Determinants of unsuccessful treatment outcomes among relapse tuberculosis patients in selangor registered in National Tuberculosis Registry from year 2015 – 2019

Nur Adila Che Rameli, MD¹, Siti Sara Yaacob, DrPH¹, Nurhuda Ismail, DrPH¹, Meram Mohammed Ali Azzanni, DrPH¹, Harishah Talib, MPH²

¹Department of Public Health Medicine, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh, Selangor, Malaysia, ²Tuberculosis/Leprosy Unit, Selangor State Health Department, Malaysia

ABSTRACT

Introduction: Despite the availability of highly effective treatment for tuberculosis (TB), patients with TB may experience a relapse, which can be either a result of the disease reactivating or a new episode induced by reinfection. In Malaysia, there has been a noticeable rise in relapse TB cases, with a substantial rate of unsuccessful treatment outcomes among this population. This study seeks to examine the trends of unsuccessful treatment outcomes in relapse TB patients and explore how factors such as sociodemographic characteristics, TB disease profile, TB treatment profile, and comorbidities contribute to the outcomes.

Materials and Methods: This is a retrospective cohort study utilising secondary data from the National Tuberculosis Registry (NTBR). The study was conducted in Selangor among relapsed TB patients who were registered in NTBR from 1 January 2015 to 31 December 2019. TB disease profile, TB treatment profile, comorbidities, and sociodemographic data were examined. The determinants of unsuccessful treatment outcomes among relapsed TB patients were identified using multiple (binary) logistic regression analyses.

Results: 896 patients who experienced relapsed tuberculosis were included in this study. 32.25% were reported to have unsuccessful treatment outcomes. Multiple (binary) logistic regression revealed that the absence of sputum smear examination at 5 months and beyond was a determinant of unsuccessful treatment outcome (AOR 1.70 (95% CI: 1.19, 2.44). Additionally, being treated in government facilities, such as government hospitals and government primary health clinics, was a protective factor (AOR 0.06 (95% CI: 0.03, 0.15) and AOR 0.02 (95% CI: 0.01, 0.04), respectively.

Conclusion: The high proportion of unsuccessful treatment outcomes among relapse TB patients stresses the importance of adherence to routine sputum monitoring and public-private partnerships.

KEYWORDS:

Tuberculosis, Relapse, Recurrent, Retreatment

INTRODUCTION

Adapting the World Health Organization (WHO) definition and reporting framework for tuberculosis (TB) in 20131, Malaysia uses the term "relapse" to describe all TB recurrences during programmatic assessments. The term "relapse" refers to patients who had previously received treatment for TB and were declared cured or completed treatment during their most recent treatment and are now being diagnosed with a recurrence episode of tuberculosis. It can be either due to a true relapse from reactivation of the disease or a new episode of TB caused by reinfection.² Many studies used the term "recurrent TB" to describe previously treated patients who had successfully treated and later presently had active TB.3,4 The WHO standard 6-month regimen is recognized as highly effective in drug-susceptible TB. However, even with effective treatment, patients can still develop a relapse TB.5,6 Approximately 2-4% of individuals who get the treatment in trial settings encounter a relapse and need retreatment over a span of 2 years.7 However, a higher proportion may be seen under programmatic conditions in high-burden regions.^{8,9} In 2015, the WHO estimated that 430,000 individuals who had previously received treatment for tuberculosis were diagnosed with relapse TB. This accounted for around 7% of all reported cases of TB.10

In Malaysia, an increasing trend in retreatment cases was reported between 2012 and 2015, from 6.4% to 6.7%, 7.3%, and 7.4%, respectively. In 2015, the highest proportion contributing to retreatment were relapse cases (4.71%), followed by treatment after default cases (2.33%) and treatment after failure cases (0.36%).² Rising relapse TB cases will contribute to an increasing number of TB incidences, and this vulnerable group of patients tends to have unsuccessful treatment outcomes. Unsuccessful treatment outcomes can be defined as treatment failure, loss to follow-up and death.¹²² Relapse TB patients are more inclined to suffer higher mortality, loss to follow-up and treatment failure compared to those with the first episode of TB.³¹¹¹¹²²

Selangor is the most populated and multi-ethnic state in Malaysia and recorded the highest number of TB cases in 2018 with 5,071 cases and from 2019 to 2021, contributed up to 20% of total TB mortality in Malaysia. According to the National TB Registry data for 2019, only 70% of relapsed TB patients in Selangor had achieved treatment success. 6

This article was accepted: 13 November .2024 Corresponding Author: Siti Sara Yaacob Email: sitisara@uitm.edu.my Among risk factors contributing to unsuccessful treatment outcome among relapsed TB patients reported in previous literatures worldwide were male, positive sputum smear after 3 months of treatment, alcohol abuse, inadequate adherence to treatment, substance abuse, being current smoker, homelessness, staying in rural areas, drug resistant TB, smear positive pulmonary TB, HIV co-infection, working while on treatment and lack of family support. 11,17-20

Despite efforts made in the implementation of the TB control program and the availability of effective treatment, Malaysia is facing a challenge and has yet to achieve the target of 90% successful TB treatment set by the WHO. The proportion of successful treatment achieved is 81.5% for new cases and 77.1% for relapse TB cases.21 Numerous studies were conducted in Malaysia on unsuccessful TB treatment outcomes, but insufficient attention was given to relapse TB. Previous studies included overall and mixed categories of TB cases (combination of new cases, relapse cases, as well as return after loss to follow-up cases), however none of the previous studies focused specifically on relapse TB and how determinants such as sociodemographic, TB disease profile, TB treatment profile and comorbidities contribute to unfavourable treatment outcome. Relapse TB poses a significant threat to the emergence of drug resistance and its secondary spread in the community.^{22,23} Therefore, this study would like to investigate the determinants of unsuccessful treatment outcomes among relapsed TB patients to highlight various areas to focus on in tuberculosis control efforts.

MATERIALS AND METHODS

Study Design

This study is a retrospective cohort study utilizing secondary data acquired from the National Tuberculosis Registry (NTBR).

Locations and Study Population

The study was carried out in Selangor among relapsed TB patients who were registered in NTBR from 1 January 2015 to 31 December 2019.

Data Collection and Sampling Strategy

The inclusion criteria encompassed all individuals aged 18 years or older who had been diagnosed with relapse TB. NTBR is an online tuberculosis registry utilized by the Ministry of Health Malaysia to oversee the national tuberculosis control program. TB case notification, investigation, and treatment is documented in the registry. The exclusion criteria were patients with insufficient data on treatment outcome, patients initially registered as TB cases but subsequently diagnosed with other conditions, patients whose treatment outcome remained incomplete (e.g., those still undergoing treatment with unknown outcome), and patients with Multidrug-resistant tuberculosis (MDR-TB). As per WHO reporting system, it is recommended to separate and exclude cases with MDR-TB from the general TB main cohort when calculating treatment outcomes. 1 This is because the criteria for determining treatment outcome for MDR-TB cases are different. The study included all patients who met the eligibility criteria by using universal sampling.

Sample Size

The sample size was determined using OpenEpi for a single population proportion based on the largest sample size identified in a study by Tok et al.²¹ which reported a proportion of 22.9% for unsuccessful TB treatment outcomes in relapsed TB patients. With a 95% confidence interval (CI) and 5% desired precision, the minimum sample size required for this study was 354 after an estimated 30% was added to the final sample size estimates to account for potential incomplete data. Nevertheless, this study included all relapse TB patients registered in the Selangor NTBR database between 2015 and 2019, resulting in a total sample size of 896.

Operational Definition

The outcomes of TB treatment were defined and monitored during surveillance over a one-year period. The treatment outcome operational definitions employed in the study were based on the WHO definitions and reporting framework for TB, the Clinical Practice Guidelines for Management of Tuberculosis, and the Ministry of Health Malaysia National Tuberculosis Information System Manual (2018 Revision). 1,24-27 The operational definition for treatment outcome in this study was as follows:

- Cure: A tuberculosis patient who was initially bacteriologically confirmed and had a negative smear or culture during the last month of treatment or on at least one previous occasion.
- Completed treatment: A tuberculosis patient who has successfully completed treatment without meeting the criteria for cure or failure.
- 3. Treatment Failure: A TB patient whose sputum smear or culture was positive at any point during treatment, whether it was at five months or later.
- 4. Loss to follow-up: A TB patient who failed to initiate treatment or whose treatment was interrupted for a period of two consecutive months or more.
- 5. Died: A TB patient who passes away for any reason prior to or during TB treatment (all-cause mortality).

In this study, the dependent variable for this study was the treatment outcome. It was categorized as a dichotomous variable, either an unsuccessful or successful treatment. Unsuccessful treatment was defined as treatment failure, mortality, and loss of follow-up. On the other hand, successful treatment was defined as completed treatment or the cure of patients. Relapse TB patients were defined by category of TB cases and according to their history of previous cases, individuals who were previously treated for tuberculosis and were declared cured or completed their treatment but presented again and diagnosed with a new recurrent episode of tuberculosis. This recurrence can be either a true relapse or a new episode of tuberculosis caused by reinfection.

Data Analysis

All statistical analyses were performed by using Statistical Package for Social Science (SPSS) software version 29.0. Descriptive statistics were used to describe the study population's characteristics. Categorical variables were presented in frequency and percentage (%), while numerical

Table I: Sociodemographic	characteristic of R	Palanca TR nationts	(n-806)
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Variables	Total (n = 896) n (%) ^a	Unsuccessful TB treatment (n = 261) n (%) ^b	Successful TB treatment (n = 635) n (%) ^b
Socio-demographic			
Age (in years) c	43.0 (23.0)	43.0 (20.0)	42.5 (23.0)
Personal income (in RM)	350 (2000)	400 (2000)	350 (2000)
Nationality			
Non-Malaysian	40 (4.5)	10 (3.6)	30 (4.9)
Malaysian	856 (95.5)	270 (96.4)	586 (95.1)
Gender			
Female	274 (30.6)	84 (30.0)	190 (30.8)
Male	622 (69.4)	196 (70.0)	426 (69.2)
Ethnicity			
Chinese	114 (12.7)	37 (13.2)	77 (12.5)
Malay	555 (61.9)	187 (66.8)	368 (59.7)
Indian	159 (17.7)	40 (66.82)	119 (59.7)
Others	52 (8.4)	16 (5.7)	68 (7.6)
Education status			
Tertiary	170 (19.0)	58 (20.7)	112 (18.2)
Secondary	535 (59.7)	161 (57.5)	374 (60.7)
Primary	72 (8.0)	26 (9.3)	46 (7.5)
Others	119 (13.3)	35 (12.5)	84 (13.6)
Employment status			
Yes	448 (50.0)	139 (49.6)	309 (50.2)
No	448 (50.0)	141 (50.4)	307 (49.8)
Location of residence			
Rural	189 (21.1)	52 (18.6)	137 (22.2)
Urban	707 (78.9)	228 (81.4)	479 (77.8)

^aWithin total sample. ^bWithin the relapse TB who had unsuccessful treatment ^cMedian (IQR)

variables were expressed in mean with standard deviation (SD) or median with interquartile range (IQR) depending on the normality of the data. Then, Inferential statistics were done to determine factors associated with unsuccessful TB treatment outcomes in relapse TB patients. Simple logistic regression analysis was used to determine the association between socio-demographic, TB treatment-related, TB disease-related, and comorbidities factors with unsuccessful TB treatment outcomes in relapsed TB patients. Only variables with a p-value <0.25 in simple logistic regression or that are clinically important were selected for multiple logistic regression (binary) analysis to obtain the adjusted odds ratio (aOR). A p-value of 0.05 with a 95% confidence interval was used to indicate statistical significance in all analyses.

Ethics Approval

This study utilized secondary data and did not contain any patient-identifying information. As all cases were anonymized, informed consent was not obtained from individual patients. The Medical Research and Ethics Committee, Ministry of Health Malaysia, Faculty Ethics Review Committee, Faculty of Medicine, MARA University of Technology (UiTM) approved this study.

RESULTS

From 2015 to 2019, 1291 relapse TB cases were recorded out of 24644 TB cases in the National TB registry in Selangor. The total number of relapse TB cases included in the analyses was 896, after excluding cases with incomplete data on treatment outcomes (n: 8), cases with a change of diagnosis (n: 54), and

MDR-TB (n: 38), and duplicated data (n: 284). By using a total number of relapse TB patients with complete treatment outcomes at one year of surveillance (N: 869), 32.25% of relapse TB patients had unsuccessful outcomes. The flow diagram of data extraction was summarized in Figure 1. The trends of unsuccessful outcomes among relapsed TB patients in Selangor were noted to increase from 2016 to 2019, with the highest being in 2018, which reported a 36% unsuccessful rate. (Figure 2)

Characteristics of relapses in TB patients

The sociodemographic characteristics of the study population were illustrated in Table I. The median age for overall relapse TB cases was 43 years (IQR 23). In terms of relapse TB patients with unfavourable treatment outcomes, most of them were Malaysian citizens (96.4%), the male was predominant (69.4%), 66.8% were Malays, 81.4% were from urban areas, and almost 80% had secondary, lower, and informal education.

Table II depicted clinical profiles of relapse TB patients, which combined TB disease profile, treatment profile, and comorbidities characteristics. Most patients with unsuccessful outcomes had smear-positive pulmonary TB (62.9%), follow-up sputum monitoring at 2 months noted that 3.9% still had positive smears, and 26.8% of them had no sputum examination done. For subsequent sputum monitoring at 5 months and beyond, 1.4% was noted to have positive smear, and unfortunately, 65.7% of patients had no sputum examination done at 5 months of treatment and upon treatment completion.

Table II: Clinical profile of among Relapse TB patients (n=896)

Variables	Total	Unsuccessful TB treatment	Successful TB
	(n = 896) n (%) ^a	(n = 261) n (%) ^b	(n = 635) n (%) ^b
Clinical profile			
TB case detection			
Active	38 (4.2)	13 (4.6)	25 (4.1)
Passive	858 (95.8)	267 (95.4)	591 (95.9)
Anatomical site of TB infection			
Extrapulmonary	117 (13.1)	44 (15.7)	73 (11.9)
Pulmonary	779 (86.9)	236 (84.3)	543 (88.1)
Sputum AFB at diagnosis			,
Negative	300 (33.5)	98 (35.0)	202 (32.8)
Positive	582 (65.0)	176 (62.9)	406 (65.9)
Not done	14 (1.6)	6 (2.1)	8 (1.3)
Sputum AFB at 2 month			_ (,
Negative	668 (74.6)	194 (69.3)	474 (76.9)
Positive	32 (3.6)	11 (3.9)	21 (3.4)
Not done	196 (21.9)	75 (26.8)	121 (19.6)
Sputum AFB at ≥ 5 month	(2.1.3)		.=. (,
Negative	388 (43.3)	92 (32.9)	296 (48.1)
Positive	11 (1.2)	4 (1.4)	7 (1.1)
Not done	497 (55.5)	184 (65.7)	313 (50.8)
Chest Radiography	457 (55.5)	104 (03.7)	313 (30.0)
No lesion	81 (9.0)	30 (10.7)	51 (8.3)
Minimal lesion	500 (55.8)	155 (55.4)	345 (56.0)
Moderate lesion	271 (30.2)	82 (29.3)	189 (30.7)
Far advanced	31 (3.5)	8 (2.9)	23 (3.7)
Not done	13 (1.5)	5 (1.8)	8 (1.3)
	13 (1.3)	3 (1.6)	8 (1.3)
Type of health facilities	E3 (E 0)	47 (16.9)	6 (1.0)
Private	53 (5.9)	47 (16.8)	6 (1.0)
Government Hospital	647 (72.2)	213 (76.1)	434 (70.5)
Government Primary Health Clinic	196 (21.9)	20 (7.1)	176 (28.6)
Treatment duration	FF0 (64 4)	4.55 (50.0)	205 (62.5)
≥6 months	550 (61.4)	165 (58.9)	385 (62.5)
<6 months	346 (38.6)	115 (41.1)	231 (37.5)
DOTS (intensive)	(o o)	222 (22 1)	
Yes	760 (84.8)	230 (82.1)	530 (86.0)
No	136 (15.2)	50 (17.9)	86 (14.0)
DOTS (Supervisor)	()		
Healthcare worker (HCW)	427 (47.7)	138 (49.3)	289 (46.9)
Family member	422 (47.1)	124 (44.3)	298 (48.4)
No supervisor	11 (1.2)	4 (1.4)	7 (1.1)
Others	36 (4.0)	14 (5.0)	22 (3.6)
BCG scar			
Yes	826 (92.2)	264 (94.3)	562 (91.2)
No	70 (7.8)	16 (5.7)	54 (8.8)
Smoking			
No	581 (64.8)	181 (64.6)	400 (64.9)
Yes	315 (35.2)	99 (35.4)	216 (35.1)
HIV			
No	771 (86.0)	235 (83.9)	536 (87.0)
Yes	95 (10.6)	32 (11.4)	63 (10.2)
Not known	30 (3.3)	13 (4.6)	17 (2.8)
Diabetes			
No	675 (75.3)	210 (75.5)	465 (75.5)
Yes	221 (24.7)	70 (25.0)	151 (24.5)

^aWithin total sample. ^bWithin the relapse TB who had unsuccessful treatment

Determinant of unsuccessful treatment outcome among relapse TB patients

The study variables were analysed using simple logistic regression and multiple logistic (binary) regression, as shown in Table III. This study identified two factors that were linked to unsuccessful outcomes. The first factor was the lack of sputum examination at 5 months of treatment and upon treatment completion (AOR 1.70; 95% CI 1.19,2.44). The

second factor was the type of health facilities: government hospitals and government primary health clinics (AOR 0.06; 95% CI 0.03,0.15) and (AOR 0.02; 95% CI 0.01,0.04), respectively. The absence of Sputum AFB examination after the intensive phase was found to be a confounder as it was statistically significant in simple logistic regression; however, after adjustment was made in multiple logistic regression, this factor was found to be insignificant. The final model of

Table III: Determinants of Unsuccessful treatment outcome among Relapse TB patients

Variables	COR (95% CI) a	p-value a	AOR (95% CI) b	p-value b
Socio-demographic factor				
Age, (in years)	1.00 (0.99, 1.01)	0.397	1.00 (0.99, 1.01)	0.613
Gender				
Female	1	ref.	1	ref.
Male	0.44 (0.77, 1.42)	0.799	1.10 (0.78, 1.55)	0.596
Ethnicity				
Chinese	1	ref.	1	ref.
Malay	1.06 (0.69, 1.62)	0.799	0.66 (0.43, 1.00)	0.052
Indian	0.70 (0.41, 1.19)	0.187	0.68 (0.41, 1.13)	0.133
Others	0.64 (0.32, 1.27)	0.201	0.56 (0.30, 1.04)	0.068
Clinical factor				
DOTS (intensive)				
Yes	1	ref.	1	ref.
No	1.34 (0.92, 1.96)	0.133	1.06 (0.65, 1.74)	0.811
Type of health facilities				
Private	1	ref.	1	ref.
Government Hospital	0.06 (0.03, 0.15)	<0.001 *	0.06 (0.03, 0.15)	<0.001 *
Government Primary Health Clinic	0.01 (0.01, 0.04)	<0.001*	0.02 (0.01, 0.04)	<0.001 *
Sputum AFB at 2 month				
Negative	1	ref.	1	ref.
Positive	1.28 (0.61, 2.71)	0.52	1.62 (0.68, 3.85)	0.272
Not done	1.51 (1.09, 2.11)	0.015 *	0.98 (0.62, 1.56)	0.934
Sputum AFB at ≥ 5 month				
Negative	1	ref.	1	ref.
Positive	1.84 (0.53, 6.42)	<0.001 *	2.10 (0.54, 8.10)	0.282
Not done	1.89 (1.41, 2.54)	<0.001 *	1.70 (1.19, 2.44)	0.004 *

AOR (Adjusted Odds Ratio), Confidence Interval (CI). The Cox & Snell R2 value is 0.150, indicating the proportion of variance explained by the model. The Hosmer and Lemeshow test yield a value of 0.687, suggesting good model fit. Classification: 73.5%, and the Area Under the Curve (AUC) is 70.0% (95% CI: 66.0-74.0; p-value=<0.001). ^aTest employed: Simple logistic regression ^bTest employed: Multiple Logistic Regression Analysis (Enter Method) Constant value: 0.842 and the model assumption is met. There is a no interaction and multicollinearity.

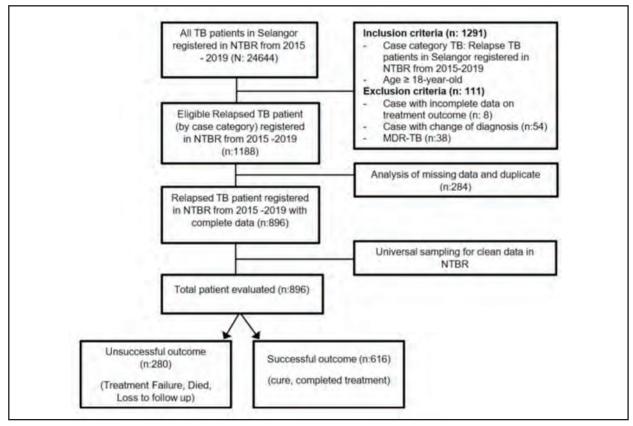


Fig. 1: Flow chart of data retrieval and extraction

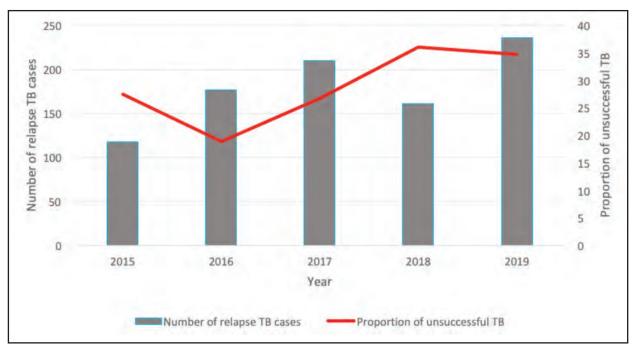


Fig. 2: Trends of unsuccessful treatment outcome among relapse TB cases in Selangor from 2015 -2019

determinants comprised all significant factors and three clinically relevant factors: age, gender, and DOTs during the intensive phase.28-30 The prediction of this model was 70% (95% CI 66.4, 73.7).

DISCUSSION

In this retrospective cohort study, we highlighted the high proportion of unsuccessful treatment outcomes among relapse TB patients in Selangor. The increasing trends seen were alarming, especially from the year 2016 to the year 2019 (18.8%, 26.7%, 36%, and 34%), respectively. One of the critical indicators being monitored to achieve target under the End TB strategy by WHO is a successful TB treatment rate of 90%, thus allowing only 10% of unsuccessful rate.³¹ A study done using Malaysia's national-wide data (2014 until 2017), revealed a high rate of unsuccessful treatment outcomes among relapse TB patients compared to new patients (22.9% and 18.5%) respectively.²¹ This current study suggests that Selangor had a high rate of unsuccessful treatment outcome that was above the national level.

A study from Tanzania utilizing national wide data however reported much lower rate of unfavourable outcome among relapse TB patients compared to Malaysia which was 10%.¹¹

Factors associated with unsuccessful treatment outcomes among relapse TB patients

We found that not doing Sputum AFB examination after 5 months and before the end of treatment, was associated with a higher likelihood of unfavourable outcomes in relapse TB patients AOR 1.70 (95% CI: 1.19,2.44). Furthermore, the current study revealed that 55% of relapse TB patients that had not been checked for sputum at 5 month and beyond reported much higher rate of incomplete monitoring

compared to a study done in Uganda that showed 16% of patients did not have sputum AFB follow up at 2 months, 39% at 3 months and 28% at 5 months and later. Lack of proper sputum monitoring has been linked to not being on DOTs, inability to produce sputum, long time spent at the laboratory, and poor health education among patients and health care providers.³² In Malaysia, for instance, according to the Clinical Practice Guideline (CPG) of Management of Tuberculosis, all patients with pulmonary tuberculosis must undergo routine monitoring during their treatment. This includes monitoring the presence of acid-fast bacilli (AFB) in sputum samples at specific intervals: during the initial assessment stage, after 2 weeks of commencing treatment, after 1 month, after 5 months, and at the end of treatment. This is in line with WHO's recommendation to use sputum smears to evaluate treatment outcomes and monitor the result of the treatment.25,33

This study also found that being treated in government facilities that include government hospital and government primary health clinic were protective factor for an unsuccessful treatment outcome in relapse TB patients AOR 0.06 (95% CI 0.03, 0.15) and 0.02 (95% CI 0.01, 0.04) respectively compared to being treated in private facilities.

A mixed method study done in Nigeria³³ found that most patients diagnosed with TB in private sectors were referred to public facilities while 25% being treated in private facilities and reported that 10.5% of patient were treated with unconventional regimens, 21% were cured, 11% died, 16% loss to follow up and 53% were not evaluated. This study revealed that 5% of patients received unconventional treatment regimens, 21% of the patients were cured, 11% died, 16% defaulted, and 53% were not assessed.

The knowledge about TB among the healthcare providers was not up to date, and most of the healthcare providers had not undergone any formal training in tuberculosis. ^{34,35} Most patients that were suspected or confirmed to have TB were referred to the public sector without any feedback. ³³ Also, the private healthcare providers were not very sure of the diagnostic procedures and necessary tests for the definite diagnosis of TB. ³⁶

The findings are in line with other previous studies conducted in Malaysia's high TB burden neighbouring countries such as Indonesia and Pakistan. 37,38 have also pointed to shortcomings in the diagnosis, management and treatment of TB patients by private practitioners. It was reported that 19-53% of TB cases and about 4-18% of smear-positive Pulmonary TB cases were not treated with standardized diagnosis and treatment. 37 A systematic review was conducted in India, which reported barriers to engagement with private sectors in TB care includes lack of coordination mechanisms and inadequate knowledge of private practitioner on programmatic aspects. 34

The study finding highlights the lack of routine sputum smear examination upon completion of 5 months of treatment and upon treatment completion. It is a predictor for poor treatment outcomes in relapse TB patients and signifies the importance of the clinical managing team adhering to the recommendations suggested by the CPG, which are routine monitoring of sputum smears being practiced, including the procedure to induce sputum in patients who have difficulty to produce the phlegm.

Apart from that, this study also highlighted the increased risk of unsuccessful treatment outcomes associated with private treatment facilities; this signifies that strengthening the multisectoral and TB public-private partnership and regular training to have updates on recent knowledge is important. TB program managers, public and private practitioners, and NGOs all have a critical role in TB prevention and Control efforts and to end TB epidemics.

The strength of our study is that it is the first study done in Selangor focusing solely on relapse TB patients and its associated factors for unsuccessful treatment outcomes. This evidence would be beneficial for TB Control teams to plan out tailored strategies and approaches specific to this group of patients which have a higher risk of unsuccessful treatment.

A limitation of our study is that this study utilized secondary data that have limited variables, for example, the factors that can affect the adherence to TB medication, including side effects of TB regimes, other comorbidities associated with TB, such as alcohol abuse, and chronic obstructive pulmonary disease.

CONCLUSION

This study has identified one of the determinants of unsuccessful treatment among relapse TB patients is the lack of routine sputum smear examination after completing 5 months of therapy, and being treated in government facilities is a protective factor. The study also highlights the high

proportion of unsuccessful treatment outcome among relapse TB patients and the importance of adherence to routine sputum monitoring and strengthening public-private partnerships.

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REFERENCES

- World Health Organization. Definitions and reporting framework for tuberculosis – 2013 revision: updated December 2014 and January 2020 [Internet]. Définitions et cadre de notification pour la tuberculose – révision 2013. Geneva: World Health Organization; 2013 [cited 2024 Jan 6]. Available from: https://iris.who.int/handle/10665/79199
- MOH. Malaysia Ministry of Health. National strategic plan for tuberculosis control (2016-2020). Kuala Lumpur: MOH; 2016
- 3. Kim L, Moonan PK, Heilig CM, Woodruff RSY, Kammerer JS, Haddad MB. Factors associated with recurrent tuberculosis more than 12 months after treatment completion. Int J Tuberc Lung Dis 2016; 20(1): 49-56.
- 4. Vega V, Rodríguez S, Van der Stuyft P, Seas C, Otero L. Recurrent TB: a systematic review and meta-analysis of the incidence rates and the proportions of relapses and reinfections. Thorax 2021; 76(5): 494-502.
- Dartois VA, Rubin EJ. Anti-tuberculosis treatment strategies and drug development: challenges and priorities. Nat Rev Microbiol 2022; 20(11): 685-701.
- 6. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. Geneva, Switzerland: World Health Organization; 2021.
- Romanowski K, Balshaw RF, Benedetti A, Campbell JR, Menzies D, Ahmad Khan F, et al. Predicting tuberculosis relapse in patients treated with the standard 6-month regimen: an individual patient data meta-analysis. Thorax 2019; 74(3): 291-
- 8. Dooley KE, Lahlou O, Ghali I, Knudsen J, Elmessaoudi MD, Cherkaoui I, et al. Risk factors for tuberculosis treatment failure, default, or relapse and outcomes of retreatment in Morocco. BMC Public Health 2011; 11(1): 140.
- Anaam MS, Alrasheedy AA. Recurrence Rate of Pulmonary Tuberculosis in Patients Treated with the Standard 6-Month Regimen: Findings and Implications from a Prospective Observational Multicenter Study. Tropical Medicine and Infectious Disease [Internet]. 2023 Feb 1 [cited 2024 Feb 8];8(2):110. Available from: https://www.mdpi.com/2414-6366/8/2/110
- Jiang H, Yin J, Liu F, Yao Y, Cai C, Xu J, et al. Epidemiology of recurrent pulmonary tuberculosis by bacteriological features of 100 million residents in China. BMC Infect Dis. 2022; 22(1): 638.
- Njiro BJ, Kisonga R, Joachim C, Sililo GA, Nkiligi E, Ibisomi L, et al. Epidemiology and treatment outcomes of recurrent tuberculosis in Tanzania from 2018 to 2021 using the National TB dataset. PLOS Neglected Tropical Diseases 2024; 18(2): e0011968
- Hermans SM, Zinyakatira N, Caldwell J, Cobelens FGJ, Boulle A, Wood R. High rates of recurrent tuberculosis disease: A population-level cohort study. Clinical Infectious Diseases 2020; 72(11): 1919-26.

- Kaur K, Said S, Norkhadijah S, Lim PY. Risk factors of unfavourable TB treatment outcomes in Hulu Langat, Selangor. Malaysian Journal of Medicine and Health Sciences 2022; 18: 52– 60.
- 14. Mohidem NA, Osman M, Hashim Z, Muharam FM, Mohd Elias S, Shaharudin R. Association of sociodemographic and environmental factors with spatial distribution of tuberculosis cases in Gombak, Selangor, Malaysia. Wen TH, editor. PLOS ONE 2021; 16(6): e0252146.
- 15. Mohammad Haikal Suhairi, Mohamad M, Mohamad Rodi Isa, Sherzkawee A, Ismail N. Risk factors for tuberculosis-related death among adults with drug-sensitive pulmonary tuberculosis in Selangor, Malaysia from 2013 to 2019: a retrospective cohort study using surveillance data. BMJ open 2024; 14(2): e080144-4.
- Selangor Health State Department. National Tuberculosis registry (NTBR) [Internet]. 2019. Available from: https://ntbr.moh.gov.my/
- 17. Mutembo S, Mutanga JN, Musokotwane K, Kanene C, Dobbin K, Yao X, et al. Urban-rural disparities in treatment outcomes among recurrent TB cases in Southern Province, Zambia. BMC Infect Dis 2019; 19(1): 1087.
- 18. Slama K, Tachfouti N, Obtel M, Nejjari C. Factors associated with treatment default by tuberculosis patients in Fez, Morocco. East Mediterr Health J 2013; 19(08): 687-93.
- Matulyte E, Davidaviciene E, Kancauskiene Z, Diktanas S, Kausas A, Velyvyte D, et al. The socio-demographic, clinical characteristics and outcomes of tuberculosis among HIV infected adults in Lithuania: A thirteen-year analysis. Lee YT, editor. PLOS ONE 2023; 18(3): e0282046.
- Velavan A, Purty AJ, Shringarpure K, Sagili KD, Mishra AK, Selvaraj KS, et al. Tuberculosis retreatment outcomes and associated factors: a mixed-methods study from Puducherry, India. Public Health Action. 2018; 8(4): 187-93.
- 21. Tok PSK, 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. Ehtesham HS, editor. PLOS ONE 2020; 15(4): e0231986.
- Zong Z, Huo F, Shi J, Jing W, Ma Y, Liang Q, et al. Relapse versus reinfection of recurrent tuberculosis patients in a national tuberculosis specialized hospital in Beijing, China. Frontiers in Microbiology 2018; 9.
- 23. Zereabruk K, Kahsay T, Teklemichael H, Aberhe W, Hailay A, Mebrahtom G, et al. Determinants of multidrug-resistant tuberculosis among adults undergoing treatment for tuberculosis in Tigray Region, Ethiopia: a case–control study. BMJ Open Resp Res 2024; 11(1): e001999.
- 24. Ministry of Health, Malaysia. Manual Sistem Maklumat Tibi Kebangsaan (Semakan 2018). Putrajaya: Disease Control Division, Ministry of Health; 2019; 8-9.
- 25. Ministry of Health Malaysia. Clinical Practice Guidelines: Management of Tuberculosis (4th edition). MOH/P/PAK/258.12(GU). Putrajaya: Ministry of Health Malaysia; 2012
- 26. Limenh LW, Kasahun AE, Sendekie AK, Seid AM, Mitku ML, Fenta ET, et al. Tuberculosis treatment outcomes and associated factors among tuberculosis patients treated at healthcare facilities of Motta Town, Northwest Ethiopia: a five-year retrospective study. Scientific Reports 2024; 14(1): 7695.

- 27. Debash H, Nega J, Bisetegn H, Tesfaw G, Feleke DG, Ebrahim H, et al. Tuberculosis treatment outcomes and its predictors among tuberculosis patients registered at Tefera Hailu Memorial General Hospital, Sekota Town, Northeast Ethiopia: a seven-year retrospective study. Sharma D, editor. Canadian Journal of Infectious Diseases and Medical Microbiology 2023; 2023: 1-9.
- Rostam Niakan Kalhori S, Nasehi M, Zeng XJ. A logistic regression model to predict high risk patients to fail in tuberculosis treatment course completion. IAENG International Journal of Applied Mathematics 2010; 40.
- 29. Murphy ME, Wills GH, Murthy S, Louw C, Bateson ALC, Hunt RD, et al. Gender differences in tuberculosis treatment outcomes: a post hoc analysis of the REMoxTB study. BMC Medicine 2018; 16(1): 189.
- 30. Wang S. Development of a nomogram for predicting treatment default under facility-based directly observed therapy short-course in a region with a high tuberculosis burden. Ther Adv Infect Dis 2021; 8: 20499361211034066.
- 31. Global Tuberculosis Report 2023. Geneva: World Health Organization; 2023.
- Nakaggwa P, Odeke R, Kirenga BJ, Bloss E. Incomplete sputum smear microscopy monitoring among smear-positive tuberculosis patients in Uganda. Int J Tuberc Lung Dis 2016; 20(5): 594-9.
- 33. Chijioke-Akaniro O, Onyemaechi S, Kuye J, Ubochioma E, Omoniyi A, Urhioke O, et al. Challenges in engaging the private sector for tuberculosis prevention and care in Nigeria: a mixed methods study. BMJ Open 2023; 13(9): e069123.
- 34. PS R, Shannawaz M, Mathew ME, Sachdeva KS. Facilitators and barriers for private health sector engagement for tb care in india: A systematic review and meta-synthesis of qualitative research. Glob Health Sci Pract 2024; 12(4): e2400034.
- 35. Wippel C, Farroñay S, Gilbert HN, Millones AK, Acosta D, Torres I, et al. Exploring the role of the private sector in tuberculosis detection and management in Lima, Peru: a mixed-methods patient pathway analysis. medRxiv. 2023.
- 36. Shah HD, Chaudhary S, Desai B, Patel J, Yasobant S, Bhavsar P, et al. Exploring private sector perspectives on barriers and facilitators in availing tuberculosis care cascade services: a qualitative study from the Indian state. BMC Primary Care 2024; 25(1): 5.
- 37. Probandari A, Lindholm L, Stenlund H, Utarini A, Hurtig AK. Missed opportunity for standardized diagnosis and treatment among adult Tuberculosis patients in hospitals involved in Public-Private Mix for Directly Observed Treatment Short-Course strategy in Indonesia: a cross-sectional study. BMC Health Services Research 2010; 10(1): 113.
- 38. Naseer M, Khawaja A, Pethani AS, Aleem S. How well can physicians manage Tuberculosis? A Public-Private sector comparison from Karachi, Pakistan. BMC Health Services Research 2013; 13(1): 439.