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Occupational Risk of Latent Tuberculosis Infection in Health Workers of 14 Military Hospitals

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Tuberculosis (TB) is a known occupational risk to health workers. Identifying risk factors in health care settings is critical to the prevention of TB for health workers and patients. In 2014, we carried out a TB screening and survey for 902 health workers from 14 selected military hospitals to determine the prevalence rate of latent tuberculosis infection (LTBI) as well as occupational risk factors. Of all subjects, 19.5% reported having provided TB patient care for 1 year or more (176/902), and 26.9% (243/902) were positive for the tuberculin skin test (TST) (10 mm or more of induration). Additionally, 21.4% (52/243) of those who tested positive were also positive for the interferon-gamma release assay (IGRA). The proportion of LTBI in the study population was 5.8% (52/902). In a multivariate logistic regression analysis, providing TB patient care for one year or more was the only significant occupational risk factor (adjusted odds ratio [aOR], 2.27; 95% confidence interval [CI], 1.13–4.56). This study suggests that military health workers working with TB patients should be regularly examined by chest radiography, TST and IGRA to detect LTBI in the early stage and control nosocomial infection of TB.

Keywords: Military; Health Worker; Occupational Exposure; Latent Tuberculosis

INTRODUCTION

Tuberculosis (TB) causes a serious disease burden with an estimated 1.4 million deaths worldwide in 2015 (1). In Korea, more than 30,000 new TB cases are identified annually and the notification rate of new TB cases was 60.4 per 100,000 population in 2016 (2). According to the Korean mortality statistics, TB resulted in 2,209 deaths and was the leading cause of death from infectious diseases in 2015 (2,3). In 2013, the Ministry of Health and Welfare endorsed the National TB Control Scheme that aimed to halve the current incidence rate by 2020. The scheme seeks to achieve this goal through enhanced TB outbreak investigation, treatment of latent tuberculosis infection (LTBI), public-private collaboration to minimize treatment failure, the mandatory inpatient treatment of highly contagious TB patients, and the early identification of high-risk groups (4).

According to guidelines of the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), health workers providing care to TB patients are categorized as a high-risk group (5,6). The guidelines recommend implementing a national TB surveillance system, the evaluation of TB infection control measures in healthcare facilities, and implementing an annual TB screening program for health workers providing treatment for 3 or more TB patients per year.

Several Korean studies have sought to determine the occupational risks of TB in civilian health care settings (7-10). Laboratory technicians were found to be vulnerable to TB infection through exposure to contagious specimens from patients (7). Jo et al. (8) reported a 5-fold higher incidence rate of TB for nurses working in departments for TB patients than that of the general population.

The incidence rate of pulmonary TB in young soldiers in Korea was 63.1 per 100,000 population in 2004 (11), which is slightly less than that of the general population, 75.0 per 100,000 population (12). In providing treatments to conscripted and professional solders infected with TB, military health workers are often exposed to contagious TB patients through aerosols and other modes of transmission. Despite this, occupational risk factors of TB in military health care settings have not been thoroughly evaluated. In this study, we sought to measure the prevalence of LTBI in military health workers and identify occupational risk factors by a survey done in 14 selected military hospitals in 2014.

MATERIALS AND METHODS

Data collection

A cross-sectional study was undertaken for health workers in

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military hospitals from June to December 2014. The Ministry of National Defense currently operates 19 military hospitals nationwide to provide medical services primarily to active duty soldiers. While 5 military hospitals with limited clinical capabilities are commanded by the army, navy, and air force headquarters, 14 military hospitals are supervised by the Armed Forces Medical Command (AFMC), providing outpatient, inpatient, and emergency cares. Since AFMC hospitals are mainly providing treatments for infectious disease patients such as TB and other notifiable diseases, this study did not include the 5 hospitals under the 3 service headquarters.

Despite the official definition of military health worker only covering medical officers, nursing officers, and other paramedics holding specialized license (13), medics, who are qualified to provide basic health services, are generally expected to assist military health workers at health care facilities in peacetime or at the battlefield in wartime. This study thus included military health workers and medics for the screening and survey.

A total of 962 of the 14 chosen military hospitals finished the screening and survey of the study. However, 60 people were excluded based on past TB history and TB history of family members to identify the relationship of recent TB infection and occupational exposures. In the survey, we collected the following information from the subjects: sex, age, smoking history, alcohol intake, comorbidities at present, weight, height, profession, work duration, and work duration of TB patient care. After the study, we recommended subjects with LTBI to get proper management and treatments. Fig. 1 describes the study protocol.

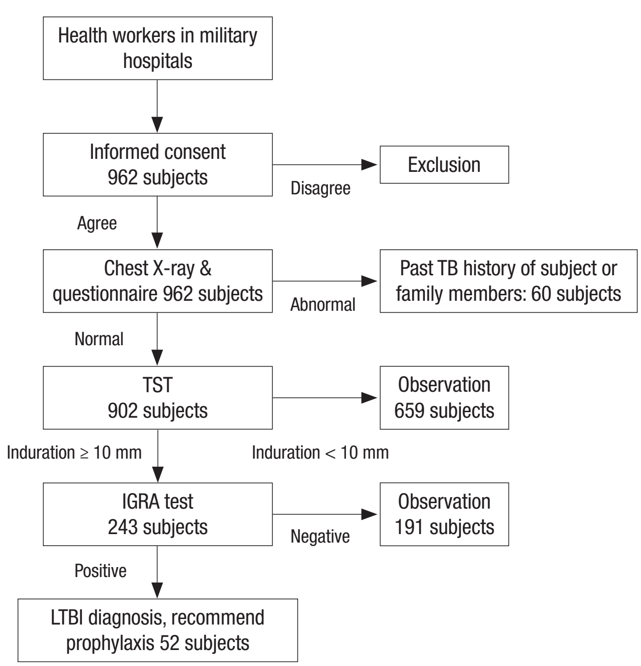

Fig. 1. Latent TB infection screening process of military health workers.
TB = tuberculosis, TST = tuberculin skin test, IGRA = interferon-gamma release assay, LTBI = latent tuberculosis infection.

Screening for the detection of LTBI cases

LTBI is defined as a state that shows a persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifested active TB (14). To measure the prevalence rate of the study population, we adopted a dual strategy of identifying LTBI cases for immunocompetent adults: the tuberculin skin test (TST) followed by the interferon-gamma release assay (IGRA). If a person showed a positive result in TST, IGRA followed to confirm the diagnosis as the latest guidelines recommend (15,16). In order to assess occupational risk, subjects with various occupations were enrolled: physicians, nurses, laboratory technicians, radiological technicians, and medics. All participants underwent chest radiography to exclude pulmonary TB or any diseases in the lung and TST to measure the sensitivity to *M. tuberculosis*.

The government of Korea has implemented the Bacillus Calmette-Guerin (BCG) vaccination in the National Immunization Program (NIP) from 1952 (17). We set a cut-off of 10 mm or more for the induration size after a tuberculin injection to exclude any reaction by previous immunization. In the test, 0.1 mL of purified protein derivative test reagent (PPD RT23 [2TU]; Statens Serum Institute, Copenhagen, Denmark) was injected into the intradermal skin of the left forearm of each subject. Seventy-two hours after injection, a TB specialist nurse measured the induration with a digital caliper to judge positivity. If a subject showed a positive reaction to TST, subsequent IGRA was performed to diagnose LTBI. In performing IGRA, staff of the Korean Institute of Tuberculosis drew 3 mL of blood from a vein of a TST positive subject. A commercial diagnostic tool, QuantiFERON-TB Gold in-tube blood test (QIAGEN, Hilden, Germany), which determines blood reaction to a specific antigen of *M. tuberculosis*, was applied to obtain the results. This diagnostic tool quantifies serum interferon-gamma (IFN-γ) secreted by effector T lymphocytes by enzyme-linked immunosorbent assay (ELISA). We set 0.35 IU/mL for a cutoff value that is recommended by CDC (18).

In order to identify occupational risks, we designed a structured survey that collected the following information: demographics, weight, height, smoking history, alcohol consumption history, occupation, work period in current position, work experience in TB-related departments, TB history, TB history of family members, comorbidities, and BCG vaccination history.

Statistical analysis

Data were analyzed using the statistical analysis system (SAS) statistical software package version 9.3 (SAS Institute, Cary, NC, USA). After performing a descriptive analysis using the χ^2 test, we performed multivariable logistic regressions to identify associations between LTBI and occupational factors. Statistical significance was set at $P < 0.05$, and 95% confidence intervals (CIs) were reported where appropriate.

Ethics statement

The protocol of this study was reviewed and approved by the Institutional Review Board of the Korean Institute of Tuberculosis (2014-KIT-IRB-01). Written informed consents were provided by all participants.

RESULTS

A total of 962 health workers from the 14 military hospitals participated in the study. No active TB was identified in the screening, and inactive TB lung lesions were found in 21 subjects. No one reported TB symptoms at the moment of the screening. We underwent TST and IGRA to identify LTBI cases and collected completed questionnaires from 902 subjects (Table 1). The mean age of participants was 24.4 ± 5.6 (men: 23.1 ± 4.6; women: 28.5 ± 6.5), and 75.7% (683/902) of subjects were men. A third (33.8%) of all subjects reported having provided TB patient care and 19.5% of all subjects had been involved in the care for one year or more in the past.

Positive TST results were found in 26.9% of all subjects and positive IGRA results were identified in 21.4% of positive TST subjects (Table 2). Overall, the proportion of those who were diagnosed as LTBI in the study group was 5.8% (52/902). Old age, comorbidity, a higher number of BCG scars, and having provided TB patient care were found to be associated with LTBI in the univariate analysis. In the multivariate analysis, controlling for demographic and health-related variables (Table 3), work experience in TB-related departments for 1 year or more was

Table 1. General characteristics of study participants

Characteristic	Total (n = 902)		Male (n = 683)		Female (n = 219)		*P* value
	No.	%	No.	%	No.	%	
Demographics							
Age, yr							< 0.001
Mean ± SD	24.4 ± 5.6		23.1 ± 4.6		28.5 ± 6.5		
19–29	756	83.8	601	87.9	155	70.8	
30–39	118	13.1	73	10.7	45	20.6	
≥ 40	28	3.1	9	1.3	19	8.7	
Health related factors							
Smoking							< 0.001
Never	604	67.0	388	56.8	216	98.6	
Past-smoker	61	6.8	59	8.6	2	0.9	
Smoker	237	26.3	236	34.6	1	0.5	
Alcohol intake							< 0.001
No/quit alcohol drinking	498	55.2	401	58.7	97	44.3	
Yes	404	44.8	282	41.3	122	55.7	
Comorbidities							0.802
No	888	98.5	672	98.4	216	98.6	
Yes	14	1.6	11	1.6	3	1.4	
BCG scar							< 0.001
None	260	28.8	210	30.8	50	22.8	
1	602	66.7	454	66.5	148	67.6	
> 2	40	4.4	19	2.8	21	9.6	
BMI							< 0.001
< 18.5	35	3.9	15	2.2	20	9.1	
18.5–25.0	748	82.9	556	81.4	192	87.7	
≥ 25.0	119	13.2	112	16.4	7	3.2	
Occupational factors							
Position							< 0.001
Physician	65	7.2	64	9.4	1	0.5	
Nurse	242	26.8	41	6.0	201	91.8	
Radiologic technician	29	3.2	23	3.3	6	2.7	
Laboratory technician	19	2.1	8	1.2	11	5.0	
Medic	547	80.1	547	80.1	0	0	
Work period in current position, yr							< 0.001
≤ 1	719	79.7	633	92.7	86	39.3	
< 3	84	9.3	31	4.5	53	24.2	
> 3	99	11.0	19	2.8	80	36.5	
Work experience in TB-related departments, yr							< 0.001
No	597	66.2	510	74.7	87	39.7	
Yes, < 1	129	14.3	85	12.5	44	20.1	
Yes, ≥ 1	176	19.5	88	12.9	88	40.2	

SD = standard deviation, BCG = Bacillus Calmette-Guerin, BMI = body mass index, TB = tuberculosis.

Table 2. Result of LTBI test and related factors

Characteristic	TST			IGRA		
	No./total	%	*P* value	No./total*	%	*P* value
Demographics						
Sex			0.014			0.249
Male	170/683	24.9		33/170	19.4	
Female	73/219	33.3		19/73	26.0	
Age, yr			< 0.001			0.216
19–29	169/756	22.4		36/169	21.3	
30–39	58/118	49.2		10/58	17.2	
≥ 40	16/28	57.1		6/16	37.5	
Health related factors						
Smoking			0.506			0.629
Never	169/604	27.9		39/169	23.1	
Past-smoker	17/61	27.9		3/17	17.7	
Smoker	57/237	24.1		10/57	17.5	
Alcohol intake			0.004			0.903
No/quit alcohol drinking	115/498	23.1		25/115	21.7	
Yes	128/404	31.7		27/128	21.1	
Comorbidities			0.639			0.612
No	240/888	27.0		51/240	21.3	
Yes	3/14	21.4		1/3	33.3	
BCG scar			< 0.001			0.016
None	47/260	18.1		15/47	31.9	
1	170/602	28.2		28/170	16.5	
> 2	26/40	65.0		9/26	34.6	
BMI			0.049			0.317
< 18.5	8/35	22.9		0/8	0	
18.5–25.0	192/748	25.7		43/192	22.4	
≥ 25.0	43/119	36.1		9/43	20.9	
Occupational factors						
Position			< 0.001			0.808
Physician	29/65	44.6		4/29	13.8	
Nurse	81/242	33.5		18/81	22.2	
Radiologic technician	16/29	55.2		3/16	18.8	
Laboratory technician	10/19	52.6		7/10	30.0	
Medic	107/547	19.6		24/107	22.4	
Work period in current position, yr			< 0.001			0.599
≤ 1	169/719	23.5		34/169	20.1	
< 3	28/84	33.3		8/28	28.6	
> 3	46/99	46.5		10/46	21.7	
Work experience in TB-related departments, yr			0.053			0.024
No	156/597	26.1		28/156	18.0	
Yes, < 1	28/129	21.7		4/28	14.3	
Yes, ≥ 1	59/176	33.5		20/59	33.9	
Total	243/902	26.9		52/243	21.4	

LTBI = latent tuberculosis infection, TST = tuberculin skin test, IGRA = interferon-gamma release assay, BCG = Bacillus Calmette-Guerin, BMI = body mass index, TB = tuberculosis.

Table 3. Result of multivariate logistic analysis

Duration of TB patient care, yr	Model I		Model II		Model III	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
No	Reference	-	Reference	-	Reference	-
< 1	0.72	0.24–2.14	0.76	0.25–2.28	0.78	0.26–2.36
≥ 1	2.38*	1.25–4.55	2.36*	1.23–4.55	2.27*	1.13–4.56

Model I: adjusted for sex and age; Model II: model I + adjusted for smoking, alcohol intake, comorbidities, number of BCG scars, and BMI; Model III: model II + adjusted for job position and duration of current position.
TB = tuberculosis, aOR = adjusted odds ratio, CI = confidence interval, BCG = Bacillus Calmette-Guerin, BMI = body mass index.
*$P < 0.050$.

the only factor significantly associated with LTBI (adjusted odds ratio [aOR], 2.27; 95% CI, 1.13–4.56). The associations between LTBI and other occupational factors such as occupation and duration of employment were not significant.

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DISCUSSION

This study sought to identify LTBI cases in military health workers with TST and IGRA. A third of subjects reported work experience in TB-related departments. We conducted IGRA for subjects with positive TST results to exclude false-positive cases that had been vaccinated for BCG in the NIP. Positive TST results were identified in 26.9% (243/902) of subjects by a cut-off of 10 mm diameter skin duration. Of the subjects with positive TST results, positive IGRA results were found in 21.4% (52/243). We applied IGRA only to subjects with positive TST results, considering cost effectiveness of the test since high negative results are expected from TST negative reactors.

According to the study protocol, the prevalence of LTBI in the study population was 5.8%. An occupational risk, having been in TB patient care for one year or more, was significantly associated with LTBI, controlling for demographic and health-related variables in the multivariate analysis. This result emphasizes the importance of annual LTBI screenings as a certain portion of health workers are always exposed to TB patients in the practice. The guidelines for TB control in the health facility developed by Korea Centers for Disease Control and Prevention (KCDC) recommend that every health worker in health facilities should be examined by chest radiography annually to detect active lung lesion of TB (15,16,19). However, this study suggests the application of TST and IGRA to identify health workers who might be infected with TB during the practice. This provides a chance of treating LTBI in the early stage before the disease would develop to the active form.

Nosocomial TB infection has been a concerning issue in both hospital infection control and public health (20,21). As TB can be transmitted via aerosolized droplet nuclei from infectious TB patients and the diagnosis for the disease may require invasive and non-invasive examinations, TB can spread to other patients and health workers in outpatient and inpatient settings. After developed countries recognized TB as an occupational hazard since the 1950s, effective control measures were introduced to reduce the risk of TB infection in healthcare settings (6).

In Korea, a country with an intermediate TB burden, TB infection in health workers has been a serious issue in occupational health. Chung et al. (22) reviewed annual occupational safety and health reports to determine common occupational infections that had occurred in employees. From 2000 to 2007, *M. tuberculosis* was the most common infectious disease in compensation claims. Several studies were conducted to identify specific occupations being involved with increased risk of TB infection in hospitals. Jo et al. (8) analyzed medical records of health workers in a tertiary hospital to investigate TB incidence, using prevalence ratios adjusted by age and sex, compared with that of general population. The prevalence ratio was 3.4 (95% CI, 1.52–8.25) for nurses working in TB-related departments. However, those who work in non-TB-related departments did not show a significant difference with that of the general population. Lee et al. (23) followed up 196 newly employed nurses in a teaching hospital, using TST and IGRA to screen for LTBI. It showed that the nurses were exposed to 3% of the annual risk of TB infection. A study involving 173 laboratory personnel in a tertiary hospital demonstrated significant associations between working in microbiology sections and positivity in IGRA (7). Park et al. (9) also presented that 3.3–5.7 of the 244 health workers who were IGRA negative upon recruitment were infected after the first year of employment, depending on department. In a study by Kim et al. (10), the proportion of positive IGRA in a high-exposure group in a general hospital was 1.2 times higher than that of a low-exposure group.

A number of limitations should be noted. Firstly, as we applied the dual strategy, TST followed by IGRA, we could not conclude the proportion of only IGRA positive cases with TST negative results in all subjects. Nonetheless, it may have little influence on identifying occupational risks of LTBI as TST negative but IGRA positive cases are expected to be few. Secondly, we used self-reported information to exclude subjects with past TB history and TB history of family members. This was done to identify only LTBI cases infected during professional practice. However, it might have created a recall bias that systematically influenced the response. Thirdly, BCG vaccination and nontuberculous mycobacterium infection may increase the number of TST positive cases that are false-positive (24). As the vaccination has been implemented since 1948, the government of Korea has tried to maintain a high vaccination coverage rate to prevent TB infection in general population (25). With regard to the effect of the vaccination, we examined BCG scars on their arms, revealing that 71.1% of all subjects had been vaccinated in their lifetime. BCG revaccination policy for year one students in elementary school with no scar had been in effect until 2008 (4). In addition, a revaccination policy for year 6 children with negative TST results had been implemented until 1996 (25-27). To minimize false-positive results in TST, we set 10 mm of cut-off to judge the positivity, considering high BCG immunization rate. In this regard, the application of IGRA helps to minimize the number of false-positives. Farhat et al. (28) reported only 1% difference between unvaccinated subjects and subjects who had been vaccinated 10 years earlier as infants younger than 1 year old. A study of Korean elementary school students found no significant difference in TST prevalence between subjects with BCG scars and those without (26). Thus, those support that this study identified the prevalence of LTBI in the study population with rare false-positive cases.

In conclusion, we examined the LTBI prevalence in military health workers working in 14 military hospitals and occupation risk factors significantly associated with LTBI in the hospital settings. Of the 902 subjects, 26.9% (243/902) were positive for the TST, and the proportion of LTBI in the study population was 5.8% (52/902). We demonstrated that providing TB patient care for 1 year or more was the only statistically significant risk of LTBI in the multivariate analysis. This result calls for policy makers to implement a regular TB screening program including TST and IGRA to provide immediate chemoprophylaxis treatments for health workers when they are found to be exposed to contagious TB patients in workplaces.

DISCLOSURE

The authors have no potential conflicts of interest todisclose.

AUTHOR CONTRIBUTION

Conceptualization: Yoon CG, Oh SY, Yang J, Bae KJ, Yang ES, Kim HJ. Investigation: Yoon CG, Oh SY, Yang J, Bae KJ, Yang ES, Kim HJ. Formal analysis: Yoon CG, Oh SY, Lee JB, Kim MH, Seo Y, Bae KJ, Hong S, Kim HJ. Visualization: Yoon CG, Oh SY, Lee JB, Kim MH, Seo Y, Bae KJ, Hong S, Kim HJ. Writing - original draft: Yoon CG, Kim HJ.

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