Factors associated with tuberculosis treatment success among tuberculosis and human immunodeficiency virus coinfected patients in Kelantan

Siti Romaino Mohd Nor, MSc^{1,2}, Nyi Nyi Naing, MMedStats¹, Mat Zuki Mat Jaeb, MMed³

¹Faculty of Medicine, Universiti Sultan Zainal Abidin, Medical Campus, Kuala Terengganu, Terengganu, Malaysia, ²Ministry of Health, Clinical Research Centre Kelantan, Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan, Malaysia, ³Ministry of Health, Respiratory Unit, Department of Medicine, Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan, Malaysia

ABSTRACT

Introduction: Tuberculosis (TB) and human immunodeficiency virus (HIV) co-infection is a global public health issue among people living with HIV. The objective was to assess the prevalence of TB treatment outcomes (successful and unsuccessful) and associated factors with TB treatment success among TB and HIV co-infected patients in Kelantan for 5 years (2014–2018). The successful TB treatment was defined as the sum of cured patients and those who completed the treatment. The unsuccessful treatment was defined as the sum of treatment failed, died, and default.

Materials and methods: A cross-sectional study was conducted at the TB/Leprosy Unit of the State Health Department of Kelantan (JKNK) using secondary data from January 2014 to December 2018 assessed in the MyTB online system. The data were analyzed using SPSS 25.0 and STATA 14. Ethics approvals were obtained from Medical Research Ethics Committee (MREC) and UniSZA Human Research Ethics Committee (UHREC).

Results: Kelantan had 6,313 TB cases from January 2014 to December 2018. There were 703 (11.1%) cases of TB and HIV co-infection. The prevalence of successful treatment among TB and HIV co-infected patients was 57.1%. The duration of treatment and anatomy of TB location was significantly associated with TB treatment success.

Conclusion: This study's findings showed that the prevalence of TB treatment success rate was 57.1%, and the unsuccessful rate was 42.9%. The treatment duration and the TB location's anatomy were significantly associated with the treatment success rate. Improving TB treatment outcomes should be started with anti-TB treatment immediately after TB diagnosis. Therefore, the government should strengthen the TB/HIV collaborative efforts to achieve good treatment outcomes among these vulnerable patients.

KEYWORDS:

Factor associated, Tuberculosis (TB), treatment outcome, human immunodeficiency virus (HIV), co-infected patients

INTRODUCTION

Tuberculosis (TB) is an infectious disease that remains a major global health issue. It is one of the top 10 causes of mortality worldwide, and each year millions of people fall sick with TB. Due to decreased immunity, the risk of developing active TB was 20–37 times higher among people living with human immunodeficiency virus (PLHIV) than people who did not have human immunodeficiency virus (HIV).¹ The appearance of HIV has led to a resurgence of TB around the world. When the two diseases occur simultaneously in the same individuals, one will exacerbate the effects of the other.² Therefore, early detection of TB and HIV allows for early treatment of these two diseases and thus a better chance of survival. Without treatment, both diseases actively paralyse vital functions in the body until the infected person dies.

In 2019, 7.1 million new and relapsed TB cases were reported to the National Tuberculosis Programs (NTPs) and the World Health Organization (WHO). This figure increased from 7.0 million in 2018, 6.4 million in 2017, and 5.7 to 5.8 million per year between 2009 and 2012. Among all those affected in 2019, 8.2% of those were PLHIV. In 2018 globally, the treatment success rate for newly enrolled TB cases was 85% and 57% for people with Multidrug/rifampicin-resistant TB (MDR/RR-TB). Even though the global TB incidence rate and death rate are decreasing, most WHO regions and many high TB burden countries are still not on track to meet the End TB Strategy 2020 milestones by the end of 2019.³

Malaysia is located in the southeast Asia region and is categorised as an intermediate TB burden country. Several studies were conducted in Malaysia to assess the parameters associated with successful and unsuccessful treatment outcomes among TB patients. However, the results were varied and inconsistent. The treatment outcomes studies from a few states in Malaysia reported a very high heterogeneity in the results.⁴⁻⁸ To date, TB and HIV co-infected patients have a lower treatment success rate than TB patients (75.0% vs 83.0%), but their death rate is much higher than TB patients (14% vs 3%).⁹

Kelantan is a Malaysian state in the east of the country that shares a border with Thailand. In Kelantan alone, the

This article was accepted: 28 September 2022 Corresponding Author: Nyi Nyi Naing Email: syedhatim@unisza.edu.my

treatment success rate in 2017 among TB and HIV coinfection was only 27.9%.⁶ Based on this, a practical method for improvement was needed, particularly in achieving a better cure rate. Many factors are recognised as barriers to treatment success, including lack of communication between patients and healthcare providers, Directly Observed Treatment Short-Course (DOTS) implementation, incentives, lost patients, difficult treatment access, supervision, and other limitations in the treatment units.¹⁰⁻¹²

To our knowledge, a published study looking at treatment outcomes and associated factors among TB and HIV coinfected patients in Kelantan is still lacking. We need to understand the socio-demographic characteristics and clinical characteristics that may contribute to and affect the outcome of TB treatment. Further clarity and quantification of the prevalence and associated factors are needed to better understand and evaluate management for TB and HIV coinfected patients. Thus, our study aimed to assess the prevalence of TB treatment outcomes (successful and unsuccessful) and associated factors with TB treatment success among TB and HIV co-infected patients in Kelantan for 5 years (2014–2018).

MATERIALS AND METHODS

Study design

A cross-sectional study reviewed the 5-year secondary data from January 2014 to December 2018 retrieved from the MyTB online system at the TB/Leprosy Unit of the State Health Department of Kelantan (JKNK). The population consisted of all TB and HIV co-infected patients in Kelantan based on the recommendation by WHO to evaluate patients separately.

Sample size

All TB and HIV co-infected patients who met the inclusion criteria and registered for TB treatment during the study were included. A single proportion equation was used to calculate the sample size with a treatment success rate for TB and HIV of 27.9%.⁶ The minimum required sample size was 309 patients with a 95% confidence interval (CI) within a 5% precision. Assuming 15.0% dropouts, the number of the sample size should be at least 364 patients. We used 15% dropouts because the study needed to increase the sample size by the expected predicted reasons for losing subjects and were concerned about the large proportion of missing data. In this study, as the data available was 667, we decided to include all. Non-probability sampling method was applied because it was based on convenience sampling from secondary data.

Data collection procedure

The person in charge of the TB/Leprosy Unit extracted the data from MyTB online system in December 2019. They downloaded the data into excel for patients who identified themselves as TB and HIV co-infection and submitted it to the investigator. The subject ID number identified the list of all TB and HIV co-infected patients. Then, the investigator exported the data from excel to IBM SPSS statistics version 25.0 for further analysis.

The secondary data contained patients' socio-demographic characteristics, clinical characteristics, and TB treatment outcomes. The missing data (i.e., marital status and monthly income) cannot be minimised. Their records were unavailable, and their medical results were ambiguous, so these variables could not be included.

Inclusion criteria

Our target population is TB and HIV co-infected patients. The selected patients included in this study were based on secondary data from MyTB online system. Patients with TB and HIV who were \geq 18 years old and proved positive for both TB and HIV were eligible.

Exclusion criteria

Patients who recorded transferred out and ongoing treatment were excluded since their treatment results could not be determined. Patients whose TB diagnoses changed were also excluded since they were later diagnosed with a different disease.

Operational definitions

According to the Malaysian Ministry of Health Clinical Practice Guidelines for Tuberculosis Management,¹³ the following TB treatment outcome and operational terms were utilised in this study:

- 1. "Cured: Former smear-positive patient who was smearnegative in the last month of treatment and at least one previous occasion."
- 2. "Completed treatment: A patient who completed treatment but did not meet the criteria classified either as a cure or a failure."
- 3. "Treatment failed: A patient whose sputum was smearpositive at five months or later during treatment."
- 4. "Died: A patient died for any reason during treatment."
- 5. "Default: A patient who has interrupted treatment for two consecutive months or more."

In the analysis of treatment outcomes, successful TB treatment was defined as the sum of cured patients and those who completed treatment. In contrast, treatment failed, died, and default was considered as unsuccessful TB treatment.

The X-ray findings were extracted from MyTB online system reported by District TB Organizer Team based on chest X-Ray (CXR) results reported by the clinician. The severity of the lesion on the X-ray film was used to classify the CXR presentation at the time of diagnosis. It was categorised into:

- 1. No lesion if CXR showed no lesions,
- 2. Minimal if CXR showed a few lesions,
- 3. Moderate advance if CXR showed many lesions,
- 4. Far advance if CXR showed extensive lesions or miliary appearance, and
- 5. Not performed if CXR was not done during the diagnosis

Ethical Considerations

Privacy and confidentiality of patients were maintained. Ethics approvals were obtained from the Medical Research Ethics Committee, Ministry of Health Malaysia (NMRR-19-2628-50776 (IIR), KKM/NIHSEC/P19-2067(11)), and UniSZA Human Research Ethics Committee (UniSZA/UHREC/2019/150).

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Statistical Analysis

IBM SPSS statistics version 25.0 were used to analyse the data. The socio-demographic data were presented descriptively. The numerical data were presented as a mean (standard deviation, SD), whereas the categorical data were expressed as frequency (percentage, %). Multiple logistic regression analysis determined the association between the independent variables and the outcomes. Simple logistic regression was used to determine the candidate variables to be included in multiple logistic regression. The variables with *p* value <0.25 were included in multiple logistic regression. Principles of best fit and biological plausibility were used to obtain the parsimonious model. Forward and backward stepwise regression analyses were applied. Multicollinearity and interaction problems were checked. The Hosmer-Lemeshow goodness of fit (GOF) test, overall properly categorised percentage, and area under the receiver operation characteristic (ROC) curve were used to assess the model fit. The outcomes were presented in the form of crude and adjusted odds ratios (OR), a 95% confidence interval (CI) and corresponding *p* values.

Variable Under Study

Independent Variables: The socio-demographic characteristics included age, gender, race, duration of treatment, level of education, place of residence, and occupation. The clinical characteristics retrieved were diabetes mellitus status, Bacillus Calmette-Guérin (BCG) scar, anatomy of TB location, CXR status, case TB category, treatment regime, DOTS status, Highly Active Antiretroviral Therapy (HAART) treatment, and detection method. Other characteristics included in the study were smoking status, source of notification, place of treatment, and district area. Outcome variables: The study outcome was either successful (cured, completed treatment) or unsuccessful (treatment failed, died, default) TB treatment.

RESULTS

Baseline characteristics and treatment outcomes

A total of 6,313 TB cases in Kelantan were registered in the MyTB online system from January 2014 to December 2018. A total of 703 (11.1%) of these cases had TB and HIV co-infection. However, 36 cases were excluded due to transfer out (3), change of diagnosis (24) and ongoing treatment (9). Therefore, 667 cases were evaluated in this study based on inclusion criteria (Figure 1).

Table I illustrates the socio-demographic characteristics and other related factors among all study subjects (n = 667). Their ages ranged from 18 to 77, with a mean (SD) of 38.7 (7.9) years. The range of TB treatment duration was 0 to 722 days, with a mean (SD) of 202.8 (131.27) days. The treatment success rate was 57.1% (95% CI; 53.34,60.86). Successful outcomes were achieved in 381 cases, with 132 (19.8%) cases cured and 249 (37.3%) cases completed treatment. In contrast, the unsuccessful outcomes were 42.9% (95% CI; (39.14,46.66) achieved in 286 cases, with 67 (10.1%) cases defaulted and 219 (32.8%) cases of death. There were no treatment failure cases identified.

Factors associated with TB treatment successful outcomes

Table II illustrates the results of a simple logistic regression revealed that age, duration of treatment, level of education, occupation, Anatomy of TB location, CXR Status during diagnosis, smoking status, the regime of treatment, DOTS by healthcare providers, HAART treatment, source of notification, place of treatment, method of detection, and district were significantly associated with the successful treatment among TB and HIV co-infected patients.

On the other hand, gender, race, residency, diabetes mellitus status, BCG scar, and type of TB category cases were shown to have no significant association with TB treatment success.

Table III illustrates the factors associated with TB treatment success among subjects using multiple logistic regression. After adjusting confounding variables, duration of treatment and anatomy of TB location was significantly associated with TB treatment success. A person with an increased 1-day duration of treatment had 1.02 times higher odds of TB treatment success (OR: 1.02, 95% CI: 1.018, 1.025, p<0.001). A person with PTB (Pulmonary Tuberculosis) had 2.42 times higher odds of TB treatment success than those a person with EPTB (Extrapulmonary Tuberculosis) (OR: 2.42, 95% CI: 1.344, 4.361, p=0.003).

DISCUSSION

This study included 667 cases, 381 successful and 286 unsuccessful TB treatment outcomes. Among these 667 cases, 82.8% of new TB cases were reported, which is similar to that observed from 2010 to 2012 in Southwest Ethiopia (85.2%)¹⁴ and in rural South Africa (84.9%).¹⁵ The previous studies found that TB and HIV co-infection prevalence differed depending on study sites and population. In this study, TB and HIV co-infection was discovered in 11.1% of participants. It was comparable to the patients in Klang Valley, Malaysia (11.8%)⁴ but higher than national TB surveillance between 2014 and 2017 $(6.0\%)^7$ and in Aurangabad city, Maharashtra, in 2017 (7.28%).¹⁶ However, the co-infection prevalence in this study was lower than Nigerian at 20.5%¹⁷, Lagos, Nigeria at 21.6%,¹⁸ Northern Ethiopia at 24.3%,¹⁹ Ethiopia at 29.4%²⁰ and Malawi at 56.0%.²¹ The co-infection prevalence was higher in third-world countries because of the diagnosis method for TB (diagnosed by chest radiography) and HIV (diagnosed based on blood analyses) than in those which used other diagnostic methods.²²

According to the TB report, the global treatment success rate for TB/HIV patients was 78.0%.²³ In our study, data analysis revealed that TB and HIV patients had poor treatment outcomes with a success rate of only 57.1%. The high death rate (32.8%) and default rate (10.1%) contributed to this study's lower treatment success rate. Moreover, TB and HIV co-infected patients have a high risk of experiencing adverse treatment outcomes²⁴ due to immunosuppression, drug interactions, and lack of a rapid and sensitive TB diagnostic test. The success rate in this study is almost similar to the study in Malaysia (56.0%),¹ Klang Valley (53.4%),⁴ and Western Ethiopia (58.06%).²⁵ This finding reveals why Malaysia is classified as an intermediate TB burden country in the world by the WHO.²⁶ The treatment success rate in this

		Treatment Outcome		n (%)	
		Unsuccessful	Successful		
		(n = 286)	(n = 381)		
Gender	Male	256 (43.4)	334 (56.6)	590 (88.5)	
	Female	30 (39.0)	47 (61.0)	77 (11.5)	
ace	Malays	276 (42.8)	369 (57.2)	645 (96.7)	
	Non-Malays	10 (45.5)	12 (54.5)	22 (3.3)	
evel of education	No education	6 (50.0)	6 (50.0)	12 (1.8)	
	Primary school	29 (39.2)	45 (60.8)	74 (11.1)	
	Secondary school	241 (45.0)	294 (55.0)	535 (80.2)	
	Form 6/diploma/certificate	7 (21.2)	26 (78.8)	33 (4.9)	
	Others	3 (23.1)	10 (76.9)	13 (1.9)	
lesidency	Urban	65 (42.5)	88 (57.5)	153 (22.9)	
esidency	Rural	221 (43.0)	293 (57.0)	514 (77.1)	
scupation	Government servant				
occupation		7 (25.0)	21 (75.0)	28 (4.2)	
	Own business	38 (47.5)	42 (52.5)	80 (12.0)	
	Unemployed	132 (44.3)	166 (55.7)	298 (44.7)	
	Prisoner	24 (32.0)	51 (68.0)	75 (11.2)	
	Others	85 (45.7)	101 (54.3)	186 (27.9)	
viabetes mellitus	No	279 (43.2)	367 (56.8)	646 (96.9)	
	Yes	7 (33.3)	14 (66.7)	21 (3.1)	
CG Scar	No	13 (38.2)	21 (61.8)	34 (5.1)	
	Yes	273 (43.1)	360 (56.9)	633 (94.9)	
natomy of TB location	EPTB	76 (46.3)	88 (53.7)	164 (24.6)	
inaterity of 15 location	РТВ	168 (39.3)	260 (60.7)	428 (64.2)	
VD status duning allo an ass	EPTB and PTB	42 (56.0)	33 (44.0)	75 (11.2)	
XR status during diagnose	No lesion	37 (39.4)	57 (60.6)	94 (14.1)	
	Minimal	154 (39.8)	233 (60.2)	387 (58.0)	
	Moderately advanced	87 (50.9)	84 (49.1)	171 (25.6)	
	Far advanced	4 (80.0)	1 (20.0)	5 (0.7)	
	Not done	4 (40.0)	6 (60.0)	10 (1.5)	
ase TB category	New case	232 (42.0)	320 (58.0)	552 (82.8)	
	Relapse case	38 (46.3)	44 (53.7)	82 (12.3)	
	Case after treatment default	16 (48.5)	17 (51.5)	33(4.9)	
moking status	No	80 (35.2)	147 (64.8)	227 (34.0)	
lineking status	Yes	206 (46.8)	234 (53.2)	440 (66.0)	
egime of treatment	2SHRZ	7 (77.8)	2 (22.2)	9 (1.3)	
egime of treatment					
	2EHRZ	125 (45.3)	151 (54.7)	276 (41.4)	
	2HRZ	2 (66.7)	1 (33.3)	3 (0.4)	
	Others	152 (40.1)	227(59.9)	379 (56.8)	
DOTS by health care providers	No	77 (98.7)	1 (1.3)	78 (11.7)	
	Yes	193 (33.7)	380 (66.3)	573 (85.9)	
HAART treatment	No	259 (44.0)	329 (56.0)	588 (88.2)	
	Yes	11 (29.7)	26 (70.3)	37 (5.5)	
Source of notification	Public hospital	253(46.4)	292 (53.6)	545 (81.7)	
	Public health clinic	32 (26.7)	88 (73.3)	120 (18.0)	
Place of treatment	Public hospital	249 (46.0)	292 (54.0)	541 (81.1)	
	Public health clinic	35 (28.5)	88 (71.5)	123 (18.4)	
lathad of datastic-	Private health sector	2 (66.7)	1 (33.3)	3 (0.4)	
Nethod of detection	Active	15 (51.7)	14 (48.3)	29 (4.3)	
	Passive	251 (44.0)	319 (56.0)	570 (85.5)	
	Screening	20 (29.4)	48 (70.6)	68 (10.2)	
District	Kota Bharu	105 (40.90)	152 (59.1)	257 (38.5)	
	Pasir Mas	22 (42.3)	30 (57.7)	52 (7.8)	
	Pasir Puteh	20 (47.6)	22 (52.4)	42 (6.3)	
	Tumpat	34 (43.0)	45 (57.0)	79 (11.8)	
	Bachok	20 (36.4)	35 (63.6)	55 (8.2)	
	Jeli	15 (55.6)	12 (44.4)		
				27 (4.0)	
	Kuala Krai	21 (55.3)	17 (44.7)	38 (5.7)	
	Machang	18 (36.0)	32 (64.0)	50 (7.5)	
	Tanah Merah	25 (52.1)	23 (47.9)	48 (7.2)	
	Gua Musang	6 (31.6)	13 (68.4)	19 (2.8)	

Table I: Socio-demographic and other related factors among all study subjects

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Table II: Factors associated with TB treatment success among subjects using simple logistic regression						
Factors		Simple logistic regression				
		b	Crude OR (95% CI)	Wald test	<i>p</i> value	
Age*	-0.02	0.98 (0.97, 1.00)	2.76	0.097		
Duration of treatment*	0.02	1.02 (1.018, 1.024)	174.00	< 0.001		
Gender	Male	0	1	20.001		
Gender				0 5 4	0.461	
B	Female	0.18	1.20 (0.74, 1.95)	0.54	0.461	
Race	Malays	0	1			
	Non-Malays	13.32	0.90 (0.38, 2.11)	13.32	0.804	
Level of education	No education	0	1			
	Primary school	0.44	1.55 (0.46, 5.28)	0.50	0.482	
	Secondary school	0.20	1.22 (0.39, 3.83)	0.12	0.734	
	Form 6/diploma /certificate	1.31	3.71 (0.91, 15.15)	3.35	0.067	
	Others	1.20	3.33 (0.60, 18.54)	1.89	0.169	
Residency	Urban	0	1			
·····,	Rural	-0.21	0.98 (0.68, 1.41)	0.01	0.910	
Occupation	Government servant	0	1	0.01		
occupation	Own business	1.00	0.37 (0.141, 0.964)	4.14	0.042	
	Unemployed	0.87	0.42 (0.173, 1.016)	3.70	0.042	
					1	
	Prisoner	0.35	0.71 (0.27, 1.89)	0.47	0.492	
	Others	0.93	0.40 (0.161, 0.977)	4.04	0.044	
Diabetes Mellitus	No	0	1			
	Yes	0.42	1.52 (0.61, 3.82)	0.80	0.372	
BCG Scar	No	0	1			
	Yes	-0.20	0.82 (0.40, 1.66)	0.31	0.575	
Anatomy of TB location	EPTB	0	1			
,	РТВ	0.29	1.34 (0.930, 1.922)	2.45	0.117	
	EPTB and PTB	-0.39	0.68 (0.392, 1.176)	1.91	0.167	
CXR status during diagnose	No lesion	0	1	1.51	0.107	
CAR status during diagnose	Minimal		-	0.01	0.020	
		-0.02	0.98 (0.62, 1.56)	0.01	0.939	
	Moderately advanced	-0.47	0.63 (0.38, 1.05)	3.21	0.073	
	Far advanced	-1.82	0.16 (0.02, 1.51)	2.55	0.110	
	Not done	-0.03	0.97 (0.26, 3.69)	0.00	0.969	
Case TB category	New case	0	1			
	Relapse case	-0.18	0.84 (0.53, 1.34)	0.54	0.462	
	Case after treatment default	-0.26	0.77 (0.38, 1.56)	0.53	0.467	
Smoking status	No	0	1			
5	Yes	-0.48	0.62 (0.44, 0.86)	8.14	0.004	
Regime of treatment	2SHRZ	0	1			
	2EHRZ	1.44	4.23 (0.86, 20.72)	3.16	0.075	
	2HRZ	0.56	1.75 (0.10, 30.84)	0.15	0.702	
	Others	1.65	5.23 (1.07, 25.50)	4.18	0.041	
DOTS by Health care providers	No	0	1			
	Yes	5.02	151.61 (20.93, 1098.31)	24.70	0.000	
HAART treatment	No	0	1			
	Yes	0.62	1.86 (0.90, 3.84)	2.83	0.093	
Source of notification	Public hospital	0	1			
	Public health clinic	0.87	2.38 (1.54, 3.69)	15.08	< 0.001	
Place of treatment	Public hospital	0				
	Public health clinic	0.76	2.14 (1.40, 3.29)	12.28	<0.001	
	Private health sector	-0.85	0.43 (0.04, 4.73)	0.48	0.487	
Method of detection	Active	0	1	0.40	0.407	
viethod of detection				0.00	0.410	
	Passive	0.31	1.36 (0.65, 2.87)	0.66	0.418	
	Screening	0.94	2.57 (1.05, 6.30)	4.27	0.039	
District	Kota Bharu	0	1			
	Pasir Mas	-0.06	0.94 (0.52, 1.72)	0.04	0.846	
	Pasir Puteh	-0.28	0.76 (0.40, 1.46)	0.68	0.411	
	Tumpat	-0.09	0.91 (0.55, 1.52)	0.12	0.731	
	Bachok	0.19	1.21 (0.66, 2.21)	0.38	0.538	
	Jeli	-0.59	0.55 (0.25, 1.23)	2.12	0.146	
	Kuala Krai	-0.58	0.56 (0.28, 1.11)	2.76	0.097	
	Machang	0.21	1.23 (0.66, 2.30)	0.41	0.097	
	5					
	Tanah Merah	-0.45	0.64 (0.34, 1.18)	2.06	0.151	
	Gua Musang	0.40	1.50 (0.55, 4.06)	0.626	0.429	

Table II: Factors associated with TB treatment success among subjects using simple logistic regression

*Mean

Table III: Factors associated with TB treatment success among subjects using multiple logistic regression

Factors		Multiple logistic regression ^a				
		b	Adjusted OR (95% CI)	Wald statistic	p value	
Duration of treatment*		0.02	1.02 (1.018, 1.025)	170.19	< 0.001	
Anatomy of TB location	EPTB	0				
	PTB	0.88	2.42 (1.344, 4.361)	8.67	0.003	
	EPTB and PTB	-2.94	0.75 (.308, 1.806)	42	0.515	

*Mean

^a Forward stepwise likelihood ratio multiple logistic regression method was applied

Multicollinearity and interaction terms were checked and not detected.

Hosmer–Lemeshow GOF test (P<0.001), classification table (overall correctly classified percentage = 89.8%), and the area under the ROC curve (92.4%) were applied to check the model fitness.

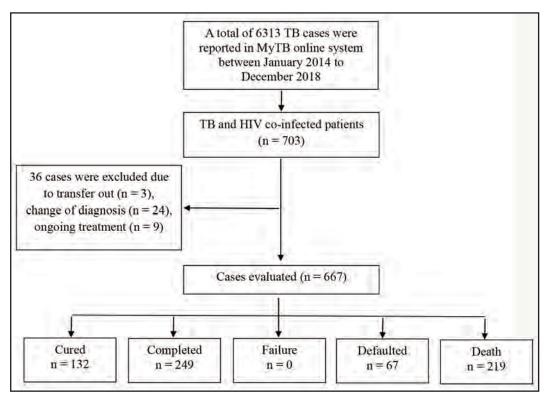


Fig. 1: Schematic diagram for selection of patients.

study was lower than the study conducted in Ghana (78.1%),²⁴ Ethiopia (88.2%),²⁰ North West Ethiopia (77.3%),²⁷ Western Ethiopia (60.7%),²⁸ and Northern Ethiopia (71.0%).²⁹ However, it was higher than the results obtained among TB and HIV co-infection in Kelantan between 2003 and 2012 (27.9%)⁶ and in the Eastern Region of Ghana (50.0%).³⁰ The reasons for comparatively poor treatment outcomes in this study might be due to late detection of HIV and TB and delays in starting antiretroviral therapy (ART) or TB treatment.

This study has shown that having PTB and EPTB, moderate advanced and far advanced CXR status during diagnosis, smoking, and from the district of Jeli, Kuala Krai, and Tanah Merah may reduce the likelihood of treatment success. In Eastern Ethiopia, smear-positive PTB patients had a greater rate of ineffective treatment than EPTB and smear-negative PTB. This difference was statistically significant.³¹ In Malaysia, a previous national TB surveillance study⁷ found

that smoking was related to unsuccessful results but not mortality. They claimed that the nature of smoking data collected in their study was self-reported by patients, influencing their findings. According to consistent evidence worldwide, smoking is linked to an increased risk of active TB, poor TB treatment results, and TB mortality.^{32,33}

While having form 6/diploma/certificate and others level of education, own business, unemployed and others occupation, PTB, taken 2EHRZ and others regime of treatment, DOTS by healthcare providers, receiving HAART treatment, source of notification from the public health clinic, place of treatment at the public health clinic, and screening method detection increases the chance of having TB treatment success. A study of the DOTS program in Western Ethiopia found that HAART treatment, sputum examination, and treatment year were significantly associated with a higher treatment success rate.²⁸ The effect of

ART treatment on TB illness prognosis, on the other hand, is related to patients' immunological improvement after starting ART treatment in addition to the TB medicine.

After adjusting for other potential confounding variables, the duration of treatment and the anatomy of TB location was significantly associated with treatment success among TB and HIV co-infected patients in Kelantan. The mean (SD) duration of treatment in this study was 202.8 (131.27) days, equivalence to more than 6 months. The study done in Ethiopia found that the duration of treatment of 2–7 months (AOR = 14.8) contributed to the treatment success. The prior standard for first-line anti-TB treatment was eight months, which was revised to 6 months recently.³⁴

In this study, PTB was more prevalent in the successful and unsuccessful groups. These findings could explain why PTB has a greater treatment success rate than EPTB and TB anatomy. A previous study in Southwest Ethiopia showed that TB/HIV co-infected patients with smear-positive PTB had a higher likelihood of treatment success.³⁵ According to studies conducted in various locations, TB and HIV coinfected patients with EPTB had a higher mortality risk during TB treatment than PTB patients.⁴ In the study in China,³⁶ EPTB inpatients accounted for 48.69% of all TB patients. Patients with PTB are generally predicted to have a much better treatment outcome than PTB and EPTB.

Contrary to this, a study in Kelantan revealed the associated factors of poor treatment outcomes among PTB patients. They found that TB and HIV co-infection is a strong predictor of unsuccessful.⁵ Another study found that smear-positive patients with PTB were 2.8 times more likely than patients with EPTB to have TB and HIV co-infection.¹⁹ The study done in Ethiopia suggested that patients with advanced age and smear-positive PTB have poor treatment results.²⁰ In a study in Eastern Ethiopia, they found that smear-positive PTB patients had a greater rate of failed treatment (18.9%) than EPTB (14.3%) and smear-negative PTB (6.7%).³¹

The study findings of TB treatment outcomes and associated factors differed from other studies conducted in other states due to multifactorial aspects such as socio-demography, socioeconomic status, culture, level of knowledge, drugs used, and tolerance to side effects. It also may have been influenced by local service provision settings of the TB patient population. Our findings indicate a need for a strategy to improve the treatment outcomes among TB and HIV coinfected patients with TB in collaborative activities. The essential data of the patient socio-demographic, the prevalence of TB treatment outcomes, and associated factors with TB treatment success among TB and HIV co-infected patients can be used as a baseline for further study. They may also contribute to the body of knowledge regarding the treatment outcomes. Healthcare facilities, particularly in Kelantan, could be encouraged to focus on these relevant areas for a better outcome of TB treatment to achieve a better outcome of TB treatment in the future.

Nevertheless, our research has certain limitations. The study data and patient information were retrieved from the MyTB online system available in the TB/Leprosy Unit. The issue is that missing data cannot be minimised as well as getting inaccurate data. Some essential variables, such as income, are not recorded. We were unable to include these variables. Transfer of outpatients and change of diagnosis that were subsequently excluded from this study could be slightly biased in our findings. It is hoped that the efforts to begin capturing those characteristics could be made regularly.

CONCLUSION

This study's findings showed that the prevalence of TB treatment success rate was 57.1%, and the unsuccessful rate was 42.9%. The duration of treatment and the anatomy of the TB location was significantly associated with the treatment success rate among TB and HIV co-infection in Kelantan. Improving TB treatment outcomes should be started with anti-TB treatment immediately after TB diagnosis. Therefore, the government should strengthen the TB/HIV collaborative efforts to achieve good treatment outcomes among these vulnerable patients.

REFERENCES

- 1. World Health Organization (WHO). Global Tuberculosis Report 2018. 2018.
- 2. GBC Health. HIV & TB : Joint Action for Maximum Impact [Internet]. 2011. Available from: www.gbchealth.org
- 3. World Health Organization (WHO). Global Tuberculosis Report 2020. 2020.
- 4. Ismail I, Bulgiba A. Determinants of unsuccessful tuberculosis treatment outcomes in Malaysian HIV-infected patients. Prev Med (Baltim) 2013; 57(SUPPL): S27-30.
- Nik Nor Ronaidi NM, Mohd NS, Wan Mohammad Z, Sharina D, Nik Rosmawati NH. Factors associated with unsuccessful treatment outcome of pulmonary tuberculosis in Kota Bharu, Kelantan. Malaysian J Public Heal Med 2011; 11(1): 6-15.
- 6. Jalal TMT, Abdullah S, Wahab FAFA, Dir S, Naing NN. Prevalence and factors associated with tuberculosis treatment success among TB/ HIV co-infection in North-East Malaysia. Malaysian J Med Sci 2017; 24(2): 75-82.
- Keng Tok PS, Liew SM, Wong LP, Razali A, Loganathan T, Chinna K, et al. Determinants of unsuccessful treatment outcomes and mortality among tuberculosis patients in Malaysia: A Registry-Based Cohort Study. PLoS One 2020; 15(4): 1-14.
- Goroh MMD, Avoi R, William T. Epidemiology of tuberculosis in Sabah, Malaysia, 2012 – 2018. Infect Dis Poverty 2020; 9: 119.
- 9. World Health Organization (WHO). TB-HIV Factsheet 2018 [Internet]. 2018.
- Hannah HA, Miramontes R, Gandhi NR. Socio-demographic and clinical risk factors associated with tuberculosis mortality in the United States, 2009-2013. Public Health Rep 2017; 132(3): 366-75.
- 11. Liu Y, Zheng Y, Chen J, Shi Y, Shan LY, Wang S, et al. Tuberculosis-associated mortality and its risk factors in a district of shanghai, china: a retrospective cohort study. Int J Tuberc Lung Dis 2018; 22(6): 655-60.
- 12. Wen, Yufeng, Zhang, Zhiping, Li, Xianxiang, et al. Treatment outcomes and factors affecting unsuccessful outcome among new pulmonary smear positive and negative tuberculosis patients in Anqing, China: a retrospective study. BMC Infect Dis 2018; 18(104): 1-12.
- 13. Ministry of Health Malaysia. Clinical Practice Guidelines; Management of Tuberculosis (3rd Edition) [Internet]. 2012. (cited 20 December 2020) Available from: http://www.moh.gov.my
- 14. Abrha H, Tsehayneh B, Massa D, Tesfay A, Kahsay H. Survival experience and its predictors among TB/HIV co-infected patients in Southwest Ethiopia. Epidemiol 2015; 5(3): 3-9.

- 15. Jacobson KB, Moll AP, Friedland GH, Shenoi S V. Successful tuberculosis treatment outcomes among HIV/TB co-infected patients down-referred from a District Hospital to primary health clinics in rural South Africa. PLoS One 2015; 10(5): 1-11.
- 16. Warkari PD, Nakel MP, Mahajan SM, Adchitre SA. Study of treatment outcome of tuberculosis among HIV co-infected patients: a cross sectional study in Aurangabad City, Maharashtra. Int J Commun Med Public Heal 2017; 4(12): 4466.
- Oshi DC, Oshi SN, Alobu I, Ukwaja KN. Profile, outcomes, and determinants of unsuccessful tuberculosis treatment outcomes among HIV-infected tuberculosis patients in a Nigerian State. Tuberc Res Treat 2014; 2014: 1-8.
- Adejumo OA, J daniel O, Otesanya AF, Adegbola AA, Femi-Adebayo T, Bowale A, et al. Factors associated with TB/HIV coinfection among drug sensitive tuberculosis patients managed in a secondary health facility in Lagos, Nigeria. African J Infect Dis 2017; 11(2): 75-82.
- 19. Mekonnen D, Derbie A, Desalegn E. TB/HIV co-infections and associated factors among patients on directly observed treatment short course in Northeastern Ethiopia: A 4 years retrospective study. BMC Res Notes 2015; 8(1): 4-9.
- 20. Ali SA, Mavundla TR, Fantu R, Awoke T. Outcomes of TB treatment in HIV co-infected TB patients in Ethiopia: a cross-sectional analytic study. BMC Infect Dis 2016; 16(1): 640.
- 21. Tweya H, Feldacker C, Phiri S, Ben-Smith A, Fenner L, Jahn A, et al. Comparison of treatment outcomes of new smear-positive pulmonary tuberculosis patients by hiv and antiretroviral status in a TB/HIV clinic, Malawi. PLoS One 2013; 8(2): e56248.
- 22. Gao J, Zheng P, Fu H. Prevalence of TB/HIV Co-infection in countries except China: a systematic review and meta-analysis. PLoS One 2013; 8(5).
- World Health Organization (WHO). Global Tuberculosis Report 2017. 2017.
- 24. Hayibor KM, Bandoh DA, Asante-Poku A, Kenu E. Predictors of adverse TB treatment outcome among TB/HIV patients compared with non-HIV patients in the Greater Accra Regional Hospital from 2008 to 2016. Tuberc Res Treat 2020; 2020: 1-8.
- 25. Fekadu G, Turi E, Kasu T, Bekele F. Impact of HIV status and predictors of successful treatment outcomes among tuberculosis patients : a six-year retrospective cohort study. Ann Med Surg 2020; 60: 531-41.
- 26. World Health Organization (WHO). Global Tuberculosis Report 2019. 2019.

- 27. Sinshaw Y, Alemu S, Fekadu A, Gizachew M. Successful TB treatment outcome and its associated factors among TB/HIV coinfected patients attending Gondar University Referral Hospital, Northwest Ethiopia: an institution based cross-sectional study. BMC Infect Dis 2017; 17: 1-9.
- 28. Eyasu E, Tadesse B, Tsedeke W. Tuberculosis treatment outcomes among tuberculosis/human immunodeficiency co-infected cases treated under directly observed treatment of short course in Western Ethiopia. J AIDS HIV Res 2014; 6(8): 164-71.
- Belayneh M, Giday K, Lemma H. Treatment outcome of human immunodeficiency virus and tuberculosis co-infected patients in Public Hospitals of Eastern and Southern Zone of Tigray Region, Ethiopia. Brazilian J Infect Dis 2015; 19(1): 47-51.
- 30. Ansa GA, Walley JD, Siddiqi K, Wei X. Assessing the impact of TB/HIV services integration on TB treatment outcomes and their relevance in TB/HIV monitoring in Ghana. Infect Dis Poverty 2012; 1(1): 1.
- Tola A, Mishore KM, Ayele Y, Mekuria AN, Legese N. Treatment outcome of tuberculosis and associated factors among TB-HIV coinfected patients at Public Hospitals of Harar Town, Eastern Ethiopia. A five-year retrospective study. BMC Public Health 2019; 19(1): 1-12.
- 32. Gegia M, Magee MJ, Kempker RR, Kalandadze I, Chakhaia T, Golub JE, et al. Tobacco smoking and tuberculosis treatment outcomes: a prospective cohort study in Georgia. Bull World Health Organ 2015; 93(6): 390-9.
- Burusie A, Enquesilassie F, Addissie A, Dessalegn B, Lamaro T. Effect of smoking on tuberculosis treatment outcomes: a systematic review and meta-analysis. PLoS One 2020;15: 1-20.
- 34. Hirpa S, Medhin G, Girma B, Melese M, Mekonen A, Suarez P, et al. Determinants of multidrug-resistant tuberculosis in patients who underwent first-line treatment in Addis Ababa: a case control study. BMC Public Health 2013; 13(1): 1-9.
- 35. Kefale AT, Ánagaw YK. Outcome of tuberculosis treatment and its predictors among HIV infected patients in southwest Ethiopia. Int J Gen Med 2017; 10: 161-9.
- 36. Kang W, Yu J, Du J, Yang S, Chen H, Liu J, et al. The epidemiology of extrapulmonary tuberculosis in China: A largescale multicenter observational study. PLoS One 2020; 15: 1-15.