Mortality Following Diagnosis of Tuberculosis in HIV-infected Patients in Asia

Awachana Jiamsakul¹, Evy Yuniastuti², Kinh Van Nguyen³, Tuti Parwati Merati⁴, Cuong Duy Do⁵, Rossana Ditangco⁶, Sasheela Ponnampalavanar⁷, Fujie Zhang⁸, Sasisopin Kiertiburanakul⁹, Man-Po Lee¹⁰, Anchalee Avihingasanon¹¹, Oon Tek NG¹², Benedict LH Sim¹³, Wingwai Wong¹⁴, Jeremy Ross¹⁵, and Matthew Law¹

¹The Kirby Institute, UNSW Sydney, NSW, Australia ²Working Group on AIDS, Faculty of Medicine, University of Indonesia/ Cipto Mangunkusumo Hospital, Jakarta, Indonesia ³National Hospital for Tropical Diseases, Hanoi, Vietnam ⁴Faculty of Medicine Udayana University & Sanglah Hospital, Bali, Indonesia ⁵Bach Mai Hospital, Hanoi, Vietnam ⁶Research Institute for Tropical Medicine, Manila, Philippines ⁷Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia ⁸Beijing Ditan Hospital, Capital Medical University, Beijing, China ⁹Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand ¹⁰Queen Elizabeth Hospital, Hong Kong, China ¹¹HIV-NAT, The Thai Red Cross AIDS Research Centre and Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand ¹²Department of Infectious Diseases, Tan Tock Seng Hospital, Singapore ¹³Hospital Sungai Buloh, Sungai Buloh, Malaysia ¹⁴Taipei Veterans General Hospital, Taipei, Taiwan ¹⁵TREAT Asia, amfAR – The Foundation for AIDS Research, Bangkok, Thailand

Keywords

TB; survival; Asia

To the Editor

Tuberculosis (TB) is highly prevalent in the Asia-Pacific region, accounting for 61% of estimated cases globally in 2015. To further expand on available data around TB co-infection and associated treatment outcomes in HIV-infected patients in Asia (1), we investigated survival outcomes in HIV-positive-TB co-infected patients.

HIV-positive-TB co-infected cases were selected from those who were recruited into the TREAT Asia's socio-economic determinants of TB in HIV-TB co-infected patients in Asia study (2). Survival time from TB diagnosis was plotted using the Kaplan-Meier (K-M) curve and analysed using Cox regression. Ethics approvals were obtained from the local ethics committees of all participating sites, the data management and biostatistical centre (UNSW

Sydney Ethics Committee), and the coordinating centre (TREAT Asia/amfAR). A written informed consent was obtained from the participants. All data management and statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA) and Stata software version 14.2 (Stata Corp., College Station, TX, USA).

A total of 146 TB-positive cases from China, Hong Kong SAR, Indonesia, Malaysia, the Philippines, Singapore, Taiwan, Thailand, and Vietnam were included. There were 20 deaths (14%). The median follow-up time from TB diagnosis was 238 days (IQR: 182-285). The overall mortality rate was 21.5 per 100 person-years (/100pys). The median age at enrolment was 33 years (IQR: 29-38) and the median CD4 cell count was 40.5 cells/ μ L (IQR: 13-87). There were 122 (84%) males.

The K-M curve (Figure 1) shows the survival probability dropping to 80% at one year from TB diagnosis. Factors associated with survival time in the univariate model were ART initiation ($p=0.014$), place of origin ($p=0.071$), employment status ($p=0.006$), and smoking history ($p=0.066$). In the multivariate model adjusting for ART, we found that patients in part-time or occasional employment had higher hazard for mortality compared to patients who were in full-time employment (HR=4.55, 95% CI (1.51-13.73), $p=0.010$). Those who had ceased smoking showed improved survival compared to those who were current smokers (HR=0.22, 95% CI (0.07-0.70), $p=0.010$).

The mortality rate in our study is considerably higher when compared to the mortality rates reported in previous studies from the same region, which ranged from 1.46/100pys to 3.77/100pys (1, 3). The large difference could be due to the short follow-up time, which is a limitation of our study. Other regions, however, have reported high short term mortality rates similar to our findings (4, 5).

Apart from employment status and smoking history, which are known risk factors for TB and poor TB treatment outcomes (5), we did not find a significant association between the available demographic or clinical characteristics and survival time.

In summary, mortality in HIV-positive TB co-infected patients enrolled in our study was high but comparable to rates reported across different regions. Patients should be closely monitored in the first year following TB diagnosis.

Acknowledgments

This study is an initiative of TREAT Asia, a program of amfAR, The Foundation for AIDS Research, with support from the U.S. National Institutes of Health's National Institute of Allergy and Infectious Diseases, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the National Cancer Institute, as part of the International Epidemiology Databases to Evaluate AIDS (IeDEA; U01AI069907). The Kirby Institute is funded by the Australian Government Department of Health and Ageing, and is affiliated with the Faculty of Medicine, UNSW Sydney. The content of this publication is solely the responsibility of the authors and does not necessarily represent the official views of any of the governments or institutions mentioned above.

TB socio-economic determinants study members: FJ Zhang, HX Zhao and N Han, Beijing Ditan Hospital, Capital Medical University, Beijing, China;

MP Lee, PCK Li, W Lam and YT Chan, Queen Elizabeth Hospital, Hong Kong, China;

TP Merati, DN Wirawan, F Yuliana and Y Gayatri, Faculty of Medicine Udayana University & Sanglah Hospital, Bali, Indonesia;

E Yunihastuti, D Imran, A Widhani, Wulunggono, and D Prahajna, Faculty of Medicine Universitas Indonesia - Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia;

A Kamarulzaman, SF Syed Omar, S Ponnampalavanar, I Azwa, A Kajindran, N Huda Ab Rahman, and A Raja Izam, Department of Medicine, University of Malaya, Kuala Lumpur, Malaysia;

BLH Sim, YM Gani, R David, A P Radhakrishnan, and H Chang, Hospital Sungai Buloh, Sungai Buloh, Malaysia;

R Ditangco, E Uy and R Bantique, Research Institute for Tropical Medicine, Muntinlupa City, Philippines;

OT Ng, PL Lim, LS Lee, PS Ohnmar, MT Tan and NA Zainuldin, Tan Tock Seng Hospital, Singapore;

WW Wong, WW Ku and PC Wu, Taipei Veterans General Hospital, Taipei, Taiwan;

S Kiertiburanakul, S Sungkanuparph, L Chumla and N Sanmeema, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand;

A Avihingsanon, S Gatechompol, P Phanuphak, C Phadungphon, P Thongpaeng, and Jaravee Jamthong, HIV-NAT/Thai Red Cross AIDS Research Centre, Bangkok, Thailand;

KV Nguyen, HV Bui, DTH Nguyen, DT Nguyen, MA Ha, and PT Dang, National Hospital for Tropical Diseases, Hanoi, Vietnam;

DD Cuong, NV An, NT Luan, TT Pham, and GH Nguyen, Bach Mai Hospital, Hanoi, Vietnam;

AH Sohn, JL Ross, N Durier and B Petersen, TREAT Asia, amfAR - The Foundation for AIDS Research, Bangkok, Thailand;

DA Cooper, MG Law, A Jiamsakul, DC Boettiger, and S Wright, The Kirby Institute, UNSW Sydney, Australia.

References

1. Han SH, Zhou J, Lee MP, et al. Prognostic significance of the interval between the initiation of antiretroviral therapy and the initiation of anti-tuberculosis treatment in HIV/tuberculosis-coinfected patients: results from the TREAT Asia HIV Observational Database. *HIV Med.* 2014; 15(2):77–85. [PubMed: 23980589]
2. Jiamsakul A, Lee MP, Nguyen KV, et al. Socio-economic Statuses and Risk of Tuberculosis – A Case-Control Study of HIV-infected Patients in Asia. *IJTL*. 2017 in press.
3. Zhou J, Elliott J, Li PC, et al. Risk and prognostic significance of tuberculosis in patients from The TREAT Asia HIV Observational Database. *BMC infectious diseases.* 2009; 9:46. [PubMed: 19383122]
4. da Silva Escada RO, Velasque L, Ribeiro SR, et al. Mortality in patients with HIV-1 and tuberculosis co-infection in Rio de Janeiro, Brazil - associated factors and causes of death. *BMC infectious diseases.* 2017; 17(1):373. [PubMed: 28558689]
5. Gesesew H, Tsehaine B, Massa D, Tesfay A, Kahsay H, Mwanri L. The role of social determinants on tuberculosis/HIV co-infection mortality in southwest Ethiopia: a retrospective cohort study. *BMC research notes.* 2016; 9:89. [PubMed: 26868489]

Figure 1. Survival time from TB diagnosis