Age is associated with latent tuberculosis in nurses

Naesinee Chaiear1, Janpen Bourpoern2, Kittisak Sawanyawisuth3,4,5, Kanlayanee Sawanyawisuth6, Panita Limparawattana7, Wipa Reechaipichitkal1,3

1Department of Community Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Isan, Thailand
2Infectious Control Unit, Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand
3Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
4Research Center in Back, Neck Other Joint Pain and Human Performance, Khon Kaen University, Khon Kaen, Thailand
5Non-communicable Diseases, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
6Department of Biochemistry, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
7The Research and Diagnostic Centre for Emerging Infectious Disease, Khon Kaen University, Khon Kaen, Thailand

Objective: To evaluate risk factors for developing latent tuberculosis (LTB) in Thai nurses.

Methods: A comparison study was conducted at Srinagarind Hospital, Khon Kaen, Thailand. Clinical factors were compared between persons with tuberculin conversion and those without tuberculin conversion identified by tuberculin skin test.

Results: There were 173 eligible persons with the LTB (34.7%). There were five workplaces where participants worked regularly including the general ward, surgical ward, pediatric ward, medical ward and critical care ward. In a multivariate model, two factors were significantly associated with LTB including age and history of tuberculosis in colleagues. The adjusted odds ratio (95% confidence interval) of both variables were 1.056 (1.004–1.104) and 0.202 (0.044–0.941).

Conclusions: Older age is associated with latent tuberculosis in nurses. LTB should be screened routinely and treated if diagnosed for nurses.

1. Introduction

Tuberculosis is still the public health problem particularly in the Southeast Asia area which accounted for 34% of total tuberculosis patients[1]. The World Health Organization also estimated that the prevalence of tuberculosis in Thailand was 163 patients per 100 000 population in 2008[1].

Latent tuberculosis (LTB) causes no symptom but it is associated with future tuberculosis[2]. Approximately 1.3% of LTB patients developed active tuberculosis within 4 years[2]. Tuberculosis occurs in most healthcare workers (HCW) due to recent infection or LT B rather than remote infection[2]. Treatment with either isoniazid or isoniazid-rifapentine is recommended by the Centers for Disease Control and Prevention to prevent further active tuberculosis[3].

LTB can be diagnosed by several methods such as the tuberculin skin test (TST). TST is cheap and has been used for a long time. It may, however, have issues with the accuracy of skin induration interpretation[4]. The interferon-gamma release assays (IGRAs) methods may be more sensitive and have less cross reactivity than TST but may have issues with cost, lack of data on future tuberculosis development and reversion of tests in healthcare workers[5]. All three tests are fairly concordant in several studies[6,7].

Prevalences of LTB varies among countries, co-morbid diseases and occupations. In the US army survey, the LTB rate was 1.3% out of 4 569 791 service members[8]. The rate in healthcare students in Italy was 3.3%, while it was 8.6% from a study conducted in Brazilian prisons[9,10]. HIV infected persons and HCW are at risk for having LTB. The prevalence of LTB in Thai HCW was 19.8%[11].

Diagnosis of LTB in HCW needs serial annual TSTs. A baseline TST may not represent LTB particularly in Thailand which is an endemic area for tuberculosis and universal bacille calmette guerin (BCG) vaccination. TST should be performed on HCWs annually.
If the consecutive TST becomes positive after being negative at baseline, LTB is established. The IGRAs method is not widely available in Thailand and other Asian countries due to high cost and unavailability.

Among several HCW, nurses and nursing assistants play important roles in tuberculosis care and are the most reported occupations to be at the highest risk for having LTB due to long contact times with tuberculosis patients. The adjusted odds ratios (OR) of having LTB in nurses from Turkey was 1.5 (1.29–1.66). The report from Thailand also showed that nurses had adjusted OR for LTB of 2.3 (1.3–4.1) compared to office workers. Several factors such as age or household contact have been shown to be related with LTB. Risk factors of LTB in nurses, particularly in Thailand, an endemic area of tuberculosis, are limited.

This study aimed to evaluate risk factors for developing LTB in Thai nurses. The results may be used to develop guidelines to identify nurses at risk for LTB in Thai or Asian population where tuberculosis is as endemic as in Thailand. The specific aims of this study are to study the prevalence of LTB among nurses and to identify predictors of LTB among nurses in the endemic area of tuberculosis.

2. Materials and methods

2.1. Study design

A comparison study was done at Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand, between nurses with tuberculin conversion and those who had negative results of TST in 2 consecutive years.

2.2. Study population

Nurses and nursing assistants who had results of TST within 2 consecutive years were recruited. Persons were excluded if they had any of these items including a history of recent or active tuberculosis, an abnormal chest X-ray, a history of diabetes mellitus, HIV infection, or had received any immunosuppressive therapy. The study population was a part of the previous study. Persons who worked in outpatient settings were excluded due to less contact time with the patients.

Participants with tuberculin conversion were compared with those who had negative results of TST in 2 consecutive years. Tuberculin conversion was defined if a person had a negative baseline TST on the first year and a positive TST in the next consecutive years. TST procedures were described elsewhere.

2.3. Data analysis

Baseline and clinical characteristics of those with and without tuberculin conversion were compared using descriptive statistics. Logistic regression analyses were executed to predict the development of LTB. All data analyses were performed with SAS software version 8.2.

3. Results

There were 213 persons who met the study criteria, among which 40 persons were excluded due to an outpatient working location. In total, 173 persons were included in the analysis, of which 60 persons (34.7%) had tuberculin conversion and were designated as the case group.

The baseline characteristics and variables related to tuberculosis of the case and control groups were presented in Table 1. The case group was characterized by being of an older age, which had more male participants, a longer duration of employment, more persons with BCG scars, more histories of tuberculosis in family members, tuberculosis exposure in the past year, of prevention by any methods and of using surgical masks.

Table 1

| Variables                          | No conversion (n = 113, %) | Conversion (n = 60, %) | P      |
|-----------------------------------|---------------------------|------------------------|--------|
| Median age (range) (years)        | 31.5 (19–50)              | 38 (23–57)             | 0.089  |
| Female gender                     | 109 (96.5)                | 54 (90.0)              | 0.097  |
| Median duration of employment (years) | 8 (2–25)               | 13.5 (2–25)            | 0.206  |
| Location                          |                           |                        |        |
| General ward                      | 19 (16.8)                 | 16 (26.7)              |        |
| Surgery                           | 18 (15.9)                 | 8 (13.3)               |        |
| Pediatric                         | 16 (14.2)                 | 7 (11.7)               |        |
| Medicine                          | 13 (11.5)                 | 10 (16.7)              |        |
| CCU                               | 47 (41.6)                 | 19 (31.7)              |        |
| Tuberculosis related variables    |                           |                        |        |
| History of tuberculosis in family | 9 (8.0)                   | 6 (10.2)               | 0.627  |
| History of tuberculosis in colleagues | 15 (13.3)               | 2 (3.4)                | 0.039  |
| History tuberculosis exposure in the past year | 63 (55.8) | 38 (64.4)            | 0.274  |
| Prevention related variables      |                           |                        |        |
| History of prevention by any methods | 88 (77.9)               | 49 (83.1)              | 0.424  |
| History of using surgical mask use | 99 (87.6)               | 54 (90.0)              | 0.640  |
| History of using N95 mask         | 10 (40.0)                 | 7 (33.3)               | 0.641  |
| History of using high efficiency particulate air mask | 0 (0.0)           | 1 (20.0)               | 1.000  |
| Use of surgical mask at all times | 47 (51.1)                 | 28 (57.1)              | 0.493  |

Data for no conversion and conversion groups may not be total of 113 and 60 persons, respectively due to missing data in individuals.

In a multivariate model that included all significant variables at the univariate level (Table 1), the only two significant factors for tuberculin conversion were age and history of tuberculosis in colleagues (Table 2). The adjusted ORs [95% confidence interval (CI)] of both variables were 1.056 (1.004–1.104) and 0.202 (0.044–0.941).

Table 2

| Variables                          | ORs (95% CI) | Adjusted ORs (95% CI) |
|-----------------------------------|-------------|-----------------------|
| Age                               | 1.053 (1.004–1.104) | 1.056 (1.004–1.104) |
| History of tuberculosis in colleagues | 0.229 (0.051–1.039) | 0.202 (0.044–0.941) |

Results of univariate and multivariate regression analyses showed independent variables, their crude ORs and adjusted ORs with 95% CI for being TST conversion.

4. Discussion

The LTB prevalence in HCW is varied among countries and can be high as 79%.[16] In the previous Thai report, it showed the overall LTB rate in HCW was 19.3%.[11] This study showed the LTB rate in nurses who worked at patient wards was 34.7%, while the LTB rates in nurses in Brazil, Saudi Arabia, and Germany were 54.5%, 12.9%, and 9.7%.[17–19].

Some work locations such as medicine or the emergency department are reported to be at a higher risk for tuberculosis.[16] In this current study, working in medicine wards had higher numbers...
of participants with tuberculin conversion (Table 1). It was not, however, statistically significant in multivariate analysis. In other words, working locations were not an independent factor for LTBI in nurses.

The only two significant factors for LTBI in nurses were age and a history of tuberculosis in colleagues (Table 2). The first one was a predictor and the latter one was a protector for LTBI. With an increase of age by one year, the chance of having LTBI will increase 5%. There were two studies also showing that older age was the important risk factor for LTBI. An age over 55 years increases risk of LTBI by 14.7 times in health care workers in Germany, while an age over 35 years had adjusted OR of 9.49 (2.22–40.50) for LTBI in a study from Malaysia[18,20]. A study from Taiwan found that age was associated with LTBI diagnosed by the IGRAs methods but not TST[21]. The study populations between these two studies were different. The study from Taiwan was more general and included HIV patients, but this study enrolled only nurses. The median age of those who had tuberculin conversion in this study was 38 years. If one has tuberculin conversion and is aged over 38 years, treatment for LTBI may be needed.

Having a history of tuberculosis in colleagues was found to be a protector for LTBI in nurses. The risk of LTBI decreases by 80% if any nurse had this history. The study from Malaysia showed that if HCW had close contact with active tuberculosis, the risk of LTBI increased 8.69 times[30]. If nurses had colleagues with tuberculosis, they may protect themselves more seriously or be more aware about tuberculosis to account for the apparent protective effect. As a result, a history of tuberculosis in colleagues was shown to be a protector in the analysis.

The main limitations of this study are the small study population and missing data. Further studies should be performed to evaluate the association between LTBI and future active tuberculosis in this study population.

Older age was positively associated with LTBI in nurses, while a history of tuberculosis in colleagues was negatively associated. TST should be performed routinely for nurses who work in the patient wards.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

The authors would like to thank Prof. James A Will for his kind manuscript English editing via Publication Clinic KKV, Thailand, the Thailand Research Fund (IRG 5780016), and the Thailand Research Fund Senior Research Scholar Grant from the Thailand Research Fund (Thailand Research Fund Grant No. RTA5880001) and the Higher Education Research Promotion and National Research University Project of Thailand, Office of the Higher Education Commission, Thailand, through the Health Cluster (SHeP-GMS), Khon Kaen University.

References

[1] Global tuberculosis control: key findings from the December 2009 WHO report. *Wkly Epidemiol Rec* 2010; 85: 69-80.

[2] Gounder PP, Harris TG, Anger H, Trieu L, Meissner JS, Cadwell BL, et al. Risk for tuberculosis disease among contacts with prior positive tuberculin skin test: a retrospective cohort study, New York City. *J Gen Intern Med* 2015; 30: 742-8.

[3] Centers for Disease Control and Prevention. Recommendations for use of an isoniazid- rifampicin regimen with direct observation to treat latent *Mycobacterium tuberculosis* infection. *MMWR Morb Mortal Wkly Rep* 2011; 60: 1650-3.

[4] Person AK, Pettit AC, Sterling TR. Diagnosis and treatment of latent tuberculosis infection: an update. *Curr Respir Care Rep* 2013; 2: 199-207.

[5] Park JS, Lee JS, Kim MY, Lee CH, Yoon HI, Lee SM, et al. Monthly follow-ups of interferon-γ release assays among health-care workers in contact with patients with TB. *Chest* 2012; 142: 1461-8.

[6] Lee SJ, Lee SH, Kim YE, Cho YJ, Jeong YY, Kim HC, et al. Risk factors for latent tuberculosis infection in close contacts of active tuberculosis patients in South Korea: a prospective cohort study. *BMC Infect Dis* 2014; 14: 566.

[7] Khawcharoenporn T, Apisarnthanarak A, Phetsuksiri B, Rudceaneksin J, Srisungnam S, Mundy LM. Tuberculin skin test and QuantiFERON-TB gold in-tube test for latent tuberculosis in Thai HIV-infected adults. *Respirology* 2015; 20: 340-7.

[8] Armed Forces Health Surveillance Center (AFHSC). Brief report: number of tuberculosis tests and diagnoses of latent tuberculosis infection in active component service members, U.S. Armed Forces, January 2004–December 2014. *MSMR* 2014; 21: 8-10.

[9] Semia S, Ortis M, Antoniotti Z, Palazzo C, Colamuesta V, D’Aguanno S, et al. [Latent tuberculosis infection: prevalence amongst healthcare students at the Sapienza University of Rome (Italy)]. *Ig Sanita Pubbl* 2014; 70: 393-400. Italian.

[10] Carbone Ada S, Païos DS, Sgarbi RV, Lenos EF, Cazanti RF, Ota MM, et al. Active and latent tuberculosis in Brazilian correctional facilities: a cross-sectional study. *BMC Infect Dis* 2015; 15: 24.

[11] Sawanyawisuth KS, Chaiar N, Sawanyawisuth KN, Limpawattana P, Bourgoën J, Rheeupichitkul W. Can job titles be predictors for recent onset latent tuberculosis in health care workers? *Asian Biomed* 2012; 6: 535-9.

[12] Jensen PA, Lambert LA, Iademarco MF, Ridzon R; CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR Recomm Rep* 2005; 54: 1-141.

[13] Mukasa JP, Glass N, Mntazaganian G. Ethnicity and patient satisfaction with tuberculosis care: a cross-sectional study. *Nurs Health Sci* 2015; 17: 395-401.

[14] Faccini M, Cantoni S, Ciconali G, Filipponi MT, Mainardi G, Marino AF, et al. Tuberculosis-related stigma leading to an incomplete contact investigation in a low-incidence country. *Epidemiol Infect* 2015; 143: 2841-8.

[15] Keskiner R, Ergönül O, Demiroglu Z, Zeren S, Baykam N, Dokuzoguz B. Risk of tuberculosis infection among healthcare workers in a tertiary-care hospital in Ankara, Turkey. * Infect Control Hosp Epidemiol* 2004; 25: 1067-71.

[16] Joshi R, Reingold AL, Menzies D, Pai M. Tuberculosis among health-care workers in low- and middle-income countries: a systematic review. *PLoS Med* 2006; 3: e394.

[17] Abbas MA, AlHamdan NA, Fiala LA, AlEnezy AK, AlQahtani MS. Prevalence of latent TB among healthcare workers in four major tertiary care hospitals in Riyadh, Saudi Arabia. *J Egypt Public Health Assoc* 2011; 36: 61-71.

[18] Schablon A, Harling M, Diehl R, Nienhaus A. Risk of latent TB infection in individuals employed in the healthcare sector in Germany: a multicentre prevalence study. *BMC Infect Dis* 2010; 10: 107.

[19] Severo KG, Oliveira Jda S, Carneiro M, Valim AR, Krumpenauer EC, Possuelo LG. Latent tuberculosis in nursing professionals of a Brazilian hospital. *J Occup Med Toxicol* 2011; 6: 15.

[20] Rafiza S, Rampal KG, Tahir A. Prevalence and risk factors of latent tuberculosis infection in health care personnel in Malaysia. *BMC Infect Dis* 2011; 11: 19.

[21] Lin WC, Lin HH, Lee SS, Sy CL, Wu KS, Chen JK, et al. Prevalence of latent tuberculosis infection in persons with and without human immunodeficiency virus infection using two interferon-gamma release assays and tuberculin skin test in a low human immunodeficiency virus prevalence, intermediate tuberculosis-burden country. *J Microbiol Immunol Infect* 2016; 49: 729-36.