ORIGINAL ARTICLE

Tuberculosis Death and Associated Risk Factors in Hulu Langat District

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ABSTRACT

Introduction: Addressing the challenge of mortality among tuberculosis (TB) patients undergoing treatment is a significant concern in Malaysia. It is essential to identify the factors linked to TB mortality to evaluate national TB control programs and identify high-risk individuals. The objective of this study was to assess the percentage of TB mortality among patients receiving treatment over a three-year duration and identify the associated factors in Hulu Langat District. **Method:** The study used secondary data collected from the national TB registry from 2019 to 2021, and all registered TB cases that met the inclusion and exclusion criteria were included. The data in the study were tested using regressions. **Results:** The results showed that 11.5% of total registered TB patients had died during their course of treatment, and multiple logistic regression identified several significant factors associated with TB mortality, including gender (aOR= 0.75, 95%CI: 0.58, 0.97; p=0.026), age (aOR= 16.94, 95%CI: 5.14, 55.81; p<0.001), household income level (aOR= 1.56, (95%CI: 1.22, 1.99; p<0.001), living area (aOR= 1.53, 95%CI: 1.00, 2.32; p=0.048) education level (aOR= 1.89, 95%CI: 1.06, 3.35; p=0.030), the severity of chest x-ray (aOR= 5.03, 95%CI: 2.95, 8.58; p<0.001), and HIV status (aOR= 3.72, 95%CI: 2.71, 5.19; p<0.001). **Conclusion:** TB mortality in the Hulu Langat district is a significant public health concern and interventions such as intensified case finding, home visits for elderly patients, and health promotion are needed to reduce TB mortality and achieve the WHO End TB strategy milestone.
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INTRODUCTION

Tuberculosis (TB) is caused by bacteria known as Mycobacterium tuberculosis, most often affecting the lungs. Transmission of tuberculosis bacteria is through air whereby when a person with lung tuberculosis sneezes, coughs, or spits the bacteria will travel airborne and has the potential to be inhaled by a healthy person. According to the World Health Organization, tuberculosis has been a significant public health issue despite being a preventable and curable disease (1). It is recorded that nearly 10 million people fall victim to tuberculosis every year and around 1.5 million people die from it, making it the global top infectious killer. The infection rate is considerably greater in third-world countries where people live with a low to middle-household income, but there are still significant active cases throughout the globe (2).

In 2018, out of the 10 million reported TB cases, men accounted for a higher prevalence at 57%, followed by women at 32% and children at 11%. These statistics clearly demonstrate that TB poses a significant risk across all age groups. Furthermore, among the 10 million new cases, a distressing 1.5 million individuals succumbed to the disease within the same year of diagnosis, highlighting the urgent need for public health interventions (3,4). Analysing the global trend over a four-year period from 2015 to 2019, there was a notable reduction of 9% in TB cases. Additionally, between 2018 and 2019 alone, there was a 2.3% decrease in cases (3,4). However, despite these reductions, progress is insufficient, particularly for many third-world countries, to achieve the targets set by the World Health Organization (WHO) and the Sustainable Development Goals (SDGs) (5). A recently published study indicates that the nation will suffer significant economic and health costs if the SDG TB mortality target is not met (6). The effects of tuberculosis on the labour force are detrimental, and the disease also strains public health budgets, reduces household savings, and destabilises regional economies (6).

Access to resources has consistently been identified as a significant contributing factor to tuberculosis (TB) mortality. For instance, a recent article highlights that developed countries have successfully implemented comprehensive national TB control programs, reducing mortality rates among patients undergoing treatment. Furthermore, the article suggests that a majority of TB-related deaths occurring during the treatment phase are not primarily caused by the disease itself (7). Meanwhile, limited resources in many countries have contributed to unsatisfactory outcomes in TB treatment, primarily because of inadequate coverage and poor adherence to treatment protocols (8). The main causes of TB mortality is due to severe TB, respiratory failure, and, comorbidity (9). Southeast Asian countries have reported a significant portion, approximately one-third (44%), of the global tuberculosis burden, as stated by (10). Furthermore, Malaysia is ranked 76th worldwide in terms of tuberculosis incidence and is classified as a country with a medium to low level of endemicity (11). In 2019, Malaysia's TB incidence rate stood at 92 cases per 100,000 population, while the estimated mortality rate was 4 cases per 100,000 population per year, as reported in the (4). Latest tuberculosis data in Malaysia according to TB overview published in the T-Spot.TB website, that it is the second cause of death among communicable, maternal, neonatal, and nutritional diseases in Malaysia. Furthermore, every year there is around 20,000 to 25,000 new tuberculosis cases and annual tuberculosis death of 1500 to 2000, in Malaysia. The average number of deaths per day is around 6 people per day from tuberculosis infection. While Malaysia has successfully been able to reduce tuberculosis-related mortality, tuberculosis incidences and the number of mortalities are still persistent which is not in par with the global End Tuberculosis Strategy milestones (4,12). Therefore, this study's objective is to determine the risk factors associated with TB mortality and try to prevent it from the root cause.

MATERIALS AND METHODS

In this study, we used a retrospective cohort approach to collect secondary data from the national TB registry from 2019 to 2021 (Table I). The study was conducted in the Hulu Langat District Health Office, which provides services to almost 1.3 million populations. Hulu Langat district was selected as the ideal location for conducting the TB mortality study due to the notable number of recorded mortality cases within the district annually. Moreover, considering that Hulu Langat is one of the largest districts in Selangor, our study will allow for the extrapolation of findings to the entire population of Selangor. The study encompassed all individuals diagnosed with tuberculosis and registered in the national TB registry within the Hulu Langat District between the years 2019 and 2021. The total sample was 3358, but Single Proportion Sampling was used to ensure the adequacy of sample size and the result was

Table I: Cumulative TB cases in Hulu Langat district from 2019–2021

Years	TB Death		Total (%)
	Alive (%)	Death (%)	
2019	1095 (89.97)	122 (10.03)	1217 (36.24)
2020	994 (88.75)	126 (11.25)	1120 (33.35)
2021	883 (86.48)	138 (13.52)	1021 (30.40)
Total	2972 (88.50)	386 (11.50)	3358 (100)

426 sample. All ages TB patients which are registered in national TB registry from 01/01/2019 to 31/12/2021 and completed treatment/ cured/ death was included in the study and patients with incomplete data/ missing data/ still on treatment after 31/12/2021 were excluded in the study. The data was extracted from national TB registry after getting permission from Medical Research & Ethics Committee Ministry of Health, Malaysia (NMRR ID – 23 – 00255 – YRJ (IIR).

Final data was tested using IBM SPSS version 28, and all the data were presented in a descriptive table. Logistic regression was chosen to determine the association between independent variables. Additionally, we employed multiple logistic regression analysis to determine the actual risk factors associated with mortality in tuberculosis cases. The dependent variable was tuberculosis death in the Hulu Langat District.

The independent variables considered in the study encompassed various socio-demographic characteristics such as age, sex, citizenship, race, location of living, house category, education level, and household income. Other independent variables included diabetic Mellitus, smoker, BCG scar, type of tuberculosis, first chest x-ray status, and HIV status.

RESULTS

A total of 3358 tuberculosis patient data was extracted from national TB registry for the year 2019 to 2021. The cumulative percentage of tuberculosis death for the year 2019 to 2021 was 11.5% (386). Meanwhile, the highest percentage of tuberculosis death recorded between the 3 years was 13.5% (138) for 2021 followed by the years 2020 (11.3%), and the year 2019 (10%).

Table II presents descriptive summaries of the secondary data collected for this study. We were able to observe that 13.5% of tuberculosis death contributed by the male and in the age category, elderly people contributed the highest percentage of TB death which is 28.2%. There is also a higher percentage of death among non-Malaysians compared to Malaysian citizens which is 15% and 10.7% respectively.

TB cases are reported to happen more in urban areas, which is 94.2%, but TB death occurs more in suburban (16.9%) compared to urban (11.2%). A similar event can

Table II: Characteristics of TB patients in Hulu Langat district from 2019–2021

Variables	TBDeath		n (%) (3358)
	Alive (%)	Death (%)	
Sex			
Male	1815 (86.46)	284 (13.54)	2099 (62.50)
Female	1157 (91.89)	102 (8.11)	1259 (37.49)
Citizenship			
Malaysian	2475 (89.25)	298 (10.75)	2773 (82.57)
Non-Malaysian	497 (84.95)	88 (15.05)	585 (17.42)
Age			
Children	133 (97.79)	3 (2.21)	136 (4.05)
Youth	475 (96.93)	15 (3.07)	490 (14.59)
Adult	2163 (88.21)	289 (11.79)	2452 (73.01)
Elderly	201 (71.78)	79 (28.22)	280 (8.33)
Place of living			
Urban	2810 (88.84)	353 (11.16)	3163 (94.19)
Sub-urban	162 (83.07)	33 (16.93)	195 (5.81)
Housing category			
Village house	2811 (88.7)	359 (11.3)	3170 (94.40)
ResidentialHouse	161 (85.68)	27 (14.32)	188 (5.59)
Education level			
None	383 (84.55)	70 (15.45)	453 (13.49)
Primary school	165 (81.68)	37 (18.32)	202 (6.02)
Secondary school	1695 (87.73)	237 (12.27)	1932 (57.53)
Above SPM, below Degree	420 (93.54)	29 (6.49)	449 (13.37)
Degree and above	309 (96.96)	13 (3.04)	322 (9.58)
Household income	1693 (92.11)	145(7.89)	1838(54.73)
Above minimal wage			
Minimal wage and below	1279 (84.14)	241(15.86)	1520(45.26)
Diabetes Mellitus			
Yes	601 (84.76)	108 (15.24)	709 (21.11)
No	2371 (89.50)	278 (10.50)	2649 (78.89)
Smoking habit			
Yes	818 (87.11)	120 (12.89)	939 (27.96)
No	2154 (89.00)	266 (11.00)	2420 (72.06)
BCG scar			
Yes	2643 (89.29)	317 (10.71)	2960 (88.15)
No	329 (82.66)	69 (17.34)	398 (11.85)
TB type			
Pulmonary	2234 (88.41)	293 (11.59)	2527 (75.25)
Extrapulmonary	615 (89.65)	71 (10.35)	686 (20.43)
Both	123 (84.82)	22 (15.18)	145 (4.32)
X-ray on diagnosis			
Nolesion	377 (92.40)	31 (7.60)	408 (12.15)
Minimal	1645 (90.43)	174 (9.57)	1819 (54.16)
Moderately advanced	852 (86.76)	130 (13.24)	982 (29.24)
FarAdvanced	98 (65.77)	51 (34.23)	149 (4.44)
HIVstatus			
Positive	193 (72.01)	75 (27.99)	268 (7.98)
Negative	2779 (89.93)	311 (10.07)	3090 (92.02)

also be observed in the housing category; more cases are documented in village houses (94.4%) but TB death happens more in residential houses (14.4%). More TB deaths happen among tuberculosis patients who only have primary school level education (18.3%) and have minimum wages and below salary (15.9%) compared to their counterparts.

In this study also we able to observe that a higher percentage of TB death occurs in the TB patient which has diabetes mellitus (15.2%), smoking habit (12.8%), HIV positive (28.0%), diagnosed with both extrapulmonary and pulmonary TB (15.2%). Furthermore, 17.3% of TB death happened among TB patients who do not have BCG scars. We also observed that 34.2% of TB death occurs among TB patients with far advanced chest x-ray followed by moderately advanced chest x-ray (13.2%).

As shown in the univariate analysis (Table III) between the sex of the TB patients in the Hulu Langat district with TB deaths, it is reported that male TB patients have 43.7% lesser odds of dying compared to females (95% CI: 0.444, 0.715 with p-value <0.001). Meanwhile, the odds of the elderly age group TB patient dying is 17 times (95% CI: 5.389, 56.34 with p-value <0.001) higher than the children age group. The analysis also reveals Non-Malaysian TB patients have 32% (95% CI: 0.526, 0.879 with p-value <0.05) lesser odds of dying than Malaysian TB patients in the Hulu Langat district. There is also a significant association between the TB patient's household income and TB death. There are 2.2 times (95% CI: 1.768, 2.737 with p-value <0.001) higher odds of TB patients who earn a minimum wage and below dying compared to their counterparts. Besides that, TB patients living in an urban location also show 1.6 times (95% CI: 1.098, 2.396 with p-value <0.05) higher odds of dying compared to TB patients living in suburban. TB patients who had no education and only primary school education has higher odds of dying compared to the one who has higher education, 2 times higher (95% CI: 1.357, 3.021 with p-value <0.001) and 3.2 times higher (95% CI: 1.934, 5.454 with p-value <0.001) respectively. TB patients who have diabetes mellitus and no BCG scar also have higher odds of dying compared to their counterparts which are 1.5 times higher (95% CI: 1.206, 1.948 with p-value <0.001) and 1.7 times higher (95% CI: 1.316, 2.324 with p-value <0.001) respectively. Furthermore, TB patients who show a minimal lesion in the 1st chest x-ray taken have 6 times higher odds (95% CI: 3.844, 10.420 with p-value <0.001) of dying than those without lesions. The analysis also found that TB patients with HIV comorbid have 3 times higher odds (95% CI: 2.585, 4.647 with p-value <0.001) of dying compared to the one which does not have HIV.

Table III also shows a multivariable analysis by including all the significant variables from the univariate analysis. The final model shows there is a significant association between the variables sex, age group, household income, living location, education level, 1st x-ray status, and HIV status with TB death among the TB patients in the Hulu Langat district. The most prevailing associated risk factors are age group where elderly TB patients have 17 times higher odds (95% CI: 5.140, 55.813 with p-value <0.001) of dying while adjusted for sex, household income, location of living, education level, 1st x-ray status and HIV status. TB patients with minimum wage and below household income have 1.5 times higher odds of dying compared to their counterparts, while adjusted for the other significant variables. Besides that, TB patients living in an urban location also show 1.5 times (95% CI: 1.004, 2.322 with p-value <0.05) higher odds of dying compared to TB patients living in suburban while adjusted for the

Table III: Association between risk factor variables withTB death amongTB patients in Hulu Langat District

Variables	Univariate		Multivariable	
	cOR (95%,CI)	p-value	aOR (95%,CI)	p-value
Sex				
Female*				
Male	0.563 (0.444,0.715)	**<0.001**	0.747 (0.578,0.965)	**0.026**
Age Category				
Children: 0-14 years*				
Youth:15-24years	1.400 (0.399,4.908)	0.599	1.672 (0.465,6.019)	0.431
Adult: 25-64 years	5.923 (1.874,18.723)	**0.002**	5.397 (1.671,17.430)	**0.005**
Elderly: 65years>	17.425 (5.389,56.34)	**<0.001**	16.937 (5.140,55.813)	**<0.001**
Citizenship			-	-
Malaysian*				
Non-Malaysian	0.680 (0.526,0.879)	**0.003**		
Household income				
Above minimal wage*				
Minimal wage & below	2.200 (1.768,2.737)	**<0.001**	1.561 (1.223,1.992)	**<0.001**
Location				
Sub-urban*				
Urban	1.622 (1.098,2.396)	**0.01**	1.527 (1.004,2.322)	**0.048**
House category			-	-
Residential house*				
Village house	1.313 (0.861,2.003)	0.206		
Educationlevel				
Degree and above*				
Above SPM, below Degree	0.609 (0.312,1.191)	0.148	0.550 (0.275,1.099)	0.090
Secondary School	2.647 (1.680,4.170)	**<0.001**	1.630 (0.987,2.693)	**0.050**
Primary school	3.248 (1.934,5.454)	**<0.001**	1.889 (1.064,3.354)	**0.030**
No education	2.025 (1.357,3.021)	**<0.001**	1.269 (0.827,1.947)	0.276
DiabetesMellitus			-	-
No*				
Yes	1.533 (1.206,1.948)	**<0.001**		
Smoking (reference = No)			-	-
Yes	1.188 (0.944,1.495)	0.142		
BCGscar			-	-
Yes*				
No	1.749 (1.316,2.324)	**<0.001**		
TB type				
Pulmonary*			-	-
Extrapulmonary	0.880 (0.669,1.158)	0.362		
Pulmonary & Extrapulmonary	1.364 (0.853,2.181)	0.196		
1st X-ray				
No lesion*				
Minimal	6.329 (3.844,10.420)	**<0.001**	5.032 (2.951,8.579)	**<0.001**
Moderately Advanced	1.286 (0.864,1.915)	0.215	1.139 (0.749,1.731)	0.543
Far Advanced	1.856 (1.231,2.796)	**0.003**	1.594 (1.031,2.465)	**0.036**
HIVstatus				
No*				
Yes	3.472 (2.595,4.647)	<0.001	3.727 (2.709,5.128)	**<0.001**

**Reference group*

other significant variables. TB patients with only primary school education have 1.9 times higher odds (95% CI: 1.064, 3.354 with p-value <0.05) of dying compared to those with higher education when adjusted for the other significant variables. Furthermore, TB patients who show a minimal lesion in the 1st chest x-ray taken have 5 times higher odds (95% CI: 2.951, 8.579 with p-value <0.001) of dying than those without lesions while adjusted for the other significant variables. The analysis also found that TB patients with HIV comorbid have 3.7 times higher odds (95% CI: 2.709, 5.128 with p-value <0.001) of dying compared to the one which do not have HIV when adjusted for the other significant variables.

DISCUSSION

Our analysis of TB data collected over a three-year period, from 2019 to 2021, reveals a concerning trend in Hulu Langat District, Selangor, Malaysia. The mortality rate for TB has been steadily increasing each year, rising from 10% in 2019 to 13.5% in 2021. This upward trend is at odds with the World Health Organization's End TB strategy milestone, which aims to reduce TB deaths by 35% (13). Unfortunately, our findings suggest that we will not be able to meet the new target to lower TB deaths by 90% by 2030, as set forth by the Malaysian government (14).

According to our study, male TB patients have a 25.5% lower risk of dying compared to their female counterparts. This finding contradicts the results of a recent study by (15) which indicates that male TB patients have higher odds of dying compared to females. However, a study conducted in Terengganu, Malaysia, reported no significant association between sex and TB death among TB patients (16). The observed discrepancy between the two results could be attributed to various demographic and environmental factors. For instance, the higher proportion of working-class females in Selangor, relative to Terengganu, could be contributing to the increased risk among the former population. Moreover, Selangor's urbanization may be another factor that could exacerbate the risk, as urbanization is often associated with overcrowding, poor sanitation, and increased exposure to infectious agents.

We also found that elderly TB patients were more likely to die from TB compared to other age groups, which is consistent with previous research (16–18).This may be due to the fact that the elderly often present with multiple comorbidities, such as hypertension, diabetes mellitus, cardiac disease, and other lung-related diseases, which complicate the condition and subsequently pose a higher risk of mortality (19). Moreover, elderly patients frequently experience compromised immune systems due to factors related to aging and the presence of other medical conditions, which can contribute to additional complications during the recovery process. Ensuring

adherence to antituberculosis treatment also is a crucial concern, particularly among the elderly population. Due to their multiple medications, there is a higher chance of elderly patients defaulting on treatment. Additionally, adverse drug reactions and intolerance to antituberculosis drugs can also contribute to the increased mortality rate among elderly TB patients (20). Overall, our study highlights the urgent need for targeted interventions to address the unique challenges faced by elderly TB patients to improve treatment adherence and reduce mortality rates.

Financial status is a common risk factor for TB death among TB patients. TB patients earning minimum wage and below were found to have 1.6 times higher odds of dying compared to their counterparts. This finding is similar with a study published in 2018, which reported a similar association between low household income and TB death (21).The reason for this association is that lower household income increases the risk of poor TB treatment outcomes, which can lead to mortality. In low-income households, the TB patient may be the breadwinner, making it more likely for them to stop or default on treatment due to the need to work to fulfil their household income needs (22,23), which can further increase the risk of mortality. Additionally, the Directly Observed Treatment, Short-course strategy (DOTS), which is used to promotes adherence to TB treatment, can also contribute to higher default rates among the low-income group. This is because while the treatment itself is free in Malaysia, hidden costs such as loss of household income and transportation costs can become barriers for the lower household income group, indirectly increasing the risk of TB death (21).

Our study also revealed that TB patients living in urban settings had a 1.5 times higher risk of dying compared to those living in suburban areas. This finding is consistent with a study conducted in Bangladesh, which found that higher TB mortality rates were detected in urban settings (24). Similarly, a local study in Malaysia also found that people residing in urban regions have a higher risk of TB, which indirectly increases the likelihood of TB-related deaths (25).The increased risk of TB mortality in urban areas can be attributed to factors such as pollution, overcrowding, and urban poverty, which are all known risk factors for TB death (26–28). Additionally, TB patients living in urban slums, with poor living conditions such as lack of proper ventilation, clean water, and poor nutrition, are at greater risk of poor immune systems, which can lead to health complications and poor adherence to treatment, contributing to loss of follow-up and ultimately, increased TB mortality (29–31).

Furthermore, there is a significant association between the education level of TB patients and TB mortality in our study. TB patients with only primary school education had 1.9 times higher odds of dying compared to those with a degree or higher education. This finding is consistent with a study conducted in Colombia which reported consistently higher mortality rates among TB patients with lower education levels (32). One potential explanation for this relationship is that individuals with lower levels of education may have poorer health-seeking behaviours and delay seeking treatment until later stages of the disease, which increases the risk of mortality (33).

Chest x-ray has been found to be a useful tool not only for diagnosing tuberculosis but also for assessing the severity of the infection (34). Our study found that TB patients with minimal lesions on chest x-ray had 5 times higher odds of dying compared to those with no lesion, while TB patients with far advanced lesions had 1.6 times higher odds of dying compared to those with no lesion. This finding is consistent with a study conducted in Malaysia and Russia that reported a higher mortality rate among TB patients with cavitary lesions or extensive lung involvement on chest x-ray (16,35). The presence of cavitary lesions in the chest x-ray of TB patients indicates a higher acid-fast bacilli load and is closely associated with a higher risk of treatment failure, which directly correlates with an increased risk of TB mortality (36,37).

It is well established that individuals with HIV have a heightened vulnerability to opportunistic infections. Tuberculosis is the most frequent opportunistic infection in HIV-positive individuals worldwide, and it is often fatal (38).Consistent with this, our study revealed that TB patients co-infected with HIV had 3.7 times higher odds of mortality compared to those without HIV. Similar findings have been reported in other studies, which highlight HIV as a significant risk factor for mortality among TB patients (39–41).

Every study has its limitations, and in our research, a notable constraint was the absent of certain well-known confounding variables. This limitation arose due to the inherent constraints associated with using secondary data. As a recommendation for future studies, we advise researchers to consider employing alternative longitudinal study designs, such as cohort studies, to gain a more comprehensive understanding of additional factors associated with tuberculosis mortality. Despite these limitations, our study successfully identified important associated risk factors, which hold significant value for informing future TB programs. Additionally, we exceeded the required sample size, enhancing the reliability of our results for generalizing them to the broader population.

CONCLUSION

In conclusion, TB death in Hulu Langat district is significantly high and we are unable to reach the World Health Organization End TB strategy milestone if this trend continues. We were able to identify that sex,

elderly age group, low household income, urban living location, low education level, chest x-ray finding and HIV positive as the significant risk factor associated with mortality among TB patients in Hulu Langat district. Hence, attention should be given to this variable to reduce TB mortality. An elderly patient with TB should be given extra attention such as home visits and counselling sections to ensure medication adherence. Early case detection also is important to ensure that TB patient does not wait till lesions are present in the lungs, which can be done by intensified case finding and screening. Meanwhile, HIV patients are at high risk of mortality due to TB, thus people living with HIV should be educated on ways to prevent TB infection and awareness regards to TB. Wider coverage of health promotion to increase knowledge and awareness mainly among the poor urban and low-educated population is crucial to reduce TB mortality and reaching the 2030 End TB milestone.

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