Original Article

Agreement of Tuberculin Skin Test and QuantiFERON®-TB Gold-In-Tube for Screening *Mycobacterium tuberculosis* Infection in Healthcare Workers in a University Hospital

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Background: Healthcare workers (HCWs) have a high occupational risk for tuberculosis (TB) infection. Common methods of screening for TB infection are the tuberculin skin test (TST) and interferon-gamma release assays (IGRAs).

Objective: The aim of this study was to investigate the agreement of TST and IGRA (QuantiFERON®-TB Gold-In-Tube; QFT-GIT) as applied to HCWs at a large university hospital in northeast of Thailand.

Materials and Methods: The study population included the preplacement medical records of new employees who were tested with both TST and QFT-GIT, comprising 212 HCWs. Eligible for data analysis were 197 participants (calculated sample size was 196). SPSS version19.0 was used to analyze Cohen's kappa coefficient.

Results: The samples included 197 HCWs: 63 males (32.0%), 134 females (68.0%), 133 physicians (67.5%) and 64 nurses (32.5%). The mean age was 25.6 years (SD = 3.12). Thirty-eight workers (19.3%) tested positive in the TST and 19 workers (9.6%) were QFT-GIT-positive. The total agreement of TST and QFT-GIT was 88.3 (K = 0.54). Forty workers (20.3%) were positive in at least one test.

Conclusion: This study showed moderate agreement of TST and QFT-GIT, which was consistent with the previous studies in high tuberculosis-burden countries (TBC). The authors suggest that pre-placement HCWs in Thailand should be screened for TB infection using the QFT-GIT method.

Keywords: Tuberculin skin test, QuantiFERON, IGRA, Healthcare workers, Tuberculosis

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Tuberculosis (TB) is a chronic disease caused by *Mycobacterium tuberculosis* that can be transmitted from one person to another. In patients with an active TB infection (ATBI), a cough expels airborne particles, diffusing droplet nuclei into the air and aiding transmission. Among people who had contact with patients with mycobacterium TB, 50 to 70% were not infected and 20 to 50% had a latent TB infection (LTBI). The number of tuberculosis patients was estimated to be between 16 to 20 million people, which 8 to 10 million of whom were infectious[(1)]. In 2016, there were 10.4 million new cases of TB infection; 95% of them were in developing countries. During this year, about 1.3 million people died from tuberculosis and 98% of these deaths occurred in poor countries.

Thailand is one of 30 high-burden countries and one of 14 countries with severe tuberculosis. In 2016, it was predicted that the incidence rate in Thailand was 172 cases per 100,000 people and that the death rate was 13 cases per 100,000 people. According to reports from the Bureau of Tuberculosis, Department of Disease Control, and the Ministry of Public Health of Thailand, 30% of the population was infected with tuberculosis. There were 70,114 registered tuberculosis patients in 2016[(2)].

Healthcare workers (HCWs) as a group are at high risk of infection with TB and a source of transmission to others. Tuberculosis prevalence among HCWs in high-burden countries is about 8.4% (95% CI 2.7% to 14.0%), 3.7 times

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higher than in the general population[3,4]. In Thailand, the prevalence of tuberculosis infection among HCWs is about 53.1% according to the tuberculin skin test (TST), with abnormal chest radiographic pictures attributed to TB in 2.0% (2.67 times higher than in the general population)[5-9].

Screening HCWs and the public for TB infection is important for prevention and elimination of tuberculosis[10]. Screening test programs often use either of two methods: the tuberculin skin test (TST) and the QuantiFERON®-TB Gold-In-Tube (QFT-GIT) test. Previous studies have found the two methods to differ in sensitivity and specificity. In high-income countries with a low incidence of TB, the QFT-GIT test is preferred because of its high specificity for tuberculosis infection[11-17]. In Thailand, use of the QFT-GIT test is very limited because of cost. According to a previous study of infected members of the general population and their in-house contacts in Northeast of Thailand, the two tests were found to agree in 71.5% of cases (k = 0.41)[12]. However, there has been no previous study of HCWs, especially in the pre-placement phase and during work-related health checks. Therefore, the purpose of this study is to examine the agreement of TST and QFT-GIT tests in TB screening for HCWs.

The results from the TST screening method can be affected by various factors: BCG vaccination history, *non-TB mycobacterium* infection and incorrect result interpretation (technical error). Moreover, it is more time consumption. In the TST screening method, the test results have to be read within 48-72 hours. Moreover, the test must be conducted using a two-step process, where the first and second tests have to be 3-5 weeks apart. This causes a loss of follow-up compared to TB screening using QFT-GIT. Additionally, the method of QFT-GIT does not cause a cross-reaction between BCG and most non-tuberculous mycobacteria (NTM), and it requires only a one-time blood test to interpret the results. The respective sensitivities of TST and QFT-GIT are 89% and 83%. Specificity of TST and QFT-GIT are 85% and 99%, respectively[15]. Despite the TST method's higher sensitivity, it has a lower specificity than QFT-GIT. Therefore, the results of this study can be used to evaluate whether TB screening in Thailand should now use the QFT-GIT test instead of the TST.

Materials and Methods

Study design

A descriptive study was conducted among healthcare workers at a large university hospital in northeast of Thailand.

Study population and sample

The required sample size was calculated using the minimum sample size determination for Cohen's kappa coefficient by the Stata Program. Judgements of the kappa estimate were performed[18]. The kappa value was set at 0.7 (kappa = 0.61 to 0.8, which is within a 'good' range). Proportions P1 and P2 were assigned as equal to 0.5; absolute precision was equal to 1.0 and 95% CI. The calculated sample population was 196.

The target population included the preplacement medical records of new employees who were tested with both TST and QFT-GIT methods, comprising a total of 217 HCWs. Normally routine method for screening in Thailand is TST but special for this group used both methods. Exclusion criteria were used for participants who had HIV Infection, chronic liver disease, chronic kidney disease, steroid drugs used and active TB infection. Those who were unwilling to disclose their information were also excluded. A total of 197 participants was selected on the basis of the time allocation technique.

Data collection

In the TST method, a standard quantity (Thai Red Cross Society) of purified protein derivative (PPD) was injected using 0.1 ml on the inside arm by a professional nurse. The test results were read within 48 to 72 hours, using a standardized ruler by the same nurse. The cut-off value for the size of the induration produced by the TST was 10 mm. In the case of a negative result in the first test, a second test was conducted 3-5 weeks later.

Blood samples from HCWs to be used for the QFT-GIT test were stored at room temperature and transported to the laboratory within a maximum of 8 hours. A method to measure interferon-gamma induced by MTB-specific antigens (TB antigen) was used following the instructions of the manufacturer. One milliliter of whole blood was collected separately in each heparin-containing tube pre-coated with nil for negative control, mitogen for positive control, and TB antigen. After an 18-hour incubation at 37°C, each tube was centrifuged and plasma was harvested. The concentration of interferon-gamma in the plasma was measured using the ELISA method and calculated using analytical software recommended by the manufacturer. The cut-off value of interferon-gamma concentration was 0.35 IU/mL calculated from TB antigen minus the negative control. Based on the algorithm of the software, the result was considered to be indeterminate if mitogen minus the nil value was less than 0.5 IU/mL. Quality control of the test was completed for each run, following the manufacturer's instructions. The results were considered positive if the IFN-γ value was ≥0.35 IU/mL following correction for negative controls in any of the two tests[15].

Data analysis

Statistical analysis was performed using SPSS (version 19.0, IMB SPSS Inc., Chicago, IL) for multiple-variable analysis. The statistic used to determine the consistency of the TST and QFT-GIT tests was Cohen's kappa (k) coefficient by STATA version 10.0 (Stata Corp., College Station, KKU). The consistency of TST and QFT-GIT tests using the agreement with k was calculated. The k value was set from 0 to 1.

Ethical considerations

The study protocol has been reviewed and

approved by the Khon Kaen University Ethics Committee for Human Research) Thailand (HE 601127).

Results

Characteristics of the participants

The sample size (n = 197) consisted of 63 males (32.0%) and 134 females (68.0%). There were 133 physicians (67.5%) and 64 nurses (32.5%), with an average age of 25.6 years (SD = 3.12 years) and a median age of 24 years (min to max; 21 to 39 years). One-hundred and eighty-one individuals (91.9%) had received BCG vaccinations previously and 4.6% did not know their BCG vaccination status. Most (194; 98.5%) had no history of household contact with tuberculosis. However, there was a high risk of history of work-related illness in 182 workers (92.4%); high risk for work-related were who worked in some hospital with tuberculosis patients more than 6 cases per year. Most 194 workers (98.5%) were not found to have symptoms related to tuberculosis (Table 1).

Results of TST and QFT-GIT

The TST tests were positive for 38 workers (19.3%). From this number, there were 24 workers whose TST test results were positive in the first test. Moreover, there were 14 more workers, whose TST test results were negative in the first test, but positive in the second test, accounting for a 37% increase. QFT-GIT tests were positive in 19 workers (9.6%). There were 40 individuals (20.3%) with a positive result for at least one test. These 40 workers were examined further as follows: sputum AFB was assessed in 32 workers (80.0%) and chest x-rays were used in 29 workers (72.5%). All received negative results and were therefore regarded as having LTBI (Table 1).

Out of 38 workers with a TST positive result, 17

Table 1. Characteristics of tested samples

Information	Total n (%)	TST		QFT	
		Negative n (%)	Positive n (%)	Negative n (%)	Positive n (%)
Occupation					
Doctors	133 (67.5)	108 (81.2)	25 (18.8)	118 (88.7)	15 (11.3)
Nurses	64 (32.5)	51 (79.7)	13 (20.3)	60 (93.7)	4 (6.3)
Gender					
Male	63 (32.0)	52 (82.5)	11 (17.5)	58 (92.0)	5 (8.0)
Female	134 (68.0)	107 (79.9)	27 (20.1)	120 (89.5)	14 (10.5)
Age (years)					
Average ± (SD)	25.6 ±(3.12)	25.4 ±(2.73)	26.6 ±(4.3)	25.5 ±(3.04)	26.8 ±(3.6)
Median (Min to Max)	24 (21 to 39)	24 (21 to 27)	25 (21 to 39)	24 (21 to 39)	25 (23 to 35)
Had received BCG vaccination					
Yes	181 (91.9)	146 (80.6)	35 (19.4)	163 (90.0)	18 (10.0)
No	7 (3.6)	6 (85.7)	1 (14.3)	7 (100)	0 (0)
Not known	9 (4.5)	7 (77.8)	2 (22.2)	8 (88.9)	1 (11.1)
History of TB contact in house					
Yes	3 (1.5)	3 (100)	0 (0)	3 (100)	0 (0)
No	194 (98.5)	156 (80.4)	38 (19.6)	175 (90.2)	19 (9.8)
History of work-related diseases					
Low	15 (7.6)	11 (73.3)	4 (26.7)	13 (86.7)	2 (13.3)
High	182 (92.4)	148 (81.3)	34 (18.7)	165 (90.6)	17 (9.4)
Current symptoms					
None	194 (98.5)	156 (79.2)	38 (19.3)	175 (88.8)	19 (9.6)
1 symptom	2 (1.0)	2 (1.0)	0 (0)	2 (1.0)	0 (0)
≥2 symptoms	1 (0.5)	1 (0.5)	0 (0)	1 (0.6)	0 (0)
Sputum AFB result					
Positive	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Negative	32 (16.2)	5 (2.5)	27 (13.7)	13 (6.6)	19 (9.6)
Not examined	165 (83.8)	154 (78.2)	11 (5.6)	165 (83.8)	0 (0)
Chest x-rays result					
Positive	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Negative	29 (14.7)	2 (1.0)	27 (13.7)	10 (5.1)	0 (0)
Not examined	168 (85.3)	157 (79.7)	11 (5.6)	168 (85.3)	19 (9.6)
Diagnosis					
Normal	157 (79.7)	157 (79.7)	0 (0)	157 (79.7)	0 (0)
LTBI	40 (20.3)	2 (1.0)	38 (19.3)	21 (10.7)	19 (9.6)
ATBI	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

workers were found QFT-GIT positive while 21 workers were found negative. There were 159 (80.7%) workers in total in the group with TST negative results. Of them, two workers were found positive while 157 other workers were found QFT-GIT negative. Evaluation of the agreement of TST (1 step) and QFT-GIT in 197 workers showed a 5.5% positive agreement between the types of tests and an 83.8% negative agreement. The total agreement was 89.3% with a kappa coefficient of 0.45 (95% CI: 0.25, 0.65) (Table 2). Evaluation of the agreement of TST (2 steps) and QFT-GIT in 197 workers showed an 8.6% positive agreement between the types of tests and a 79.7% negative agreement. The total agreement was 88.3% with k = 0.54 (95% CI: 0.38 to 0.70) (Table 3).

Discussion

The sample group consisted of 197 participants, a number sufficient for calculating agreement of the two methods of tuberculosis screening. The formula for computing the sample size for kappa was used, following the standard calculation. For the QFT-GIT test, the process of blood sampling was validated through venipuncture, types of centrifuge tubes, and the number of the tubes, centrifuge method and preservation before testing. The test was conducted by medical laboratory technologists in a laboratory of the university hospital which conformed to ISO standards (ISO 15189:2012).

For the TST, participants received the standard test dose (Thai Red Cross Society) of PPD. The PPD injected had not expired and had been kept cold. The injection was done by registered nurses who were trained by officers from a hospital tuberculosis screening unit. The results were read 48 to 72 hours later, according to standard practice. The participants were given 2-step TST with 3 to 5 weeks between the tests [17]. This study eradicated the possible effect from TST to QFT-GIT by blood drawing before PPD injected.

Table 2. Agreement between TST (1 step) and QFT-GIT tests

Test	Agreement (%)
TST+: QFT-GIT+	11 workers (5.5%)
TST+: QFT-GIT-	13 workers (6.6%)
TST-: QFT-GIT+	8 workers (4.1%)
TST-: QFT-GIT-	165 workers (83.8%)
Positive agreement	5.5%
Negative agreement	83.8%
Total agreement	89.3%
Kappa (95% CI)	0.45 (0.25, 0.65)

Table 3. Agreement between TST (2 steps) and QFT-GIT tests

Test	Agreement (%)
TST (2 steps)+: QFT-GIT+	17 workers (8.6%)
TST (2 steps)+: QFT-GIT-	21 workers (10.6%)
TST (2 steps)-: QFT-GIT+	2 workers (1.0%)
TST (2 steps)-: QFT-GIT-	157 workers (79.7%)
Positive agreement	8.6%
Negative agreement	79.7%
Total agreement	88.3%
Kappa (95% CI)	0.54 (0.37, 0.70)

This study was conducted to examine agreement of the TST and QFT-GIT tests in screening *Mycobacterium tuberculosis* infection in 197 new healthcare workers (HCWs) at a university hospital. Agreement between the two tests was moderate, with a kappa value of 0.54 (95% CI 0.38 to 0.70). This is consistent with a previous study in the same region of Thailand, which found a kappa value of 0.41. However, the previous result was obtained from a different sample group, which consisted of infectious-stage tuberculosis patients, their caregivers and co-residents[12]. Therefore, this is the first study in Thailand to compare the TST and QFT-GIT methods in screening for *Mycobacterium tuberculosis* infection in HCWs.

Our results of the present study were in accordance with other studies on HCWs in high-burden countries. Countries with the highest agreement values were India, Georgia, Vietnam, Brazil, South Korea and China: kappa values of 0.61, 0.43, 0.41, 0.31, 0.22 and 0.22, respectively[19-24]. Similar studies in intermediate-burden countries had kappa values of 0.19, while low-burden countries had kappa values of 0.25[25]. For example, the kappa values from Germany, Malaysia, Egypt and France were 0.27, 0.12, 0.11, and 0.10, respectively[26-29].

We found latent tuberculosis in 20.3% of our participants. This high percentage was consistent with other studies of LTBI in sample groups in Thailand (18.8%), tested using IGRA[30]. Similar results have also been reported from other countries, where the LTBI burden ranged from 26% to 54%[31,32]. In high tuberculosis burden countries, the highest prevalence of LTBI among HCWs were in Bangladesh (44%), China (41.4%), South Africa (38%) and India (31.4%), while the lowest was in Brazil (6.9%)[19,24,32-34]. In other low tuberculosis burden countries, prevalence of LTBI among HCWs were 8.85% in Poland, 12% in the Netherlands and 20.6% in Turkey[35-37]. Around 0.5% to 14.3% of individuals with latent tuberculosis will develop active tuberculosis in the future[31]. Consequently, the LTBI group needs to be screened regularly for TB.

We found 19.3% of our participants to be TST-positive and 9.6% to be QFT-GIT-positive. Chest x-ray and sputum AFB examinations were conducted for further diagnosis on these participants. However, active-stage tuberculosis was not detected in any member of this group. There are three interesting points to be made: first, false positives in the TST could occur in participants who had received BCG vaccinations[29,38]. According to studies in the United States of America, HCWs who had received BCG vaccination had a higher tendency to yield TST+/IGRA- results than those who had not received the vaccine, with a

high odds ratio of 25.1 (95% CI: 15.5, 40.5)[39]. In this study, 91.9% of the participants had a history of a BCG vaccination, which could explain the greater number of positive TST results. Second, the specificity of IGRA (98%) is higher than that of TST (55% to 95%)[26]. In Germany, TST+/QFT- results accounted for 80.4%, while TST+/QFT+ results were 19.6%. A TST+/QFT- result was 3.5 times more frequent than a TST+/QFT+ result (95% CI 2.4, 5.99)[40]. Lastly, other factors could affect the results, including techniques in screening, background history of tuberculosis infection or tuberculosis contact[19,41].

Among our participants, 19.3% returned a positive TST, which prompted further tuberculosis diagnostic tests (chest x-ray and sputum AFB examination). A smaller number of participants (9.6%) were positive for the QFT-GIT test, meaning that fewer individuals would require further testing. Studies conducted in Germany, which implemented *Mycobacterium tuberculosis* screening using IGRA and TST, found that accepting the results from IGRA could reduce the requirement for preventive chemotherapy and decrease the number of chest x-ray examinations from 24% to only 9.9%[41]. A similar result was reported from France, with a reduction from 65.5% to 18.9%[29]. Therefore, to reduce expenses in tuberculosis diagnosis, people who have reportedly received a BCG vaccine should be diagnosed using IGRA only[42].

Conclusion

The study showed moderate agreement between the TST and QFT-GIT methods, consistent with previous studies in high tuberculosis burden countries. The researchers suggest that HCWs in Thailand should be screened for TB using the QFT-GIT test during pre-placement programs.

What is already known on this topic?

WHO[17] recommended either IGRA or TST should be used to test for screening tuberculosis infection. In high-income countries with a low incidence of TB, the IGRA test is preferred because of its high specificity for tuberculosis infection[11-17]. In Thailand, use of the IGRA test is very limited because of cost. There has been no previous study of agreement of TST and IGRA in HCWs, especially in the pre-placement phase and during work-related health checks.

What this study adds?

This is the first study to investigate the agreement of TST and IGRA among HCWs in Thailand. Most of the Thai population has received a BCG vaccination. HCWs are at high risk of tuberculosis infection and are advised to be regularly screened for tuberculosis using the IGRA method, which is more suitable than the TST method.

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Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Kasetcharoen Y. Guidelines for tuberculosis control standards for tuberculosis clinic. Bangkok: Bureau of Tuberculosis; 2009.
2. World Health Organization. Global tuberculosis report 2017. Geneva: WHO; 2017.
3. Sepkowitz KA. Occupationally acquired infections in health care workers. Part I. Ann Intern Med 1996;125:826-34.
4. Baussano I, Nunn P, Williams B, Pivetta E, Bugiani M, Scano F. Tuberculosis among health care workers. Emerg Infect Dis 2011;17:488-94.
5. Sawanyawisuth K, Chaiear N, Sawanyawisuth K, Limpawattana P, Bourpoern J, Reechaipichitkul W, et al. Can workplaces be predictors for recent onset latent tuberculosis in health care workers? J Occup Med Toxicol 2009;4:20.
6. Phothirat C, Inchai C. Tuberculosis risk of healthcare workers for Maharaj Nakorn Chiang Mai Hospital [Internet]. 2005 [cited 2016 Jun 1]. Available from: http://www.boe.moph.go.th/boedb/surdata/index.php.
7. Apivanich S, Muntajit T, Malathum K. A tuberculosis surveillance program in healthcare workers at Ramathibodi Hospital. Rama Nurs J 2012;18:273-86.
8. Wiwanitkit V. Prevalence rate of active tuberculosis from chest radiography among Thai hospital personnel: a summary. Am J Infect Control 2005;33:313-4.
9. Wiwanitkit V. Prevalence rate of positive tuberculin test among Thai hospital personnel: a summary. J Hosp Infect 2006;62:119-20.
10. Dye C, Williams BG. Eliminating human tuberculosis in the twenty-first century. J R Soc Interface 2008;5:653-62.
11. Weinfurter P, Blumberg HM, Goldbaum G, Royce R, Pang J, Tapia J, et al. Predictors of discordant tuberculin skin test and QuantiFERON(R)-TB Gold In-Tube results in various high-risk groups. Int J Tuberc Lung Dis 2011;15:1056-61.
12. Reechaipichitkul W, Pimrin W, Bourpoern J, Prompinij S, Faksri K. Evaluation of the QuantiFERON®-TB Gold In-Tube assay and tuberculin skin test for the diagnosis of Mycobacterium tuberculosis infection in northeastern Thailand. Asian Pac J Allergy Immunol 2015;33:236-44.
13. Ketpanich A. Is it a time to replace tuberculin skin test? R Thai Army Med J 2006;59:165-78.
14. Rhode Island Department of Health. A guide for testing and treating latent tuberculosis infection (LTBI). Providence, RI: Rhode Island Department of Health; 2014.
15. Mazurek GH, Jereb J, Lobue P, Iademarco MF, Metchock B, Vernon A. Guidelines for using the

QuantiFERON-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. MMWR Recomm Rep 2005;54:49-55.
16. Krittayawiwat T. Treatment guidelines for tuberculosis patients for Don Chedi Hospital. Suphan Buri: Don Chedi Hospital; 2009.
17. World Health Organization. Guidelines on the management of latent tuberculosis infection. Geneva: WHO; 2015.
18. Cantor AB. Sample-size calculations for Cohen's kappa. Psychol Meth 1996;1:150-3.
19. Pai M, Gokhale K, Joshi R, Dogra S, Kalantri S, Mendiratta DK, et al. Mycobacterium tuberculosis infection in health care workers in rural India: comparison of a whole-blood interferon gamma assay with tuberculin skin testing. JAMA 2005;293:2746-55.
20. Mirtskhulava V, Kempker R, Shields KL, Leonard MK, Tsertsvadze T, del Rio C, et al. Prevalence and risk factors for latent tuberculosis infection among health care workers in Georgia. Int J Tuberc Lung Dis 2008;12:513-9.
21. Lien LT, Hang NT, Kobayashi N, Yanai H, Toyota E, Sakurada S, et al. Prevalence and risk factors for tuberculosis infection among hospital workers in Hanoi, Viet Nam. PLoS One 2009;4:e6798.
22. de Souza FM, do Prado TN, Pinheiro JS, Peres RL, Lacerda TC, Loureiro RB, et al. Comparison of interferon-gamma release assay to two cut-off points of tuberculin skin test to detect latent Mycobacterium tuberculosis infection in primary health care workers. PLoS One 2014;9:e102773.
23. Jo KW, Hong Y, Park JS, Bae IG, Eom JS, Lee SR, et al. Prevalence of latent tuberculosis infection among health care workers in South Korea: A multicenter study. Tuberc Respir Dis (Seoul) 2013;75:18-24.
24. He GX, Wang LX, Chai SJ, Klena JD, Cheng SM, Ren YL, et al. Risk factors associated with tuberculosis infection among health care workers in Inner Mongolia, China. Int J Tuberc Lung Dis 2012;16:1485-91.
25. Lamberti M, Uccello R, Monaco MGL, Muoio M, Feola D, Sannolo N, et al. Tuberculin skin test and Quantiferon test agreement and influencing factors in tuberculosis screening of healthcare workers: a systematic review and meta-analysis. J Occup Med Toxicol 2015;10:2.
26. Diel R, Loddenkemper R, Meywald-Walter K, Niemann S, Nienhaus A. Predictive value of a whole blood IFN-gamma assay for the development of active tuberculosis disease after recent infection with *Mycobacterium tuberculosis*. Am J Respir Crit Care Med 2008;177:1164-70.
27. Rafiza S, Rampal KG, Tahir A. Prevalence and risk factors of latent tuberculosis infection among health care workers in Malaysia. BMC Infect Dis 2011;11:19.
28. El Sokkary RH, Abu-Taleb AM, El Seifi OS, Zidan HE, Mortada EM, El Hossary D, et al. Assessing the prevalence of latent tuberculosis among health care providers in Zagazig City, Egypt using Tuberculin Skin Test and QuantiFERON-TB Gold In-Tube Test. Cent Eur J Public Health 2015;23:324-30.
29. Tripodi D, Brunet-Court, Nael V, Audrain M, Chailleux E, Germaud P, et al. Evaluation of the tuberculin skin test and the interferon-gamma release assay for TB screening in French healthcare workers. J Occup Med Toxicol 2009;4:30.
30. Nonghanphithak D, Reechaipichitkul W, Chaiyasung T, Faksri K. Risk factors for latent tuberculosis infection among health-care workers in northeastern Thailand. Southeast Asian J Trop Med Public Health 2016;47: 1198-208.
31. 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:e494.
32. Nasreen S, Shokoohi M, Malvankar-Mehta MS. Prevalence of latent tuberculosis among health care workers in high burden countries: a systematic review and meta-analysis. PLoS One 2016;11:e0164034.
33. City B. Latent tuberculosis infection among healthcare workers in chest disease hospitals, Bangladesh. Health Sci Bull [Internet]. 2014 [cited 2018 Oct 15];12:1-23. Available from: http://dspace.icddrb.org/jspui/bitstream/123456789/7783/1/2014-ICDDRBHealthScience Bulletin-Vol12(1)-English.pdf.
34. Teixeira EG, Kritski A, Ruffino-Netto A, Steffen R, Lapa e Silva JR, Belo M, et al. Medical students at risk of nosocomial tuberculosis. J Hosp Infect 2011;77:80-1.
35. Targowski T, Chelstowska S, Plusa T. Tuberculin skin test and interferon-γ release assay in the detection of latent tuberculosis infection among Polish health care workers. Pol Arch Med Wewn 2014;124:36-42.
36. Erkens CG, Dinmohamed AG, Kamphorst M, Toumanian S, Nispen-Dobrescu R, Alink M, et al. Added value of interferon-gamma release assays in screening for tuberculous infection in the Netherlands. Int J Tuberc Lung Dis 2014;18:413-20.
37. Ayubi E, Doosti-Irani A, Mostafavi E. Do the tuberculin skin test and the QuantiFERON-TB Gold in-tube test agree in detecting latent tuberculosis among high-risk contacts? A systematic review and meta-analysis. Epidemiol Health 2015;37:e2015043.
38. Nahid P, Pai M, Hopewell PC. Advances in the diagnosis and treatment of tuberculosis. Proc Am Thorac Soc 2006;3:103-10.
39. Dorman SE, Belknap R, Graviss EA, Reves R, Schluger N, Weinfurter P, et al. Interferon-γ release assays and tuberculin skin testing for diagnosis of latent tuberculosis infection in healthcare workers in the United States. Am J Respir Crit Care Med 2014;189:77-87.
40. Schablon A, Harling M, Diel 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.
41. Zwerling A, van den Hof S, Scholten J, Cobelens F,

Menzies D, Pai M. Interferon-gamma release assays for tuberculosis screening of healthcare workers: a systematic review. Thorax 2012;67:62-70.
42. Marra F, Marra CA, Sadatsafavi M, Moran-Mendoza O, Cook V, Elwood RK, et al. Cost-effectiveness of a new interferon-based blood assay, QuantiFERON-TB Gold, in screening tuberculosis contacts. Int J Tuberc Lung Dis 2008;12:1414-24.