Tuberculosis Treatment Outcome in Patients with Tb-hiv Co-infection in Kuala Lumpur, Malaysia

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Abstract

Background: Tuberculosis (TB) is a serious health threat to people living with human immunodeficiency virus (HIV). Directly observed treatment, short course (DOTS) is one of many efforts done as part of ending TB, in which all confirmed TB sputum smear positive cases properly given treatment and monitored by the healthcare providers or family members to ensure treatment adherence. This study aimed to identify the characteristics, to determine the rate of unsuccessful TB treatment rate and to determine determinants of unsuccessful TB treatment outcome among patients with TB-HIV co-infection in Kuala Lumpur.

Methods: This was a cross-sectional study. The data of all patients with TB-HIV co-infection in the federal territory of Kuala Lumpur from 2013 to 2017 were collected and reviewed. The data were retrieved from the national database (TB Information System) at the Kuala Lumpur Health Department from 1 March 2018 to 31 May 2018.

Results: Out of 235 randomly selected patients with TB-HIV co-infection, TB treatment outcome was successful in 57.9% (cured and completed treatment) and unsuccessful in 42.1% (died, failed or defaulted treatment). Patients who did not receive DOTS (adjusted odds ratio [aOR] 21.71; 95% confidence interval [CI]: 5.36–87.94) and those who received shorter treatment duration of <6 months (aOR 34.54; 95% CI: 5.97–199.93) had higher odds for unsuccessful TB treatment outcome.

Conclusions: Nearly half of the patients with TB-HIV co-infection had unsuccessful TB treatment outcome. Therefore, it is important to ensure that such patients receive DOTS and continuous TB treatment of >6 months. It is crucial to strengthen and widen the coverage of DOTS, especially among high-risk groups, in healthcare settings. Strict follow-up by healthcare providers is needed for patients with TB-HIV co-infection to gain treatment adherence and for better rates of successful TB treatment.

Introduction

It is undeniable that tuberculosis (TB) and human immunodeficiency virus (HIV) co-infection poses a major public health threat worldwide[1, 2]. Worldwide, it has been estimated that more than one-third of people living with HIV (PLHIV) are infected with TB[2, 3]. An estimated 70.0% of PLHIV are from Sub-Saharan African countries[4]. Despite the Southeast Asian Region (SEAR) experiencing 34% decreased TB incidence among PLHIV within an 11-year period until 2013, high TB-HIV disease burden was still observed in Indonesia, Myanmar, Thailand, India and Nepal[5]. The prevalence of TB-HIV co-infection in Malaysia was 12.6%[6].

TB is known as the most common opportunistic infection among PLHIV; treatment management is complicated and TB is the main culprit in most HIV deaths[2, 3, 7]. The World Health Organization (WHO) has reported that around 400,000 PLHIV deaths are due to TB infection[3]. PLHIV have a higher risk for latent TB infection to progress to active TB. As a result of active TB, the immune system of PLHIV is suppressed further as the viral load increases and CD4 levels decrease. Managing TB-HIV co-infection presents enormous challenges to physicians[8].

In the future, concurrent TB-HIV infection will become a burden on a country's expenses, as prolonged treatment may be required as compared to countries with only TB infection[3, 9]. In 2013, the Malaysian government spent about USD15 million on TB intervention and control[10].

Patients with TB-HIV co-infection without anti-retroviral therapy (ART) tend to have poorer TB outcome compared to those who are on ART[6, 11, 12]. Recent literature showed that the risk of death in patients with TB-HIV co-

infection that did not receive ART were 3 times higher as compared to those who received ART [13]. ART should not been delayed especially among MDR-TB patients with HIV co-infection [14]. Study showed that the rate of unsuccessful MDR-TB treatment is proportionately increase with the increase frequency of missed clinic visits [15]. TB infection with late presentation and HIV diagnosis are further risk factors for unsuccessful TB treatment outcome among patients with TB-HIV co-infection [16-18]. Other than that, patients with positive sputum culture upon TB diagnosis are at higher risk for unsuccessful TB treatment outcome[19].

The Directly Observed Treatment, Short Course (DOTS) strategy has been introduced by WHO since year 1994. It is an effort required full support and commitment from every government for its implementation. TB case detection are done via passive case findings. This strategy highlighted a standardization of short-course TB treatment to all confirmed TB sputum smear positive cases which can be given by the healthcare providers or family members to ensure compliance of TB treatment. Other than that, this strategy also ensure all essential anti-TB drugs are supplied regularly. Programme supervision and evaluation are also established as part of its monitoring system. [20].

The Regional Strategic Plan towards Ending TB in the SEAR 2016–2020 was implemented to achieve successful TB elimination in the region by 2035. Hence, TB and HIV programmes need to be strengthened and aimed towards successful implementation by understanding the characteristics of patients with TB-HIV co-infection with successful or unsuccessful treatment outcomes[5]. Recent study done in North-East Malaysia showed that being male and had negative tuberculin test were at disadvantage for having unsuccessful TB treatment outcome [21]. However, studies, especially local studies, for determining the characteristics of such patients, including their clinical status[22], are scarce, especially in this setting, to date. Study from South Africa that evaluated the incidence of adverse events among MDR-TB patients with HIV co-infection showed that almost all patients will experience at least one adverse effect. Among these patients, one third death were due to HIV progression or MDR-TB status as a result of non- compliance to medications. Other deaths were contributed by clinical status such as renal failure, abdominal wall abscess, and related to TB or HIV treatment [14].

This study adds to the literature related to the factors of unsuccessful TB treatment among patients with TB-HIV co-infection in high density population areas like Kuala Lumpur. Despite all the efforts done by the government, the gap which could be filled to ensure future success of TB treatment especially in patients with TB-HIV co-infection could be identified. It is translatable to other settings especially in Malaysia, as the aim of this study is reproducible, by using the same source of data and by using the similar method.

This study aimed to identify the characteristics of patients with TB-HIV co-infection, to determine the rate of unsuccessful TB treatment outcome among patients with TB-HIV co-infection and to identify the associated factors for unsuccessful TB treatment outcome in such patients in Kuala Lumpur, Malaysia.

Methods

Study population and sampling

This was a cross-sectional study involving patients with TB-HIV co-infection in Kuala Lumpur, Malaysia. The sample population was patients with TB who were notified and registered with the National Registry for TB database, i.e. the National Tuberculosis Information System (TBIS), by the Kuala Lumpur Federal Territory Health Department. Patients with TB-HIV co-infection were included via simple random sampling from the patient name

list, and TBIS served as the sampling frame. Sample size was calculated based on the formula by Kish[23] and in reference to a previous local study[6]. After considering 20% missing data, a minimum of 235 patients with TB-HIV co-infection was included in this study.

Data collection

The TB records of all patients with TB-HIV co-infection in Kuala Lumpur from 2013 to 2017 were retrieved, reviewed and collected from the TBIS database at the Kuala Lumpur Federal Territory Health Department.

TBIS database is a health database, under Ministry of Health Malaysia. Data in this database were collected nationwide, for the purpose of monitoring and surveillance TB disease in Malaysia. However, datasets used for analysis in this study are not publicly available due to some concern, in which it contained health information which could compromise the privacy of research participants.

Outcome variables

The study outcome was successful or unsuccessful TB treatment. Unsuccessful TB treatment was defined as death (for any reason during the treatment course), treatment failure (positive sputum smear at 5 months or later during treatment) or defaulted treatment (interrupted treatment for >2 consecutive months).

Successful TB treatment was defined as when a patient was cured (previously smear-positive patients that were smear-negative in the final month of treatment and at least once on a previous occasion) and had completed treatment (patient had completed treatment but did not meet the criteria to be classified either as cure or failure). Patient need to complete their treatment in order to be defined as cured. The TB treatment was successful if the patient was cured and completed treatment but considered defaulted (unsuccessful) if the patient has interrupted treatment for two consecutive months or more [24].

Independent variables

The sociodemographic characteristics included in the study were age, sex, citizenship status, ethnicity, marital status and place of residence. Age was counted starting from the date of birth until the TB notification date. Sex was classified as male or female; citizenship status was classified as Malaysian or non-Malaysian. Ethnicity was considered race inherited from parents, e.g. Malay, Chinese, Indian or others. For place of residence, all flats and slums were considered low-cost residential areas. Apartments, condominiums, terrace houses and bungalows were considered medium- or high-cost residential areas; the place of residence of patients who were homeless or who were instutionalised, i.e. in detention centres or prisons was classified as ‘others’.

The socioeconomic characteristics included in the study were formal education, employment status (employed or unemployed) and household income. Any formal education, regardless of duration, was classified as ‘yes’, and no formal education was classified as ‘no’. Patients who were employed, including self-employment, were categorized as ‘employed’; patients who did not work were categorized as ‘unemployed’. Household income was considered low when it was under 3000 Malaysian ringgit (<MYR3000) [25] or equivalent to less than United States Dollar 738.55 (USD738.55) , and was considered high when it was ≥MYR3000 or equivalent to ≥ USD738.55.

The clinical characteristics retrieved were diabetes mellitus (DM) status, smoking status, Bacille Calmette-Guérin (BCG) scar status, ART status, TB type, TB case category, chest X-ray (CXR) presentation upon diagnosis, sputum smear upon diagnosis, sputum culture upon diagnosis, directly observed treatment, short course (DOTS) status

and duration of TB treatment. For DM status, patients with underlying DM were categorized as 'yes', and those without DM were categorized as 'no'. For smoking status, smokers were classified as 'yes', and non-smokers were classified as 'no'. Patients with a BCG scar on any part of the body, as it varies by country, were categorised as 'present', and those without a BCG scar were categorised as 'absent'. Patients who received ART were categorised as 'yes', and those who did not receive ART were categorised as 'no'. TB type was divided into two categories: pulmonary and extrapulmonary. TB case categories were divided into new cases, relapse and return after default. New cases were all new TB cases notified among HIV patients, 'relapse' indicated previously successfully treated TB cases among patients with HIV but who became infected again with TB; 'return after default' was defined as stopping TB treatment before the completion of treatment. CXR presentation upon diagnosis was categorized according to how severe the lesion appeared on the X-ray film: 'no or minimal lesion' if CXR showed no or few lesions, 'advanced lesion' if CXR showed extensive lesions or miliary appearance, and 'not performed' if CXR was not performed upon diagnosis. Sputum smear and sputum culture were both categorised as 'positive' if the first result was positive, 'negative' if the first result was negative, and 'not performed' if no sputum smear or culture were performed upon diagnosis. DOTS status was 'yes' if the patient received DOTS, and 'no' if the patient did not receive DOTS. TB treatment duration was divided into three categories: <6 months, 6–12 months and >12 months.

Statistical analysis

Data were analysed using SPSS 22 [26]. For descriptive analysis, continuous data were reported as the mean and standard deviation (SD), as the data were distributed normally. Categorical data are reported as the frequency (*n*) and percentage (%). The association between the independent variables and outcome variable (unsuccessful TB treatment outcome) was determined using simple logistic regression (SLR). Multivariable analysis was conducted using multiple logistic regression (MLR) analysis to obtain the adjusted odds ratio (aOR) and 95% confidence interval (CI) and to control for possible confounders. The significance level was set at $p < 0.05$.

Results

From 2013 to 2017, there were total of 690 patients with TB-HIV co-infection. Of these, 235 patients were included in the study. Patients who were transferred out, aged <18 years and with multi-drug resistance TB (MDR-TB) were excluded from the study. The mean patient age was 39.49 (SD 9.35) years. Most of the patients were Malaysians (89.8%), male (85.5%), Malay (48.9%) and lived in medium- or high-cost residences (62.1%) (Table 1).

Most of the patients had received formal education (79.6%), were unemployed (51.1%) and had low household income, i.e. <MYR3000 (88.5%) (Table 1).

The majority of patients was classified as new TB cases (84.7%); 74% were classified as pulmonary TB. Most patients did not receive ART (60.9%), were non-diabetic (96.2%), non-smokers (51.5%) and had BCG scars (90.6%). Upon diagnosis, the majority had no or minimal lesion on CXR (67.7%), 50.6% had negative sputum smear and 50.6% had negative sputum culture. Most patients were under DOTS (66%); 48.1% had 6–12 months' TB treatment. One hundred and thirty-six patients (57.9%) had successful TB treatment outcome, and 99 patients (42.1%) had unsuccessful TB treatment outcome (Table 2).

SLR showed that a few significant factors were associated with TB treatment outcome, namely citizenship status, ethnicity, formal education received, employment status, household income, BCG scar, ART, CXR upon diagnosis, sputum culture upon diagnosis, DOTS status and TB treatment duration. In terms of socio-demographic

characteristics, being non-Malaysian, Malay or Chinese were at higher risk for unsuccessful TB treatment outcome. Socio-economic characteristics showed that patients with TB-HIV co-infection that did not receive formal education, unemployed or low household income were at greater risk to get unsuccessful TB treatment outcome. Clinical characteristics such as absence of BCG scar, received ART, positive or did not perform sputum culture, did not received DOTS, and duration of TB treatment of less than six months among patients with TB-HIV co-infection increase the risk of unsuccessful TB treatment outcome (Table 3).

After adjusting for other factors, the determinants for TB treatment outcome were determined using binary logistic regression. Table 4 shows the final model, by using Forward LR method. Patients who did not receive DOTS had 22 times higher odds of having unsuccessful TB treatment outcome (aOR 21.71, 95% CI: 5.36–87.94, $p \leq 0.001$). Patients with shorter TB treatment duration, i.e. <6 months, had 35 times higher odds of having unsuccessful TB treatment outcome (aOR 34.54, 95% CI: 5.97–199.93, $p \leq 0.001$). This model had no multicollinearity and was stable (variance inflation factor [VIF] < 10), and there was no interaction problem. We also provided the preliminary model which was obtained from enter method of logistic regression which is comparable to binomial regression (Generalized Linear Model) results (Appendix A). Binary logistic regression method was used for this study as it was stable.

In order to assess the model discrimination, area under the ROC curve (AUC) has been obtained (Figure 1). The ROC curve showed that AUC was 0.986. This means that this model will assign almost 98.6% higher probability to the subject with unsuccessful TB treatment outcome compared to successful TB treatment outcome. The optimal sensitivity/ specificity was obtained from the point which was nearest to the left upper corner of the box. Therefore, the optimal sensitivity = 96% and specificity = 1 - 0.022 = 98%.

Discussion

This study reveals that 42.1% of patients with TB-HIV co-infection had unsuccessful TB treatment outcome. The main socio-demographic characteristics of TB-HIV co-infected patients in this study were: aged 18 to 39 years old, male, Malaysian, Malay and residents of medium or high cost residency. Majority received formal education, unemployed and had low household income. Most of the patients with TB-HIV co-infection in this study had clinical characteristics of: non-DM, non-smoker, did not receive ART, pulmonary TB, new TB case, no or minimal CXR lesion, negative sputum smear, negative sputum culture, received DOTS, and received treatment between 6 to 12 months. The main determinants of unsuccessful TB treatment rate among patients with TB-HIV co-infection were: not receiving DOTS and TB treatment of less than six months.

In the present study, TB treatment outcome in patients TB-HIV was closely associated with that of a study performed in 2010 in the Klang Valley, Malaysia, that reported 53.4% successful treatment outcome and 46.6% unsuccessful treatment outcome[6]. However, in the district of Kota Baharu, Malaysia, 93% of patients with TB-HIV co-infection had successful treatment outcome[27]. By comparison, other studies conducted in South Africa also showed better TB treatment outcome in patients with TB-HIV co-infection [28]. Therefore, these differences must be due to multifactorial aspects such as diverse outlook on sociodemographic structure and service provision settings.

Study shown that ART should be initiated as early as possible in MDR-TB patients with HIV co-infection [14]. It is important to start ART earlier among these patients, as higher mortality were found among TB-HIV patients who had not been started with ART prior [12]. It is also shown that higher risk for unsuccessful MDR-TB treatment

occurs with the increase frequency of missed visits which were: 1.50 times, 2.25 times and 3.37 times for once missed visit, twice missed visit and thrice missed visits respectively [15].

Not receiving DOTS and TB treatment duration of <6 months were the most important determinants of unsuccessful TB treatment. Our findings are supported by other studies that reported that DOTS can improve the cure rate[7, 29]. By contrast, a qualitative study showed that the rigidity of DOTS was one of the factors of treatment non-adherence by patients with TB-HIV co-infection, which led to treatment default and therefore unsuccessful treatment outcome[30].

Taking anti-TB medications for at least 6 months is another determinant factor for successful treatment of TB, which supports the present findings[31]. Most patients with TB-HIV co-infection are cured with a standard 6-month treatment regimen[8]. Another study comparing 6-month and 9-month treatment reported similar treatment outcomes but with significantly lower recurrence rates compared to a 6-month, thrice-weekly regimen[32]. It has also been proven that a longer treatment regimen can yield a more favourable treatment outcome for patients with TB-HIV co-infection [33], which supports our observations. Besides, low TB treatment adherence may lead to increased risk of drug resistance, treatment relapse as well as mortality. Therefore, it is important for healthcare providers to ensure that patients with TB-HIV co-infection adhere to the TB treatment regimen[30].

The present study shows that non-Malaysians had higher odds of having unsuccessful TB treatment outcome but it was not statistically significant; thus, it was not included as a determinant in this study. This is in concordance with another study performed in Malaysia[27]. The small number of non-Malaysian patients with TB-HIV co-infection could have contributed to the non-significant findings of both studies. Migration is a risk factor for TB, especially for migrants from high–TB burden countries. Immigrants tend to have a higher risk for defaulting treatment, which further contributes towards unsuccessful TB treatment outcome[31]. WHO has emphasised efforts to control TB in order to assist governments worldwide in terms of policies for migrants by preventing HIV/AIDS among migrants, as they are a vulnerable group[34].

In this study, lack of formal education, being unemployed and low household income were significantly associated with unsuccessful treatment outcome, compared to having received formal education, being employed and high household income. These findings are in concordance with other studies that show that people with low socioeconomic backgrounds tend to have a higher risk of poorer TB treatment outcome[30, 31]. The risk of developing TB increases among people with low socioeconomic backgrounds, as they usually live in areas with poor ventilation, have poor knowledge and behavioural practices regarding the disease itself, and are malnourished, which may lead to low immunity[31].

DM is a risk factor for developing TB. Similar to another study, the present findings show no significant difference in TB treatment outcome between patients with and without DM[27]. Patients with DM tend to have poorer TB treatment outcome compared to those without DM comorbidity, as DM patients with TB can have worsened glycaemic index[35]. However, patients with TB-HIV co-infection have low immunity due to the underlying HIV. On the other hand, patients with underlying HIV have higher chances of developing TB compared to patients with underlying DM[31].

The presence of a BCG scar may be a protective factor against developing TB infection. The present study suggests that patients with TB-HIV co-infection without a BCG scar have 4.2 times higher odds of having unsuccessful TB treatment outcome compared to patients with a BCG scar, but it was not significantly associated

with unsuccessful TB treatment outcome. Likewise, this finding is supported by the findings of Nik Nor Ronaidi et al.[27].

In this study, we found that not receiving ART was significantly associated with unsuccessful TB treatment outcome, and this is consistent with previous studies worldwide[6, 11, 12, 36, 37]. However, our results contradict that of a study in India[38]. A study from Iran found that patients with TB-HIV who had not been started with ART prior had a higher chance of dying earlier. Physicians had limited time to start such patients on ART due to the shorter duration of hospitalisation because they died earlier[12].

In the present study, advanced CXR presentation was not significantly associated with unsuccessful TB treatment outcome. In contrast, advanced CXR findings have been suggested as a determinant factor for unsuccessful TB treatment outcome[27]. In patients with TB-HIV, up to 10–15% of such patients with proven TB may have normal CXR due to the delayed immune response[24].

In this study, sputum smear upon diagnosis was not significantly associated with unsuccessful TB treatment outcome. The numbers of patients with smear-negative and smear-positive TB were almost identical in the present study, and this might explain why it was not associated with the treatment outcome. Nevertheless, this condition can also be due to the non-specific symptoms and broad-spectrum immune response among patients with TB-HIV co-infection, which may produce false negative sputum smear results among such patients[24, 39-42]. These findings were concordant with that of Nguyen et al. and Nik Nor Ronaidi et al.[19, 27]. Others have however showed that positive sputum smear is significantly associated with unsuccessful TB treatment outcome[1, 37].

In this study, positive sputum culture upon diagnosis was significantly associated with unsuccessful TB treatment outcome. This finding was supported by similar findings by Prado et al., Nguyen et al. and Swaminathan et al.[1, 19, 32]. Patients with TB-HIV co-infection with positive sputum culture may have higher TB bacterial loads, which may thus worsen the prognosis. Sputum culture is more accurate for diagnosing TB and for determining the prognosis in patients with TB-HIV co-infection, even though their sputum smear is negative[40]. This is consistent, as sputum culture is the gold standard for TB diagnosis, especially among patients with HIV, as it has higher sensitivity compared to sputum smear[24, 43].

Nevertheless, this study has some limitations. Although the patients were selected randomly, they were all from the Kuala Lumpur Federal Territory Health Office registry. Hence, the outcome of this study is mainly limited to patients within the Federal Territory of Kuala Lumpur, and it is not known if it can be generalised to other states in Malaysia or to other countries. Second, as it was secondary data, it was very difficult to determine the sputum conversion rate after 2 months of treatment, as not all patients with TB-HIV co-infection have these data. Besides, the transferred-out patients excluded from the study would produce bias results because they could not be included in the study due to the inability to assess the treatment outcome, as their records were unavailable.

The present study identifies the determinants of TB-HIV treatment outcome, which could guide healthcare facilities, especially those in Kuala Lumpur, to focus on those areas for better treatment outcome among patients with TB-HIV co-infection so that better treatment outcome can be achieved in the future. Other than that, the TB data were obtained from a reliable source (TBIS), which represent the population studied.

This study explored the recent factors related to unsuccessful TB treatment outcome among patients with TB-HIV co-infection. As the findings showed that not receiving DOTS and TB treatment of less than six months were the

determinants of unsuccessful TB treatment outcome, it is important to focus on these factors to ensure future success of TB treatment. Results of this study may provide knowledge to the clinician, researchers and the community for better TB management among patients with TB-HIV co-infection. The method of this study can also be adapted to other settings especially in Malaysia settings which had the same source of TB database, for future research.

This study adds to the literature related to the factors of unsuccessful TB treatment among patients with TB-HIV co-infection in high density population areas like Kuala Lumpur. It revealed the important factors needed to be focused in TB management to ensure future success of TB treatment especially in patients with TB-HIV co-infection.

Conclusions

Nearly 50% of patients with TB-HIV co-infection have unsuccessful TB treatment outcome. The socio-demographic characteristics of TB-HIV co-infected patients in this study were mostly: aged 18 to 39 years old, male, Malaysian, Malay and residents of medium or high cost residency. Majority received formal education, unemployed and had low household income. Most of patients with TB-HIV co-infection in this study had clinical characteristics of: non-DM, non-smoker, did not receive ART, pulmonary TB, new TB case, no or minimal CXR lesion, negative sputum smear, negative sputum culture, received DOTS, and received treatment between 6 to 12 months. The main determinants of unsuccessful TB treatment rate among patients with TB-HIV co-infection are not receiving DOTS and TB treatment of less than six months. Therefore, crucial measures are needed to ensure that such patients receive DOTS and continuous TB treatment of >6 months. Healthcare settings are required to strengthen and widen DOTS service coverage and to prioritize DOTS, especially among the high-risk groups. Accordingly, rigorous follow-ups from healthcare professionals are needed to ensure intensified treatment adherence and better rates of successful TB treatment outcome among patients with TB-HIV.

Declarations

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and analysed in this study are not publicly available due to restriction in which it contained health information that could compromise the privacy of research participants but are available from the corresponding author upon reasonable request.

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ETHICAL APPROVAL

This study was conducted in compliance with the ethical principles and approval by MREC (NMRR-18-872-40791) and with ethics permission from UKMMC REC (UKM PPI/111/8/JEP-2019-017).

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AUTHORS' CONTRIBUTIONS

DSS and AI designed the study and wrote the article. RI helped in the design of the study and provided the data, DSS, NFMA, and AA analysed the TB data. NA and AI supervised the study, reviewed and edited the article. All of the authors read and approved the final manuscript.

COMPETING INTERESTS

None declared.

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Tables

Table 1. Characteristics of patients with TB-HIV co-infection (n = 235).

Sociodemographic characteristics	
Age (years)	*n* (%)
18–39	120 (51.1)
40–59	110 (46.8)
≥60	5 (2.1)
Sex	
Male	201 (85.5)
Female	34 (14.5)
Citizenship	
Malaysian	211 (89.8)
Non-Malaysian	24 (10.2)
Ethnicity	
Malay	115 (48.9)
Chinese	61 (26)
Indian	26 (11.1)
Others	33 (14)
Place of residence	
Low-cost	64 (27.2)
Medium-/high-cost	146 (62.1)
Others (homeless/institutional)	25 (10.6)
Socioeconomic characteristics	
Formal education	
Yes	187 (79.6)
No	48 (20.4)
Employment status	
Employed	115 (48.9)
Unemployed	120 (51.1)
Household income (MYR or USD*)	
Low (<MYR3000 or <USD738.55)	208 (88.5)
High (≥MYR3000 or ≥USD738.55)	27 (11.5)

*1USD=MYR4.062, according to exchange rate from Central Bank of Malaysia 2017

Table 2. Clinical characteristics of patients with TB-HIV co-infection ($n = 235$).

	n (%)
DM	
Yes	9 (3.8)
No	226 (96.2)
Smoking status	
Yes	114 (48.5)
No	121 (51.5)
BCG scar	
Present	213 (90.6)
Absent	22 (9.4)
ART	
Yes	92 (39.1)
No	143 (60.9)
Type of TB	
Pulmonary	174 (74)
Extrapulmonary	61 (26)
TB case category	
New case	199 (84.7)
Relapse	25 (10.6)
Return after default	11 (4.7)
CXR presentation upon diagnosis	
No/minimal lesion	159 (67.7)
Advanced	70 (29.8)
Not performed	6 (2.6)
Sputum smear upon diagnosis	
Positive	93 (39.6)
Negative	119 (50.6)
Not performed	23 (9.8)
Sputum culture upon diagnosis	
Positive	93 (39.6)
Negative	119 (50.6)
Not performed	23 (9.8)
DOTS status	
Yes	155 (66)
No	80 (34)
Duration of TB treatment (months)	
<6	103 (43.8)
6–12	113 (48.1)
≥12	19 (8.1)
TB treatment outcome	
Cured	47 (20)
Completed treatment	89 (37.9)
Died	72 (30.6)
Failure	22 (9.4)
Defaulted treatment	5 (2.1)

Table 3. SLR identification of factors associated with unsuccessful TB treatment outcome in patients with TB-HIV co-infection in Kuala Lumpur

Variable	Unsuccessful outcome *n* (%)	Successful outcome *n* (%)	SLR Unadjusted OR	(95% CI)	χ^{2} [a]	*p*-value
A. Sociodemographic characteristics						
Age (years)					1.34	0.511
18–39	47 (39.2)	73 (60.8)	1			
40–59	49 (44.5)	61 (55.5)	1.25	(0.74, 2.11)	0.68[b]	0.409
≥60	3 (60)	2 (40)	2.33	(0.38, 14.47)	0.82[b]	0.364
Sex						
Male	82 (40.8)	119 (59.2)	0.69	(0.33, 1.43)	1.00	0.317
Female	17 (50)	17 (50)	1			
Citizenship						
Non-Malaysian	17 (70.8)	7 (29.2)	3.821	(1.52, 9.61)	9.00	0.003*
Malaysian	82 (38.9)	129 (61.1)	1			
Ethnicity					11.67	0.009*
Malay	44 (38.3)	71 (61.7)	0.31	(0.14, 0.70)	7.93[b]	0.005*
Chinese	20 (32.8)	41 (67.2)	0.24	(0.10, 0.60)	9.45[b]	0.002*
Indian	13 (50)	13 (50)	0.50	(0.17, 1.44)	1.66[b]	0.198
Others	22 (66.7)	11 (33.3)	1			
Place of residence					0.41	0.813
Others (homeless/institutional)	12 (48)	13 (52)	1.32	(0.57, 3.10)	0.42[b]	0.519
Low-cost	27 (42.2)	37 (57.8)	1.05	(0.58, 1.90)	0.02[b]	0.882
Medium-/high-cost	60 (41.1)	86 (58.9)	1			
B. Socioeconomic characteristics						
Formal education						
No	31 (64.6)	17 (87.5)	3.19	(1.65, 6.19)	12.38	<0.001*
Yes	68 (36.4)	119 (63.6)	1			
Employment status						
Unemployed	60 (50)	60 (50)	1.95	(1.15, 3.30)	6.27	0.012*
Employed	39 (33.9)	76 (66.1)	1			
Household income						
Low	93 (44.7)	115 (55.3)	2.83	(1.10, 7.30)	5.31	0.021*
High	6 (22.2)	21 (77.8)	1			
C. Clinical characteristics						
DM						
Yes	3 (33.3)	6 (66.7)	0.68	(0.17, 2.78)	0.30	0.581

No	96 (42.5)	130 (57.5)	1			
Smoking status						
Yes	49 (43)	65 (57)	1.07	(0.64, 1.80)	0.07	0.797
No	50 (41.3)	71 (58.7)	1			
BCG scar						
Absent	16 (72.7)	6 (27.3)	4.18	(1.57, 11.11)	9.32	0.002*
Present	83 (39)	130 (61)	1			
ART						
Yes	30 (32.6)	62 (67.4)	1.93	(1.12, 3.33)	5.69	0.017*
No	69 (48.3)	74 (51.7)	1			
Type of TB						
Pulmonary	73 (42)	101 (58)	0.97	(0.54, 1.76)	0.01	0.927
Extrapulmonary	26 (42.6)	35 (57.4)	1			
TB case category					0.19	0.910
Relapse	11 (44)	14 (56)	1.08	(0.47, 2.49)	0.03[b]	1.076
Return after default	4 (36.4)	7 (63.6)	0.78	(0.22, 2.76)	0.15[b]	0.782
New case	84 (42.2)	115 (57.8)	1			
CXR presentation upon diagnosis					7.75	0.021
Not performed	5 (83.3)	1 (16.7)	1.70	(0.96, 2.99)	3.31[b]	0.069
Advanced	35 (50)	35 (50)	8.48	(0.97, 74.30)	3.72[b]	0.054
No/minimal lesion	59 (37.1)	100 (62.9)	1			
Sputum smear upon diagnosis					0.12	0.944
Positive	40 (43)	53 (57)	1.04	(0.60, 1.80)	0.02[b]	0.884
Not performed	9 (39.1)	14 (60.9)	0.89	(0.36, 2.21)	0.07[b]	0.797
Negative	50 (42)	69 (58)	1			
Sputum culture upon diagnosis					15.14	0.001*
Positive	14 (73.7)	5 (26.3)	5.54	(1.89, 16.26)	9.73[b]	0.002*
Not performed	35 (52.2)	32 (47.8)	2.17	(1.20, 3.90)	6.64[b]	0.010*
Negative	50 (33.6)	99 (66.4)	1			
DOTS status						
No	71 (88.8)	9 (11.3)	35.78	(15.99, 80.05)	117.22	<0.001*
Yes	28 (18.1)	127 (81.9)	1			
Duration of TB treatment (months)					206.98	<0.001*
<6	93 (90.3)	10 (9.7)	79.05	(15.90,	28.52[b]	<0.001*

				393.03)		
6–12	4 (3.5)	109 (96.5)	0.31	(0.05, 1.84)	1.66[b]	0.198
≥12	2 (10.5)	17 (89.5)	1			

[a] Likelihood ratio (LR) test.

[b] Wald test.

* Significant at $p < 0.05$.

Table 4. Significant determinant factors of unsuccessful TB treatment outcomes in patients with TB-HIV co-infection in Kuala Lumpur, the final model ($n = 235$).

Characteristic	MLR			
	aOR[a]	(95% CI)	χ^2 [b]	*p*-value
DOTS status				
No	21.71	(5.36, 87.94)	24.52	<0.001*
Yes	1	-	-	-
Duration of TB treatment (months)				
<6	34.54	(5.97, 199.93)	15.63[c]	<0.001*
6–12	0.19	(0.03, 1.38)	2.72[c]	0.099
≥12	1	-	-	-

[a] Adjusted for citizenship status, ethnicity, formal education, employment status, household income, BCG [s]car, ART, CXR upon diagnosis, sputum culture upon diagnosis, DOTS status and duration of TB treatment using the forward LR method.

[b] Likelihood ratio (LR) test.

[c] Wald test.

* $p < 0.05$.

There was no multicollinearity (VIF < 10) and no interaction problem.

1 = reference.

Figures

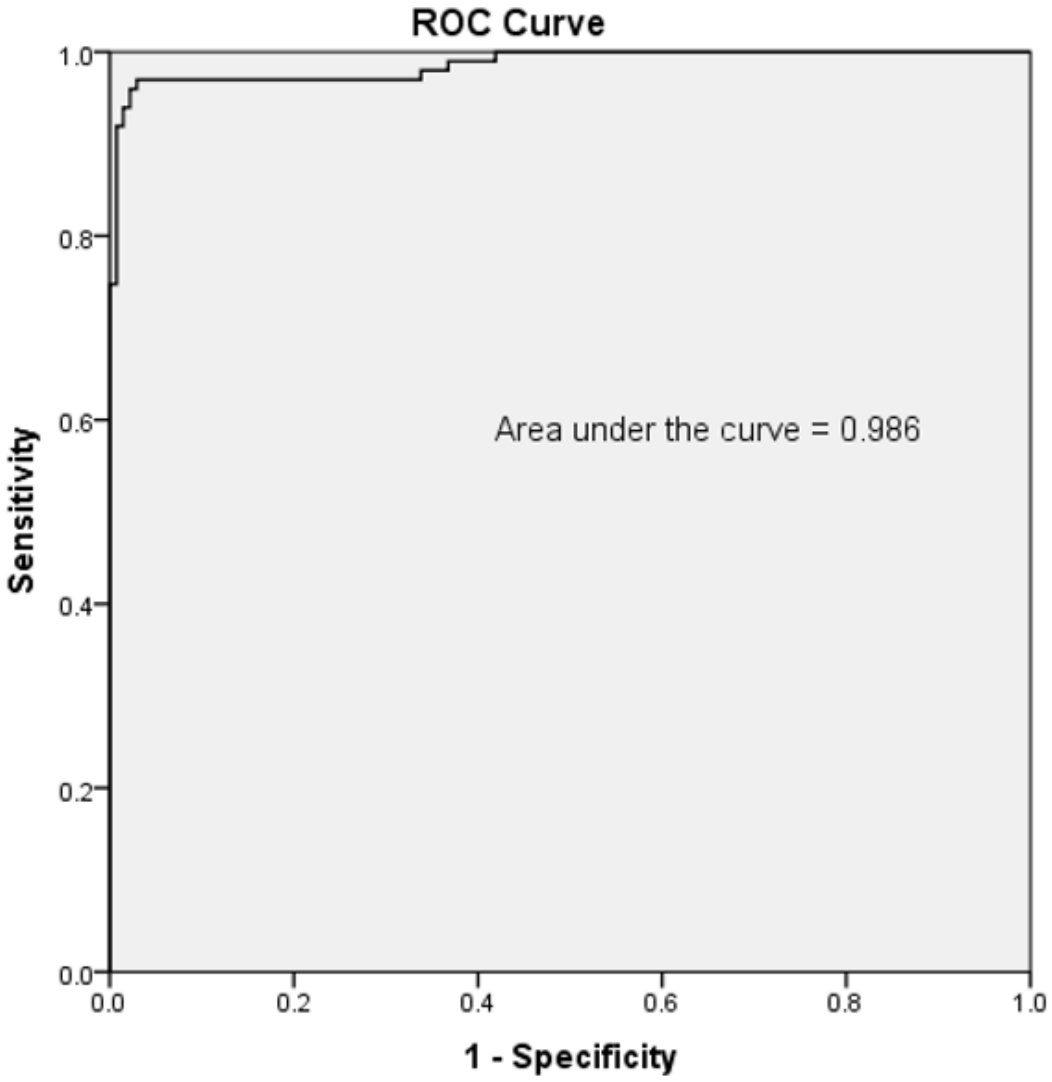

Figure 1

ROC curve

Supplementary Files

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- AppendixA230120.docx