced social distancing. However, TB infection usually depended on the duration, frequent traveling and proximity of exposure; the number of organisms that are expelled into the air from an infected person or index cases to the contacts, and the degree of virulence of the organism.

Limitation of the study

Our study is subject to limitations. There are insufficient data to investigate some risk factors such duration of migration to Malaysia, history of homelessness, history of incarceration and socio-economic stress. These risk factors have been proven to be related to exposure to the disease and might be closely associated with TB among high-risk populations. The present analysis would also have missed unobtainable unpublished data from clinical trials that may influence the findings. Moreover, the present analysis may be subject to publication bias as studies with more TB case among migrants may be less likely to be published. Some migrants do not proactively seek treatment. This may have led to an over- or underestimation of notification rate among local and foreign populations. However, the outcome may be opposite. This may not fully explain the real case and may impact the reliability and generalizability of the research findings.

Another challenge was defining what groups are hard to reach which may vary between different institutional settings. The study analyzed prisoners but sex workers could not be detected by systematic review. This identified gap in knowledge provides an opportunity for future studies among sex workers that been infected with TB which might improve the treatment access and adherence for the patients. Further, the association between household income with TB disease is also unclear, which should be investigated in future studies.

The other limitations of this review include the bias in reporting results from thresholds between studies being published with significant and non-significant findings.

In summary, it is noteworthy that the present analysis is the first study to describe the demographic, socio-economic and behavioral risk factors of TB infection in Malaysian.

Conclusion

Our study highlights that the unrecognized TB transmission in high burden and resource constraint settings is the

major contributor to the ongoing transmission compared to the general population. Instead, migrant workers are part of the chains of TB epidemics that carry the disease from their country of origin to Malaysia. The low socio-economic conditions among migrant population results in overcrowded living conditions, poor hygiene habits, poor ventilation and unpleasant sanitary conditions and spreads the air-borne bacteria from people with active TB. However, these unequal social determinants do not directly link with the physical environment such as indoor air pollution and air conditioning that likely increase the risk of TB transmission. One other point, there is a significant heterogeneity between the studies. High-risk populations are constantly changing together with migratory patterns and the demographic profiles of communities in Malaysia. Future research is needed towards investigating the interaction between the spread of TB and determinants of social mixing patterns among different population group in Malaysia. In relation to this, there is a necessity to further integrate demographic, socio-economic, behavioral and environmental factors to retrospectively collect data for TB prediction. If Malaysia really wants to embark on an elimination phase, it is crucial to implement screening of high-risk populations.

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References

- World Health Organization. In: Global tuberculosis report 2017. Geneva: WHO. Available at: <http://apps.who.int/iris/bitstream/handle/10665/259366/9789241565516-eng.pdf;jsessionid=5CC A27FE2E9F6BFCD227B96125049254?sequence=1>.
- Ministry of Health Malaysia. Communicable disease control division. National tuberculosis control programme. Annual Report; 2016.
- Rosser A, Marx FM, Pareek M. Recurrent tuberculosis in the pre-elimination era. *Int J Tuberc Lung Dis* 2018;22(2):139–50.
- Khajanchi S, Das DK, Kar TK. Dynamics of tuberculosis transmission with exogenous reinfections and endogenous reactivation. *Physica A Stat Mech Appl* 2018;497:52–71.
- Shahidatul-Adha M, Zunaina E, Liza-Sharmini AT, Wan-Hazabbah WH, Shatriah I, Mohtar I, et al. Ocular tuberculosis in Hospital Universiti Sains Malaysia – A case series. *Ann Med Surg* 2017;24:25–30.
- Dias A, Gao R, Sousa P, Gomes M, Oliveira O, Duarte R. Migration flow and its impact on tuberculosis notification in Portugal. *Arch Bronconeumol (English Edition)* 2018;54(1):18–23.
- Wong J, Lowenthal P, Flood J, Watt J, Barry PM. Increased tuberculosis risk among immigrants arriving in California with abnormal domestic chest radiographs. *Int J Tuberc Lung Dis* 2018;22(1):73–9.
- Di Nuzzo M, Trentini A, Grilli A, Massoli L, Biagi E, Maritati M, et al. Extrapulmonary tuberculosis among immigrants in a low-TB burden and high immigrant receiving city of northern Italy. *J Infect Dev Ctries* 2018;12(02):73–9.
- Mendeley. Getting started with Mendeley. Mendeley Desktop. London, UK: 2017 Mendeley Ltd. Retrieved from <http://www.mendeley.com/>
- Kurniawati F, Sulaiman SAS, Gillani SW. Study on drug-resistant tuberculosis and tuberculosis treatment on patients with drug resistant tuberculosis in chest clinic outpatient. *Alcohol* 2012;340:52–1.
- Liew SM, Khoo EM, Ho BK, Lee YK, Mimi O, Fazlina MY, et al. Tuberculosis in Malaysia: predictors of treatment outcomes in a national registry. *Int J Tuberc Lung Dis* 2015;19(7):764–71.
- Dujaili JA, Sulaiman SAS, Awaisu A, Muttalif AR, Blebil AQ. Outcomes of tuberculosis treatment: a retrospective cohort analysis of smoking versus non-smoking patients in Penang, Malaysia. *J Public Health* 2011;19(2):183–9.
- Khan AH, Sulaiman SAS, Muttalif AR, Hassali MA, Khan TM. Tuberculous lymphadenitis at Penang General Hospital, Malaysia. *Med Princ Pract* 2011;20(1):80–4.
- Shariff NM, Shah SA, Kamaludin F. Predictors of death among drug-resistant tuberculosis patients in Kuala Lumpur, Malaysia: a retrospective cohort study from 2009 to 2013. *J Glob Antimicrob Resist* 2016;102–7.
- Aung MMT, Naing N, Rusli AM, Jaeb M, Zuki M, Wan-Arfah N, et al. Risk factors associated with recurrence of tuberculosis at the chest clinic, Hospital Raja Perempuan Zainab II Kota Bharu Malaysia. *Int J Pharm Sci Res* 2015;7(2):77.
- Rafiza S, Rampal KG, Tahir A. Prevalence and risk factors of latent tuberculosis infection among health care workers in Malaysia. *BMC Infect Dis* 2011;11(1):19.
- Syed Suleiman SA, Ishaq Aweis DM, Mohamed AJ, Razakmuttalif A, Moussa MAA. Role of diabetes in the prognosis and therapeutic outcome of tuberculosis. *Int J Endocrinol* 2012;2012:645362. doi: 10.1155/2012/645362. Epub 2012 Apr 18.
- Kurniawati F, Sulaiman SAS, Gillani SW. Study on drug-resistant tuberculosis and tuberculosis treatment. Study on drug-resistant tuberculosis and tuberculosis treatment on patients with drug resistant tuberculosis in chest clinic outpatient department. *Int J Pharm Sci* 2012;4:733–7.
- Elmi OS, Hasan H, Abdullah S, Jeab MZM, Zilfalil BA, Naing NN. Prevalence and associated factors with transmission of latent tuberculosis among household contacts of multidrug resistant tuberculosis patients in Malaysia. *WJMS* 2014;10(3):285–94.
- Jetan CA, Jamaiah I, Rohela M, Nissapatorn V. Tuberculosis: an eight year (2000–2007) retrospective study at the University of Malaya Medical Centre (UMMC), Kuala Lumpur, Malaysia. *Southeast Asian J Trop Med Public Health* 2010;41(2):378–85.
- Elmi OS, Hasan H, Abdullah S, Jeab MZM, Ba Z, Naing NN. Treatment outcomes of patients with multidrug-resistant tuberculosis (MDR-TB) compared with non-MDR-TB infections in peninsular Malaysia. *Malays J Med Sci* 2016;23(4):17.

22. Nik NR, Mohd NS, Wan M, Sharina D, Nik RN. Factors associated with unsuccessful treatment outcome of pulmonary tuberculosis in Kota Bharu, Kelantan. *MJPHM* 2011;11:6–15.
23. Elmi OS, Hasan H, Abdullah S, Jeab MZM, Nadiyah WA, Ba Z, et al. Factors associated with new and previously treated multidrug-resistant tuberculosis in Malaysia: a retrospective record review study. *Int Med J* 2014;21(5):1–5.
24. William T, Parameswaran U, Lee WK, Yeo TW, Anstey NM, Ralph AP. Pulmonary tuberculosis in outpatients in Sabah, Malaysia: advanced disease but low incidence of HIV co-infection. *BMC Infect Dis* 2015;15(1):32.
25. Atif M, Sulaiman SAS, Shafie AA, Asif M, Sarfraz MK, Low HC. Impact of tuber-culosis treatment on health-related quality of life of pulmonary tuberculosis patients: a follow-up study. *Health Qual Life Outcomes* 2014;12(1):19.
26. So H, Yuen CS, Yip RM. Comparison of a commercial interferon-gamma release assay and tuberculin skin test for the detection of latent tuberculosis infection in Hong Kong arthritis patients who are candidates for biologic agents. *Hong Kong Med J* 2017;23(3):246–50.
27. Liu Y, Birch S, Newbold KB, Essue BM. Barriers to treatment adherence for individuals with latent tuberculosis infection: a systematic search and narrative synthesis of the literature. *Int J Health Plann Manage* 2018;1–18.
28. Snow K, Hesseling AC, Naidoo P, Graham SM, Denholm J, du Preez K. Tuberculosis in adolescents and young adults: epidemi-ology and treatment outcomes in the Western Cape. *Int J Tuberc Lung Dis* 2017;21(6):651–7.
29. Kang W, Wu M, Yang K, Ertai A, Wu S, Geng S, et al. Factors asso-ciated with negative T-SPOT. TB results among smear-negative tuberculosis patients in China. *Sci Rep* 2018;8(1):4236.
30. Sikjær MG, Løkke A, Hilberg O. The influence of psychiatric disorders on the course of lung cancer, chronic obstructive pul-monary disease and tuberculosis. *Respir Med* 2018;135:35–41.
31. Suleiman S, Azhar S, Aweis I, Daud M, Mohamed AJ, RazakMuttalif-A, et al. Role of diabetes in the prognosis and therapeutic-outcome of tuberculosis. *Int J Endocrinol* 2012;2012:6. ArticleID645362. <http://dx.doi.org/10.1155/2012/645362>.
32. Nguyen DT, Teeter LD, Graves J, Graviss EA. Characteristics asso-ciated with negative interferon-γ release assay results in culture-confirmed tuberculosis patients, Texas, USA, 2013–2015. *Emerg Infect Dis* 2018;24(3):534–40.
33. Duke T, Tom SK, Poka H, Welch H. Holistic care of complicated tuberculosis in healthcare settings with limited resources. *Arch Dis Child* 2017;102(12):1161–8.
34. Shakri A, Bin MR, Zakaria RB, Samad A, Bin BH. Determining relationship between physical health care settings and Myco-bacterium tuberculosis. *Appl Mechanics Mater* 2011;90:2460–5.
35. Azura S, Hussin S, Rahman MM. Drug resistance and sus-ceptibility of mycobacterium tuberculosis identified at Uni-versity Kebangsaan Malaysia Medical Centre. *Pak J Med Sci* 2011;27:1107–11.
36. Hwang YW, Lee YJ, Kong SY. Epidemiology and clinical out-comes of tuberculosis among homeless persons visiting emergency department in public hospital. *Am J Emerg Med* 2018;36(1):164–6.
37. Kalan ME, Sis HY, Kelkar V, Harrison SH, Goins GD, Jafarabadi MA, et al. The identification of risk factors associated with patient and healthcare system delays in the treatment of tuber-culosis in Tabriz, Iran. *BMC Public Health* 2018;18(1):174.
38. Mokhtar KS, Rahman NHA. Social determinants of tuber-culosis contagion in Malaysia. *Ann Trop Med Public Health* 2017;10(5):1215–20.
39. Issarow CM, Mulder N, Wood R. Environmental and social factors impacting on epidemic and endemic tuberculosis: a modelling analysis. *R Soc Open Sci* 2018;5(1):170726.
40. Mehay A, Raj T, Altass L, Story A, Frater A. An audit of tuberculo-sis health services in prisons and immigration removal centres. *J Public Health (UK)* 2017;39(2):387–94.
41. Calligaro GL, Zijenah LS, Peter JG, Theron G, Buser V, McNerney R, et al. Effect of new tuberculosis diagnostic technologies on community-based intensified case finding: a multicentre ran-domised controlled trial. *Lancet Infect Dis* 2017;17(4):441–50.
42. Arroyave L, Keynan Y, López L, Marin D, Arbeláez MP, Rueda ZV. Negative latent tuberculosis at time of incarceration: iden-tifying a very high-risk group for infection. *Epidemiol Infect* 2017;145(12):2491–9.
43. Al-Darraj HAA, Tan C, Kamarulzaman A, Altice FL. Prevalence and correlates of latent tuberculosis infection among employ-ees of a high security prison in Malaysia. *Occup Environ Med* 2015;72:442–7.
44. Adane K, Spigt M, Dinant GJ. Tuberculosis treatment outcome and predictors in northern Ethiopian prisons: a five-year retro-spective analysis. *BMC Pulm Med* 2018;18(1):37.
45. Adane K, Spigt M, Johanna L, Noortje D, Abera SF, Dinant GJ. Tuberculosis knowledge, attitudes, and practices among north-ern Ethiopian prisoners: implications for TB control efforts. *PloS One* 2017;12(3):e0174692.
46. Awaisu A, Nik Mohamed MH, Abd Aziz N, Syed Sulaiman SA, Mohamad Noordin N, Muttalif AR, et al. Tobacco use preva-lence, knowledge, and attitudes among newly diagnosed tuberculosis patients in Penang State and Wilayah Persekutuan Kuala Lumpur, Malaysia. *Tob Induc Dis* 2010;8. <https://doi.org/10.1186/1617-9625-8-3>.
47. Bay V, Tabarsi P, Rezapour A, Marzban S, Zarei E. Cost of tubercu-losis treatment: evidence from Iran's health system. *Osong Public Health Res Perspect* 2017;8(5):351–7.
48. Tahseen S, Shahnavaz H, Riaz U, Khanzada FM, Hussain A, Aslam W, et al. Systematic case finding for tuberculosis in HIV-infected people who inject drugs: experience from Pakistan. *Int J Tuberc Lung Dis* 2018;22(2):187–93.
49. Masjedi MR, Hosseini M, Aryanpur M, Mortaz E, Tabarsi P, Soori H, et al. The effects of smoking on treatment outcome in patients newly diagnosed with pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2017;21(3):351–6.
50. Ariffin F, Zubaidi AA, Yasin MM, Ishak R. Management of pulmo-nary tuberculosis in health clinics in the Gombak district: how are we doing so far? *Malays Fam Physician* 2015;10(1):26–33.

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