Prevalence and Factors Associated with Tuberculosis Treatment Success among TB/HIV Co-Infection in North-East Malaysia

Tengku Mardhiah Tengku Jalal[1], Sarimah Abdullah[2], Farhanah Abd Wahab[3], Sharina Dir[4], Nyi Nyi Naing[2]

[1] Faculty of Computer & Mathematical Sciences, Universiti Teknologi MARA Cawangan (Pahang) Kampus Raub, 27600 Raub, Pahang, Malaysia

[2] Unit of Biostatistics & Research Methodology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[3] Faculty of Computer & Mathematical Sciences, Universiti Teknologi MARA, 40450 Shah Alam, Selangor, Malaysia

[4] Kelantan State Department of Health, Level 5, Wisma Persekutuan Kota Bharu, 15990 Kota Bharu, Kelantan, Malaysia

Abstract

Background: One of the six strategies developed by WHO, in order to stop Tuberculosis (TB) is addressing TB/HIV high-risk groups. This study aimed to determine the prevalence of successful TB treatment and factors associated with TB treatment success among TB/HIV co-infection patients in North-East Malaysia.

Methods: A cross-sectional study was carried out in the a-year period from 2003 to 2012 by reviewing TB/HIV records in all hospitals and health clinics. The outcome of interest was treatment success as defined by Ministry of Health (MOH) when the patients was cured or completed TB treatment.

Results: Out of 1510 total TB/HIV co-infection cases, 27.9% (95% CI: 25.2, 30.6) of the patients were having treatment success. A majority of TB/HIV co-infection cases were male (91.1%). Fifty-eight percent the patients were drug addicts and 6% were having positive tuberculin tests. The multiple logistic regression revealed that male (OR: 0.39, 95% CI: 0.22, 0.71) and positive tuberculin test result (OR: 2.61, 95% CI: 1.63, 4.19) were significantly associated with the treatment success of TB/HIV co-infection patients. Other factors such as age, comorbid, sputum smear and x-ray findings were not significantly factors in this study.

Conclusion: Female patients and those with negative tuberculin test should be emphasised for successful tuberculosis treatment.

Keywords: tuberculosis, successful tuberculosis treatment, tuberculin test, BCG, TB/HIV co-infection

Introduction

Tuberculosis (TB) has been recognised as a major global public health issue by the World Health Assembly (WHA) since 1991. Starting that year, global efforts to control TB were reinvigorated. The World Health Organisation (WHO) declared TB as a global emergency in 1993 and in 1995 recommended Directly Observed Treatment Short Course (DOTS) as a cost-effective strategy for TB control worldwide (1). Human immunodeficiency virus (HIV) is the greatest single risk factor for developing tuberculosis and life-threatening (2).

There are two forms of TB: latent TB and TB disease. Latent TB occurs when the mycobacterium infected in the body are not active and do not produce symptom (3). TB/HIV co-infection occurs when HIV patients were having either latent TB or TB disease or when TB patients are infected with HIV.

There are five TB outcomes: cure, treatment completion, treatment default, death, and treatment failure. The cure outcome refers to a patient who is smear-negative at, or one month prior to, the completion of treatment and on at least one previous occasion (4). In 1990, WHO chose 2015 as the target to cutting TB mortality and prevalence in half (5).

In Malaysia, a higher sex ratio between male to female 10.7:1 was observed in patients with pulmonary tuberculosis (PTB) in Malaysia (6). Hospital Kota Bharu, Kelantan also were having males as the majority patients with TB/HIV co-infection patients (7). Only 14 countries in the WHO European region able to provide age-disaggregated data for Lazarus et al. (2) study and it is found that majority of co-infections were reported in people aged 25–34 followed by 35–44. Most of notified cases in Zambia are also in the range of 25–44 and there is a significant difference in TB prevalence between children (< 15 years) and adult (8).

Gender and age may affect the outcome of TB treatment, where male and a higher age may contribute to failure of the treatment (9). However, as reported by Lazarus et al. (2) there was no significant gender difference in the age distribution of co-infection in the 14 countries. Another major factor that contributes to failure of TB treatment is married patients (9).

In case of sputum smear examination, many persons in late stage of HIV infection with TB are sputum smear negative. HIV-infected persons are more likely to have disseminated and extra pulmonary TB than HIV-negative persons. HIV infection sometimes reduces the skin test response to tuberculin (10). A study by Nissapatorn et al. (6) found that the other characteristics of patients with pulmonary and extrapulmonary tuberculosis were not statistically different from each other. Nik Nor Ronaidi et al. (11) also found that smoker and diabetic patients were contributing to unsuccessful TB treatment.

Regarding clinical characteristics of TB, results of sputum microscopic examinations were more often positive in diabetic patients (12). Thus, diabetes mellitus has a negative effect on the outcome of TB treatment. In Kelantan, HIV-positive, non-intravenous drug users (IVDU) were more likely to become non-compliance compared to HIV patients who were IVDU while HIV-positive patients had higher compliance compared to HIV-negative patients (13). Previous studies were not much discussing on BCG scar, sputum smear, tuberculin test, and x-ray findings of the TB treatment success. However, the factors were found to have insignificant association with the TB treatment outcome in several studies (11, 13, 14). This study aimed to determine the prevalence of successful TB treatment and its association with socio-demographic and clinical characteristics among TB/HIV co-infection cases in North-East Malaysia.

Methods

A cross-sectional study was conducted by reviewing TB records from the hospitals and health clinics in all ten districts in Kelantan. All cases diagnosed with TB/HIV co-infection and registered to the Kelantan Health Department from 2003 up to 2012 were included in this study. Using PS software, it was estimated 1588 cases needed to achieve the objective of the study (15). The parameter for this estimation included a level of significance at 5%, a power 80%, proportion of unemployed who were success at 14% (16) and a success: failure ratio of 1:3. Simple random sampling was applied to achieve the sample size.

All selected cases were retrieved from the medical records system, known as TB Wallet at chest clinic at hospitals or health clinics. Socio-demographic, clinical characteristics and outcome of the patients were recorded into a data collection form. Treatment success refers to the patients who were cured and have completed TB treatment (4). Completed TB treatment was defined as any patient who had completed a TB regime based on the Clinical Practice Guidelines created by Malaysia Ministry of Health (4). Thus, all patients with cure or completed treatment outcomes were categorised as treatment success, while other outcomes which were treatment default, treatment failure and death were categorised as treatment failure.

Data were analysed using Statistical Package of Social Science (SPSS) version 20. A 95% confidence interval was used to describe the prevalence TB treatment success. Simple Logistic Regression and Multiple Logistic Regression

were applied to determine the associated factors that contributed to TB treatment success among TB/HIV co-infection in Kelantan. For the multiple logistic regression, the multicollinearity and interaction problem were checked. The goodness of fit of the model were assessed using four methods: Pearson chi-square goodness of fit test, Hosmer-Lemeshow goodness of fit test, a classification table, and the area under Receiver Operation Characteristic (ROC) curve.

This study was approved by the Universiti Sains Malaysia (USM) Human Research Ethics Committee and the Medical Research and Ethics Committee, Ministry of Health Malaysia.

Results

A total of 1510 TB/HIV co-infection cases were analysed. The mean (SD) age of all the cases involved in this study were 35.7 (7.98) years. Most of the patients were male (91.1%) (Table 1). Prevalence of successful TB treatment was 27.9% (95% CI: 25.2, 30.6). The majority of TB/HIV patients in Kelantan were single or widowed (67.1%) and 43.2% of the cases had a job. All potential variables that might be associated with TB treatment success among TB/HIV co-infection is displayed in Table 2. The simple logistic regression showed that male (OR: 0.488, 95% CI: 0.34, 0.70), not working (OR: 0.739, 95% CI: 0.59, 0.93), drug addict (OR: 0.778, 95% CI: 0.62, 0.98), and positive tuberculin test (OR: 2.537, 95% CI: 1.59, 4.04) were significantly associated to the successful treatment of TB among TB/HIV co-infection. Meanwhile, other variables, which were age, marital status, diabetic, alcoholic, steroid treatment, BCG scar, AFB sputum and X-ray findings were found to have an insignificant association with TB treatment success among TB/HIV co-infection in Kelantan.

After adjusting for confounding variables using the multiple logistic regression, gender and tuberculin test were found to be significantly associated to TB treatment success among TB/HIV co-infection in Kelantan (Table 3). Male patients were 58% less likely to have TB treatment success compared to female patients (OR: 0.42, 95% CI: (0.23, 0.75). Those with positive tuberculin test are 2.59 times more likely to have TB treatment success compared to those with a negative result (OR: 2.59, 95% CI: 1.62, 4.15).

Table 1. Socio-demographic and clinical characteristics of TB/HIV co-infection patients

Factors		*n*	(%)
Age*		35.7	(8.0)
Gender	Female	135	(8.9)
	Male	1375	(91.1)
Marital Status	Married	463	(32.9)
	Single/Widowed	946	(67.1)
Working Status	Working	652	(43.2)
	Not Working	858	(56.8)
Drug Abusers	No	632	(42.1)
	Yes	869	(57.9)
BCG Scar	No	73	(4.8)
	Yes	1308	(86.6)
AFB Sputum	Negative	500	(43.1)
	Positive	659	(56.9)
X-ray	No lesion	166	(13.4)
	Lesion	1074	(86.6)
Diabetic	No	1469	(97.3)
	Yes	31	(2.1)
Alcoholic	No	1252	(83.8)
	Yes	242	(16.2)
Steroid Treatment	No	1220	(81.4)
	Yes	279	(18.6)
Tuberculin Test	Negative	396	(81.1)
	Positive	92	(18.9)

*Mean (SD)

Table 2. Clinical characteristics of TB/HIV co-infection patients

Factors		*n*	(%)
Drug Abusers	No	632	(42.1)
	Yes	869	(57.9)
BCG Scar	No	73	(4.8)
	Yes	1308	(86.6)
AFB Sputum	Negative	500	(43.1)
	Positive	659	(56.9)
X-ray	No lesion	166	(13.4)
	Lesion	1074	(86.6)
Diabetic	No	1469	(97.3)
	Yes	31	(2.1)
Alcoholic	No	1252	(83.8)
	Yes	242	(16.2)
Steroid Treatment	No	1220	(81.4)
	Yes	279	(18.6)
Tuberculin Test	Negative	396	(81.1)
	Positive	92	(18.9)

Table 3. Logistic Regression of successful tuberculosis treatment among TB/HIV co-infection

Factors	n (%)		Simple Logistic Regression				Multiple Logistic Regression[a]			
	Treatment Success	Treatment Failure	b	Crude OR (95% CI)	Wald test	P-value	b	Adjusted OR (95% CI)	Wald test	P-value
Age*	36.83 (8.86)	35.62 (7.61)	0.006	1.01 (0.99,1.02)	0.64	0.424				
Gender										
Female	58 (43.0)	77 (57.0)	0	1	15.52	< 0.001	0	1	8.52	0.004
Male	364 (26.5)	1011 (73.5)	-0.72	0.49 (0.34,0.70)			-0.87	0.42 (0.23,0.75)		
Marital Status										
Married	144 (31.1)	319 (68.9)	0	1	2.91	0.088				
Single/Widowed	253 (26.7)	693 (73.3)	-0.21	0.81 (0.63,1.03)						
Working Status										
Working	205 (31.4)	447 (68.6)	0	1	6.91	0.009				
Not Working	217 (25.3)	641 (74.7)	-0.30	0.74 (0.59,0.93)						
Diabetic										
No	408 (27.8)	1061 (72.7)	0	1	1.78	0.183				
Yes	12 (38.7)	19 (61.3)	0.50	1.64 (0.79,3.42)						
Alcoholic										
No	347 (27.7)	905 (72.3)	0	1	0.23	0.630				
Yes	71 (29.3)	171 (70.7)	0.07	1.08 (0.80,1.46)						
Drug Abusers										
No	195 (30.9)	437 (69.1)	0	1	4.74	0.030				
Yes	225 (25.9)	644 (74.1)	-0.25	0.778 (0.62,0.98)						
Steroid Treatment										
No	357 (29.3)	863 (70.7)	0	1	2.50	0.114				
Yes	63 (22.6)	216 (77.4)	0.39	1.48 (0.91,2.40)						
BCG Scar										
No	25 (34.2)	48 (65.8)	0	1	1.66	0.198				
Yes	357 (27.3)	951 (72.7)	0.327	1.39 (0.84,2.28)						
Tuberculin Test										
Negative	101 (25.5)	295 (74.5)	0	1	15.34	< 0.001	0	1	15.68	< 0.001
Positive	43 (46.7)	49 (53.3)	0.931	2.54 (1.59,4.04)			0.950	2.59 (1.62,4.15)		

(continued on next page)

Table 3. (*Continued*)

Factors	n (%)		Simple Logistic Regression				Multiple Logistic Regression[a]			
	Treatment Success	Treatment Failure	b	Crude OR (95% CI)	Wald test	P-value	b	Adjusted OR (95% CI)	Wald test	P-value
AFB Sputum										
Negative	147 (29.4)	353 (70.6)	0	1						
Positive	190 (28.8)	469 (71.2)	-0.04	0.97 (0.75,1.24)	1.67	0.196				
X-ray										
No lesion	53 (31.9)	113 (68.1)	0	1						
Lesion	296 (27.6)	778 (72.4)	-0.23	0.79 (0.56,1.13)	1.67	0.196				

*Mean (SD)
[a] Forward LR Multiple Logistic Regression model was applied
Multicollinearity and interaction term were checked and not found
Hosmer-Lemeshow test, (P = 0.863), classification table (overall correctly classified percentage = 71.1%) and area under ROC curve (61.0%) were applied to check the model fitness

Discussion

This study has shown that being a male patient, not working and being a drug addict may decrease the chance of having TB treatment success, while having positive tuberculin test increasing the chance of having TB treatment success. However, after adjusting for other potential confounding variables, gender and tuberculin test were the only factors that found to be significantly associated with the TB treatment success among TB/HIV co-infection cases in Kelantan. Male patients were having higher prevalence of tuberculosis in Malaysia, as well as in Kelantan where majority of TB/HIV co-infection were male patients (6, 7). These findings may help explain why this study found male patients to have a lower chance as treatment success than female patients. Another study in Klang Valley, Malaysia also discovered there was a higher prevalence of TB among male patients, but female patients had higher treatment success (17).

A study in Malawi revealed being female patients of TB/HIV co-infection compared with male patients correlated with successful outcomes of TB treatment (18). Nevertheless, other study in Nigeria found that male patients of TB/HIV co-infection either in rural or urban areas, contributed to successful TB treatment compared to female patients (19). Moreover, in the previous studies conducted among TB patients, female patients were found to have higher contribution to the unsuccessful of TB treatment (11, 13).

A study conducted in Nepal showed, unemployment leads to a high risk of non-adherence to TB treatment (OR: 9.2). This supports the finding of this study, where those who are not working have a lower chance of treatment success (9). A study conducted in Malaysia was found that there was no significant association of occupation to poor compliance with anti-TB treatment (13). However, based on the results of same cross-sectional study, the unemployed had the highest level of poor compliance compared to those with an occupation.

Many studies reported that drug addicts were also found to contribute to the treatment failure. This finding is plausible since logically, drug addicts usually tend to be homeless, and not take care of their health, leading to late diagnosis and treatment default. However, in a study conducted in Kelantan by Naing et al. (13), non-IVDU were tended to be more compliant to TB treatment compared to IVDU. It was suggested that this happens due to special attention by clinician, and strong family support or close observation of prisoners or members of drug rehabilitation centres.

In this study, those with a positive tuberculin test had a higher chance of having treatment success compared to those with a negative tuberculin test. Those who had a tuberculin positive tuberculin test were assumed to have developed an immune response to the TB bacterium (18). Indication of an individual having a past or recent TB infection that was demonstrated by a positive tuberculin test, in starting TB preventive treatment early (21). On average, for treatment of latent TB infection for HIV-infected individuals with a positive tuberculin skin test, there was approximately 60 % protection for up to three years (22). Thus, having a positive tuberculin test should lead to treatment success, a conclusion in this study supports.

Conclusion

The findings of this study showed that factors associated with treatment success among TB/HIV co-infection cases in Kelantan North of Malaysia were gender and tuberculin test. Since male and patients with negative result of tuberculin test results have a higher risk of treatment failure among TB/HIV co-infection patients, this group should strictly focus on increased awareness is important for early diagnosis, compliance and successful TB treatment. However, the males that are a part of the unemployment and drug addict groups should also receive focus since they also have a higher chance of treatment failure.

Acknowledgements

Correspondence

Associate Professor Dr Sarimah Abdullah
MD (USM), MComMed (Epidemiology and
Biostatistics) (USM)
Unit of Biostatistics & Research Methodology,
School of Medical Sciences,
Health Campus Universiti Sains Malaysia,
16150 Kubang Kerian,
Kelantan, Malaysia.
Tel: +609 767 6829
Fax: +609 765 3370
Email: sarimah@usm.my

References

1. Yoon CM. TB, the diehard disease. The Star; July 29, 2010. Retrieved January 2, 2014, from http://www.thestar.com.my/story.aspx/?file=%2f2010%2f7%2f29%2flifeliving%2f6747410 2

2. Lazarus JV, Olsen M, Ditiu L, Matic S. Tuberculosis-HIV co-infection: policy and epidemiology in 25 countries in the WHO European region. *HIV Med.* 2008:**9(6)**:406–414. https://doi.org/10.1111/j.1468-1293.2008.00567.x

3. HIV Coinfections. AIDSinfo; 2012. Retrieved April 13, 2014, from http://aidsinfo.nih.gov/contentfiles/HIVCoinfections.pdf

4. Ministry of Health Malaysia. Clinical Practice Guidelines - Management of Tuberculosis (Third Edition). Malaysia: Malaysia Health Technology Assessment Section (MaHTAS); 2012. http://www.moh.gov.my/attachments/8612.pdf

5. World Health Organization. The Stop TB Strategy-Building on and enhancing DOTS to meet the TB-related Millennium Development Goals. World Health Organization; 2006. http://www.who.int/tb/publications/2006/stop_tb_strategy.pdf

6. Nissapatorn V, Kuppusamy I, Sim BL, Quek KF, Khairul Anuar A. Tuberculosis in HIV/AIDS patients: a Malaysian experience. *Southeast Asian J Trop Med Public Health.* 2005;**36(4)**:946–953.

7. Mohammad Z, Naing NN. Characteristics of HIV-infected tuberculosis patients in Kota Bharu Hospital, Kelantan from 1998 to 2001. *Southeast Asian J Trop Med Public Health.* 2004;**35(1)**:140–143.

8. Kapata N, Chanda-Kapata P, O'Grady J, Schwank S, Bates M, Mukonka, et al. Trends of Zambia's tuberculosis burden over the past two decades. *Trop Med Int Health.* 2011;**16(11)**:1404–1409. https://doi.org/10.1111/j.1365-3156.2011.02849.x

9. Mishra P, Hansen EH, Sabroe S, Kafle KK. Socio-economic status and adherence to tuberculosis treatment: a case-control study in a district of Nepal. *Int J Tuberc Lung Dis.* 2005;**9(10)**:1134–1139.

10. Maher D. Health care in-depth. Tuberculosis and HIV. *Afr Health.* 1996;**19(1)**:17–18.

11. 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. *Malays J of Public Health Medic.* 2011:**11(1)**; 6–15.

12. Alisjahbana B, Sahiratmadja E, Nelwan EJ, Purwa AM, Ahmad Y, Ottenhoff TH, van Crevel R. The effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis. *Clin Infect Dis.* 2007;**45(4)**:428–435. https://doi.org/10.1086/519841

13. Naing NN, D'Este C, Isa AR, Salleh R, Bakar N, Mahmod MR. Factors contributing to poor compliance with anti-TB treatment among tuberculosis patients. *Southeast Asian J Trop Med Public Health.* 2001;**32(2)**:369–382.

14. Balbay O, Annakkaya AN, Arbak P, Bilgin C, Erbas M. Which patients are able to adhere to tuberculosis treatment? A study in a rural area in the northwest part of Turkey. *J Infect Dis.* 2005;**58**:152–158.

15. Dupont WD, Plummer WD: PS power and sample size program available for free on the Internet. *Controlled Clin Trials.* 1997;**18**:274. https://doi.org/10.1016/S0197-2456(97)00074-3

16. Berhe G, Enquselassie F, Aseffa A. *BMC Public Health.* 2012;**23(12)**:537. https://doi.org/10.1186/1471-2458-12-537

17. Ismail I, Bulgiba A. Determinants of unsuccessful tuberculosis treatment outcomes in Malaysian HIV-infected patients. *Preventive Medicine.* 2013;**57**:S27–S30. doi.org/10.1016/j.ypmed

18. 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. https://doi.org/10.1371/journal.pone.0056248

19. 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. *Tuberculosis Research and Treatment*. 2014;**2014**:8 p. https://doi.org/10.1155/2014/202983

20. NHS. Who should have the BCG (TB) vaccine? NHS. Retrieved April 29, 2014, from http://www.nhs.uk/Conditions/vaccinations/Pages/when-is-bcg-tb-vaccine-needed.aspx

21. World Health Organization European Region. Chapter 4 management of tuberculosis and HIV coinfection: clinical protocol for the WHO European region. Retrieved September 5, 2016, from https://www.google.com.my/url?sa=t&rct=j&q=&esrc=s&source=web&cd=3&cad=rja&uact=8&ved=0ahUKEwial4Om4PzOAhWIKY8KHd6HCMMQFggwMAI&url=http%3A%2F%2Fwww.euro.who.int%2F__data%2Fassets%2Fpdf_file%2F0004%2F78124%2FE90840_Chapter_4.pdf&usg=AFQjCNHOuLjyrAFcMMOcyCW3v1IPZmVWgg

22. Dye C, Floyd K. Disease control priorities in developing countries. In: Jamison DT, Breman JG, Measham AR et al., editors. *Chapter 16 Tuberculosis*. 2nd edition. Washington (DC): The International Bank for Reconstruction and Development/The World Bank; 2006. Retrieved September 5, 2016, from http://www.ncbi.nlm.nih.gov/books/NBK11724