

## Prevalence and risk factors for latent tuberculosis infection among health care workers in Georgia

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### SUMMARY

**BACKGROUND:** Tuberculosis (TB) is a major public health problem in Georgia, but few TB infection control measures have been implemented in health care facilities.

**OBJECTIVE:** To assess the prevalence and risk factors for latent TB infection (LTBI) among Georgian health care workers (HCWs) using two diagnostic tests, the tuberculin skin test (TST) and the QuantiFERON®-TB Gold In Tube test (QFT-3G), an interferon-gamma release assay.

**METHODS:** A cross-sectional study was conducted between June and August 2006 among HCWs at the Georgian National TB Program.

**RESULTS:** Of 265 HCWs enrolled, 177 (67%) had a positive TST and 159 (60%) had a positive QFT-3G; 203 (77%) had a positive result for at least one of the tests

and 50% tested positive for both tests. There was moderately good agreement between the tests (74%, kappa = 0.43, 95%CI 0.33–0.55). In multivariate analysis, employment for >5 years was associated with increased risk of a positive TST (OR 5.09, 95%CI 2.77–9.33) and QFT-3G (OR 2.26, 95%CI 1.27–4.01); age >30 years was associated with an increased risk of a positive QFT-3G (OR 2.91, 95%CI 1.32–6.43).

**DISCUSSION:** A high prevalence of LTBI was found among Georgian HCWs and longer duration of employment was associated with increased risk. These data highlight the need for effective TB infection control measures and provide important baseline information as TB infection control measures are implemented.

**KEY WORDS:** tuberculosis infection; IFN- $\gamma$  assay; nosocomial transmission; tuberculin skin test

NOSOCOMIAL TRANSMISSION of *Mycobacterium tuberculosis* from patients to health care workers (HCWs) has been recognized for many years; the risk of transmission is greatest in facilities with a high burden of infectious tuberculosis (TB) cases.<sup>1–3</sup> Transmission of TB in health care facilities can be reduced or prevented with the implementation of effective infection control measures.<sup>4,5</sup> A hierarchy of TB infection control measures, including administrative, engineering and respiratory protection controls, is recommended by the US Centers for Disease Control and Prevention (CDC) and others to prevent nosocomial transmission of TB.<sup>6</sup> These measures have proven effective in preventing nosocomial transmission, and administrative controls are most important.<sup>5,7</sup>

The World Health Organization (WHO) published guidelines on the prevention of TB in health care fa-

cilities in resource-limited areas in 1999<sup>8</sup> and an addendum to those guidelines in 2006 entitled, 'Tuberculosis infection control in the era of expanding HIV care and treatment'.<sup>9</sup> These WHO guidelines also emphasize the importance of administrative controls for early recognition and detection of persons with TB and separation of patients with TB or suspected of having TB from other patients in health care facilities. However, despite these recommendations, TB infection control measures are virtually non-existent in most resource-limited countries (which account for >90% of the global TB burden), where emphasis is on active TB cases.<sup>2,10</sup> The importance of TB infection control measures has been highlighted most recently by reports of the development and spread of extensively drug-resistant TB (XDR-TB), which is associated with high morbidity and mortality, especially among human immunodeficiency virus (HIV) infected persons.<sup>11</sup>

TB, including multidrug-resistant TB (MDR-TB, defined as resistance to at least isoniazid and rifampicin),

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has re-emerged as a major public health problem in the country of Georgia following the collapse of the Soviet Union.\* In 2005, a total of 6448 TB cases were reported, with an incidence and prevalence of respectively 97 and 147 cases per 100 000 population (Salakaia, unpublished). Medical care for TB in Georgia is provided through the National Tuberculosis Program (NTP) at in-patient and out-patient facilities. TB infection control measures in Georgian health care facilities are limited and are similar to most resource-limited countries. No routine program has been put in place in Georgia to screen HCWs for latent tuberculosis infection (LTBI) at the NTP or other health care facilities.<sup>1,2,10</sup>

Until recently, the tuberculin skin test (TST), which has been available for more than 100 years, was the only test available for the diagnosis of LTBI. The TST measures a delayed-type hypersensitivity response to purified protein derivative (PPD), a mixture of antigens shared among *M. tuberculosis*, bacille Calmette-Guérin (BCG) and several non-tuberculous mycobacteria (NTM).<sup>12</sup> Limitations of the TST include problems with false-positive (due to cross-reactions with BCG and NTM) and false-negative test results (e.g., due to anergy). Moreover, the test requires two trips to a health care provider, one for placement and a second 48–72 h later to have the results read.<sup>12,13</sup> A new generation of diagnostic tests for LTBI, the interferon-gamma release assays (IGRAs) have recently become available.<sup>4</sup> The whole-blood IGRA, QuantiFERON®-TB Gold, has been approved by the US Food and Drug Administration (FDA) for use in the US, and the CDC has published guidelines on its use.<sup>4</sup> A newer version of this test, the QuantiFERON®-TB Gold In Tube (QFT-3G) test, which is logistically easier to use, is now FDA-approved and also available for use in a number of countries. The QFT-3G uses antigens that are more specific to *M. tuberculosis* and not found in BCG, and most NTM. Unlike the TST, IGRAs require a single patient visit, do not boost anamnestic immune responses, eliminate the subjectivity of the TST reading and can be completed in less than 24 h.

A limited number of studies evaluating the performance of IGRAs have been conducted in TB-endemic settings. Few studies have examined the use of these tests in HCWs. The purpose of the present study was to assess the prevalence and risk factors for LTBI among Georgian HCWs working for the NTP and affiliated institutions. It was important to obtain these

data prior to the planned implementation of TB infection control measures in Georgia as part of the NTP 5-year (2007–2011) TB Control Plan. LTBI was assessed using both standard (TST) and new (QFT-3G) diagnostic tests. Concordance between the two diagnostic tests was also assessed.

## STUDY POPULATION AND METHODS

### *Participants and data collection*

We conducted a cross-sectional study from June to August 2006 at the National Center for Tuberculosis and Lung Diseases (NCTLD)/NTP and affiliated institutions in Georgia. All HCWs, including physicians, nurses, orderlies, housekeepers, laboratory workers and administrative staff from 75 health care facilities that were part of the NTP or affiliated sites, were eligible for enrollment into the study. All HCWs enrolled were required to provide written informed consent in their native Georgian language of Kartuli.

The study was approved by the Ethics Committee of the NCTLD and the Emory University Institutional Review Board.

Each HCW enrolled into the study completed a questionnaire containing data on age, sex, country of birth and ethnicity, education, number of years employed as an HCW, occupation, prior TST history, history of BCG vaccination and history of active TB. BCG status was also assessed by visual inspection for a BCG scar. Information on possible community exposure to TB was also collected, including household contacts with TB. HCWs were considered to have high occupational exposure to TB if they routinely had direct contact with infectious TB patients (e.g., on a daily basis) during the course of their duties. HCWs who worked in the NTP administration building and had no routine patient contact and HCWs at the Infectious Diseases, AIDS and Clinical Immunology Research Center were considered to have limited occupational exposure to TB.

After 3 ml of blood was drawn for the IGRA, a TST was placed using 5 tuberculin units (TU) of PPD (Tubersol, Connaught; Swiftwater, PA, USA). TST was performed using the Mantoux method<sup>13</sup> and read 48–72 h after placement. Based on published guidelines, an induration of  $\geq 10$  mm was considered a positive TST in HCWs.<sup>13,14</sup> Participants who had a positive TST or a positive QFT-3G (as defined below) were advised to have a chest radiograph performed (at no cost to them) at an NTP facility and were referred to a physician at the NCTLD for further evaluation and consideration for treatment of LTBI. There were no costs incurred for HCWs who participated in the study.

### *Laboratory methods*

The QFT3-G test (Cellestis, Carnegie, VIC, Australia) was performed according to the manufacturer's recommendations and as previously described.<sup>15,16</sup> The

\* Salakaia A. TB epidemiology in Georgia: achievements and challenges. Unpublished presentation at a US-Caucasus workshop on operational research in HIV and TB, October 25, 2005. Tbilisi, Georgia; 2005. Lomtadze N. High rates of multidrug resistant tuberculosis in the country of Georgia: a population based study. Unpublished presentation at 11th Annual Meeting North American Region of the International Union Against Tuberculosis and Lung Disease, Vancouver, BC, Canada, 2007.

QFT-3G assay uses more specific antigens for *M. tuberculosis* to test for LTBI, including the early secreted antigenic target 6 (ESAT-6), culture filtrate protein 10 (CFP-10) and TB antigen TB7.7 (Rv2654). As recommended by the manufacturer and based on previous studies,<sup>15</sup> a positive QFT-3G was defined as interferon-gamma (IFN- $\gamma$ )  $\geq 0.35$  international units (IU)/ml if the response to TB antigens minus the negative control was  $\geq 0.35$  IU/ml and  $>25\%$  of the negative control, negative if these criteria were not met, and indeterminate if either the negative control had a result of  $>8$  IU/ml or if the positive control had a result of  $<0.5$  IU/ml. Because the QFT-3G enzyme-linked immunosorbent assay cannot accurately measure absolute IFN- $\gamma$  values  $>10$  IU/ml, such values were treated as 10 IU/ml.<sup>15</sup>

#### Statistical analysis

Data were entered into Epi Info version 3.3.2 (CDC, Atlanta, GA, USA). Statistical analyses were performed using SAS software version 9.1 (SAS Institute Inc., Cary, NC, USA). Concordance between the two diagnostic tests for LTBI (TST and QFT-3G) was measured using the kappa ( $\kappa$ ) statistic, where  $\kappa > 0.75$  represents excellent agreement,  $\kappa = 0.4-0.75$  fair to good agreement and  $\kappa < 0.4$  represents poor agreement, beyond chance.<sup>17</sup> Correlation between continuous IFN- $\gamma$  values (in IU/ml) and TST induration (in mm) was assessed using Spearman's correlation coefficient.<sup>18</sup> Risk factors for a positive LTBI test result (TST or QFT-3G) were evaluated using prevalence odds ratios (PORs). To adjust for multiple covariates, we used a logistic regression method. Variables included in the final multivariate model were chosen a priori on the basis of the biological plausibility of their association with the outcome of interest, as well as on the basis of statistical and epidemiological criteria. A *P* value  $\leq 0.05$  was defined as statistically significant. A single 'chunk' test<sup>19</sup> was performed to assess the significance of all the interaction terms. The statistical significance of the 'chunk' test was addressed using the unconditional maximal likelihood ratio test.<sup>19,20</sup>

## RESULTS

#### Participant description

Of the 1231 HCWs employed at the 75 Georgian NTP and affiliated sites, 281 were enrolled in the study. Sixteen were excluded from the final analysis: 10 participants had a previous history of active TB disease, one HCW refused to have blood drawn and five others were excluded because they did not return to have their TST read. Data were analyzed for 265 Georgian HCWs.

The mean age was 42 years (range 18–74); 229 (86%) were women (reflecting the sex distribution of HCWs at the NTP) and 244 (92%) had been BCG-vaccinated. The median length of employment as an

HCW at the NTP or affiliated institutions was 8 years (range 1–42). Of the 265 study subjects, 215 (81%) had routine (e.g., daily) contact with infectious TB patients cared for by the Georgian NTP. Demographic information of HCWs enrolled into the study is presented in Table 1. The demographics of those enrolled reflect those of the overall HCW population at the NTP and affiliated sites.

#### Diagnostic tests for LTBI

Overall, 203 (76.6%) of the 265 HCWs had a positive test result for at least one of the diagnostic tests for LTBI. A total of 177 (66.8%) had a positive TST (95% confidence interval [CI] 60.8–72.4) using a cut-off point of  $\geq 10$  mm induration and 159 (60.0%) had a positive QFT-3G test result (95% CI 53.8–65.9). One hundred and thirty-three (50%) HCWs had positive results for both diagnostic tests, 62 (23%) were negative for both tests, 44 (17%) had a positive TST but a negative QFT-3G, and 26 (10%) had a positive QFT-3G and negative TST (Table 2). Absolute values for IFN- $\gamma$  concentration and TST induration are presented in the Figure. There was moderately good agreement between the two tests (74%,  $\kappa = 0.434$ , 95% CI 0.326–0.545) (Table 3). Changing the TST cut-off points (i.e., using 5 mm and 15 mm of induration instead of 10 mm) did not greatly impact concordance

**Table 1** Demographic information of health care workers (*n* = 265)

Characteristic	<i>n</i> (%)
Age, years	
18–30	45 (17.0)
31–40	65 (24.5)
>40	155 (58.5)
Sex	
Female	229 (86.4)
Male	36 (13.6)
Education level	
College graduate	121 (45.7)
Some college	111 (41.9)
Secondary school and under	33 (12.5)
Occupation	
Administrative staff	29 (11.0)
Physicians	60 (22.6)
Nurses	87 (32.8)
Other	93 (33.6)
Length of employment as HCW, years	
$\leq 1$	32 (12.1)
2–5	76 (28.7)
6–10	53 (20.0)
>10	104 (39.3)
Frequent (daily) contact with TB patients*	215 (81.1)
Positive history of BCG vaccination†	206 (77.7)

\* Defined as working in buildings where TB patients undergo TB diagnosis and treatment on a daily basis (excludes HCWs from the NTP administrative building and HCWs from the Infectious Diseases, AIDS and Clinical Immunology Research Center).

† Unknown history of BCG vaccination is classified as a negative history of BCG vaccination.

HCW = health care worker; TB = tuberculosis; BCG = bacille Calmette-Guérin; NTP = National Tuberculosis Program; AIDS = acquired immunodeficiency syndrome.

**Table 2** Prevalence of latent tuberculosis infection among Georgian health care workers ( $n = 265$ )

Results*	Positive cases $n$ (%)
Positive TST	177 (66.8)
Positive QFT-3G test	159 (60.0)
Positive TST and/or QFT-3G test	203 (77.0)
Positive TST and QFT-3G tests	133 (50.0)
Positive TST/negative QFT-3G test	44 (17.0)
Negative QFT-3G/positive TST	26 (10.0)

\* TST cut-off point  $\geq 10$  mm.

TST = tuberculin skin test; QFT-3G test = QuantiFERON®-TB Gold in Tube test.

**Table 3** Concordance between TST and QFT-3G results

TST/QFT-3G results*	TST cut-off point		
	$\geq 5$ mm	$\geq 10$ mm	$\geq 15$ mm
Negative/negative	44 (16.6)	62 (23.4)	76 (28.7)
Positive/positive	150 (56.6)	133 (50.2)	110 (41.6)
Positive/negative	62 (23.4)	44 (16.6)	30 (11.3)
Negative/positive	9 (3.4)	26 (9.8)	49 (18.5)
Agreement, %	73.2	73.6	70.3
$\kappa$	0.39	0.43	0.40
95%CI	0.29–0.50	0.33–0.55	0.29–0.51

\* QFT-3G cut-off point  $\geq 0.35$  IU/ml.

TST = tuberculin skin test; QFT-3G = QuantiFERON®-TB Gold in Tube test; CI = confidence interval.

between the TST and QFT-3G (Table 3). There was a significant correlation between absolute values of TST and QFT-3G when assessed using Spearman's correlation coefficient ( $\rho = 0.52$ ,  $P < 0.001$ ).

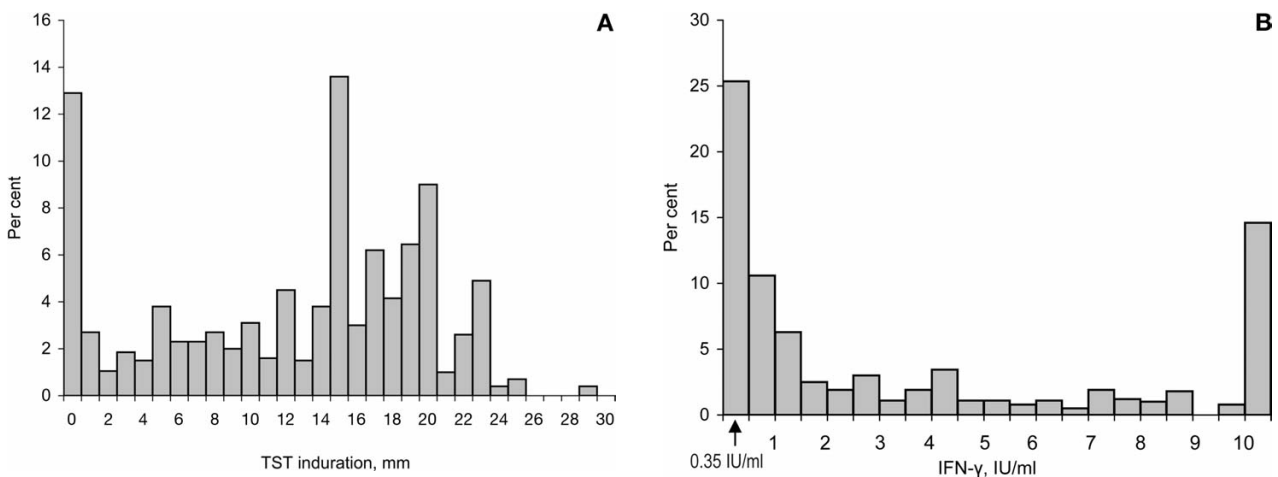
In univariate analysis, age  $>30$  years and length of employment as a HCW for  $>5$  years at the NTP were significantly associated with having a positive TST result; age  $>30$  years, female sex, direct exposure to infectious patients with TB, and length of employment as a HCW  $>5$  years was associated with increased risk of having a positive QFT-3G test (Table 4). In multivariate analysis, length of employment as a HCW for  $>5$  years (odds ratio [OR] 5.09, 95%CI 2.77–9.33) was independently associated with increased risk of a positive TST result, while age  $>30$  years (OR 2.91, 95%CI 1.32–6.43) and length of employment as an HCW  $>5$  years (OR 2.26, 95%CI 1.27–4.01) were independently associated with increased risk of a having a positive QFT-3G result (Table 5).

## DISCUSSION

We found the prevalence of LTBI among Georgian HCWs at the NTP and affiliated institutions to be higher than in the previous two reports using IGRAs for evaluation of LTBI among HCWs in resource-

limited countries.<sup>21,22</sup> Overall, 77% had a positive test result for at least one of the LTBI diagnostic tests: 66.8% had a positive TST and 60% had a positive QFT-3G. In multivariate analysis, employment as an HCW for  $>5$  years was associated with an increased risk of a positive TST (OR 5.09) or QFT-3G (OR 2.26). In addition, age  $>30$  years was associated with an increased risk of a positive QFT-3G test (OR 2.91). Our findings are consistent with other reports that increasing age and more years of work in health care are associated with higher prevalence of LTBI.<sup>23</sup> However, very few studies have reported the use of IGRAs in the evaluation of HCWs in resource-limited countries. The higher prevalence of LTBI found in our study compared to the two previous reports<sup>21,22</sup> could be due to the fact that our study population contained HCWs particularly involved in TB control.

In Georgia, patients with TB are diagnosed and treated in specialized TB facilities organized by the Georgian NTP, and generally do not receive care in other health care facilities. The high rate of LTBI among Georgian HCWs likely reflects ongoing exposure to infectious TB patients in hospitals that have had limited or no TB infection control measures. The risk of testing positive for LTBI (by either diagnostic test)



**Figure** Distribution of **A**) TST induration and **B**) IFN- $\gamma$  release assay responses ( $n = 265$ ). TST = tuberculin skin test; IFN- $\gamma$  = interferon-gamma; IU = international units.

**Table 4** Risk factors associated with a positive latent tuberculosis infection diagnostic test among HCWs in Georgia: a univariate analysis

Variable	TST*		QFT-3G test <sup>†</sup>	
	Positive tests/total tested n (%)	Unadjusted OR (95%CI)	Positive tests/total tested n (%)	Unadjusted OR (95%CI)
Age, years				
≤30	21/45 (46.6)	1.00	13/45 (28.9)	1.00
>30	156/220 (70.1)	2.79 (1.45–5.36) <sup>‡</sup>	146/220 (66.3)	4.86 (2.41–9.81) <sup>‡</sup>
Female	156/229 (68.1)	1.53 (0.74–3.13)	144/229 (66.4)	2.37 (1.16–4.85) <sup>‡</sup>
Education level				
Graduate	81/121 (45.2)	1.00	65/221 (53.7)	1.00
Some college education	72/111 (64.9)	1.60 (0.66–3.86)	70/111 (63.0)	1.47 (0.87–2.49)
Secondary school or under	25/33 (75.8)	0.95 (0.55–1.63)	24/33 (72.7)	2.30 (0.99–5.35)
Occupation				
Hospital administrative staff	19/29 (65.5)	1.00	11/29 (37.9)	1.00
Physician	40/60 (66.7)	1.05 (0.41–2.68)	36/60 (60.0)	2.45 (0.99–6.10)
Nurse	59/87 (67.8)	1.11 (0.46–2.70)	56/87 (64.4)	2.96 (1.24–7.05) <sup>‡</sup>
Other	59/93 (63.4)	1.04 (0.43–2.50)	56/93 (60.2)	2.78 (1.17–6.59) <sup>‡</sup>
Length of employment as HCW, years				
≤5	49/108 (45.4)	1.00	47/108 (43.5)	1.00
>5	128/157 (81.5)	5.32 (3.06–9.24) <sup>‡</sup>	112/157 (71.3)	3.23 (1.93–5.40) <sup>‡</sup>
Has routine direct contact with TB patients <sup>§</sup>	149/215 (69.3)	1.77 (0.95–3.33)	140/215 (65.7)	3.05 (1.61–5.75) <sup>‡</sup>
Positive history of BCG vaccination <sup>¶</sup>	162/206 (78.6)	0.79 (0.30–2.12)	142/206 (68.9)	0.33 (0.11–1.00)

\* TST induration cut-off point ≥ 10 mm.

<sup>†</sup> QFT-3G test cut-off point ≥ 0.35 IU/ml.

<sup>‡</sup> Statistically significant.

<sup>§</sup> Defined as working in buildings where TB patients undergo TB diagnosis and treatment on a daily basis (excludes HCWs from the NTP administrative building and HCWs from the Infectious Diseases, AIDS and Clinical Immunology Research Center).

<sup>¶</sup> Unknown history of BCG vaccination is classified as a negative history of BCG vaccination.

HCW = health care worker; TST = tuberculin skin test; QFT-3G test = QuantiFERON®-TB Gold in Tube test; OR = prevalence odds ratio; CI = confidence interval; BCG = bacille Calmette-Guérin; TB = tuberculosis; IU = international unit; NTP = National TB Program; AIDS = acquired immune-deficiency syndrome.

**Table 5** Risk factors associated with a positive latent tuberculosis infection diagnostic test among HCWs in Georgia: multivariate analysis

Covariate	TST* Adjusted OR <sup>†</sup> (95%CI)	QFT-3G test <sup>‡</sup> Adjusted OR <sup>†</sup> (95%CI)
Age >30 years	1.17 (0.54–2.53)	2.91 (1.32–6.43)
Female	1.30 (0.56–3.03)	1.78 (0.78–4.08)
Occupation		
Administrative staff	1.00	1.00
Physicians	0.30 (0.08–1.15)	0.82 (0.22–3.11)
Nurses	0.31 (0.07–1.34)	1.07 (0.25–4.59)
Other	0.29 (0.08–1.10)	0.97 (0.25–3.66)
Employment as HCW >5 years	5.09 (2.77–9.33)	2.26 (1.27–4.01)
Has routine direct contact with TB patients <sup>§</sup>	2.32 (0.80–6.71)	2.06 (0.71–5.98)
Positive history of BCG vaccination <sup>¶</sup>	0.74 (0.25–2.23)	0.26 (0.07–0.91)

\* TST induration cut-off point ≥ 10 mm.

<sup>†</sup> A multivariable logistic regression model includes age, sex, occupation, length of employment as HCW, daily contact with TB patients and history of BCG vaccination.

<sup>‡</sup> QFT-3G test cut-off point ≥ 0.35 IU/ml.

<sup>§</sup> Defined as working in buildings where TB patients undergo diagnosis and treatment on a daily basis (excludes HCWs from the NTP administrative building and HCWs from the Infectious Diseases, AIDS and Clinical Immunology Research Center).

<sup>¶</sup> Unknown history of BCG vaccination is classified as a negative history of BCG vaccination.

HCW = health care worker; TST = tuberculin skin test; QFT-3G test = QuantiFERON®-TB Gold in Tube test; OR = odds ratio; CI = confidence interval; TB = tuberculosis; BCG = bacille Calmette-Guérin; IU = international unit; NTP = National Tuberculosis Program; AIDS = acquired immune-deficiency syndrome.

increased with increasing length of time (i.e., >5 years) of employment as an HCW at the Georgian NTP.

The WHO has proposed interventions to reduce nosocomial transmission in settings where resources are limited.<sup>8,9</sup> These recommendations emphasize administrative controls, including careful screening and prompt diagnosis of TB, separation of TB patients and TB suspects from other patients and rapid treatment of TB. However, compliance with these TB infection control guidelines is generally poor in low-income countries.<sup>15</sup> The importance of TB infection control measures is gaining increasing attention due to reports of XDR-TB, which is associated with high rates of morbidity and mortality,<sup>11</sup> especially among immunocompromised persons such as those with HIV infection. Nosocomial transmission appears to play an important role in amplifying XDR-TB transmission.

Given the frequent exposure to infectious TB patients, it is not surprising that we found high rates of LTBI (using both the TST and QFT-3G test) among Georgian HCWs at the NTP and affiliated sites. The prevalence of LTBI in the general population in Georgia is not known, as no surveys for LTBI have been carried out. However, we suspect that rates of LTBI are much higher among HCWs at the Georgian NTP than others in the population, including other high-risk groups. For example, a previous study of LTBI using TST among internally displaced persons (IDPs) in Georgia found a prevalence of 48% among 988 IDPs.<sup>24</sup>

A systematic review of TB among HCWs in low- and middle-income countries reported a prevalence of LTBI of 54% (range 33–79) using the TST.<sup>2</sup> Our findings of a positive TST were at the higher end of this range, likely reflecting frequent exposure to infectious TB cases. We are aware of only two prior cross-sectional studies that have assessed the use of new IGRA diagnostics tests for LTBI such as the QFT-3G among HCWs. One was reported from Samara, Russia<sup>21</sup> and the other from India.<sup>22</sup> Both noted an LTBI prevalence of about 40% using the QFT-3G. These studies included HCWs who did not provide care for TB patients. We focused on HCWs at the Georgian NTP who exclusively cared for patients with TB; this may explain the higher prevalence in our study.

There was moderate concordance between the TST and the QFT-3G test in our study (agreement of 74%,  $\kappa = 0.43$ ). In a study of HCWs in India, the agreement between the tests was higher (81%,  $\kappa = 0.61$ ). The use of 1 TU PPD RT23 in the study from India may have improved TST specificity and could have been a reason for the observed higher agreement.<sup>23</sup> In the case of our study, the observed moderate or fair agreement between the diagnostic tests for LTBI might be explained by the high prevalence of TB infection and the high BCG vaccination coverage in the study participants.

There are several limitations to our study. First, because testing for LTBI is not routinely performed in Georgia, participation in our study was voluntary and did not include all HCWs at the Georgia NTP and affiliated sites. Using a convenience sampling method, we enrolled approximately 23% of the eligible population, with enrollment taking place at eight of a possible 75 eligible facilities. The TB facilities at which patients were enrolled were diverse in nature and included hospitals, administration offices, TB clinics and laboratory facilities, and were geographically widely spread throughout the country. We tended to choose larger facilities, and there was a 75% participation rate at the facilities where HCWs were enrolled. The demographics of those HCWs enrolled in the study were similar to those of the entire HCW population at the NTP. Although we collected data on BCG vaccination status, we did not collect information about the number of BCG vaccinations. During the Soviet era, it was not unusual for HCWs and others to receive multiple doses of BCG. Since Georgia became independent in the early 1990s, BCG vaccination has been given only to infants. The number of BCG vaccinations may be important, as data suggest that those with BCG vaccination after infancy produce more frequent, more persistent and larger TST reactions.<sup>25</sup>

## CONCLUSIONS

We found high LTBI rates among HCWs at the Georgian NTP using both TST and IGRA. The IGRA was

well accepted by HCWs in this study. Our study provides important baseline information on the prevalence of LTBI among Georgian HCWs involved in TB control. Obtaining baseline information and establishing surveillance for LTBI among Georgian HCWs is important, as one of the priorities of TB control in Georgia for the next 5 years is the implementation of effective TB infection control measures. Further research is needed to assess the utility of longitudinal IGRA use among HCWs, how to implement and gain acceptance from HCWs for treatment of LTBI among high risk HCWs and how best to implement TB infection control measures to protect the health and safety of HCWs and patients in Georgia.

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## RÉSUMÉ

**CONTEXTE :** La tuberculose (TB) constitue un problème majeur de santé publique en Géorgie, mais peu de mesures de lutte contre l'infection tuberculeuse ont été mises en œuvre dans les services de soins de santé.

**OBJECTIF :** Évaluer la prévalence et les facteurs de risque d'infection tuberculeuse latente (LTBI) chez les travailleurs de soins de santé (HCW) de Géorgie en utilisant deux tests de diagnostic, le test cutané tuberculique (TST) et le test QuantiFERON®-TB en tube (QFT-3G), un test de libération de l'interféron-gamma.

**MÉTHODES :** On a mené, entre juin et août 2006, une étude transversale parmi les HCW dans le Programme National Géorgien de Lutte contre la Tuberculose.

**RÉSULTATS :** On a enrôlé dans l'étude 265 HCW ; chez 177 (67%) le TST était positif et chez 159 (60%) le test QFT-3G était positif. Un résultat positif a été obtenu pour au moins un des tests chez 203 sujets (77%) et une

réponse positive pour les deux tests chez 50%. La concordance est modérément bonne entre les tests (74% ;  $\kappa = 0,43$  ; IC95% 0,33–0,55). Lors de l'analyse multivariée, on a trouvé que le fait d'avoir un emploi depuis >5 ans est en association avec un risque accru de TST positif (OR 5,09 ; IC95% 2,77–9,33) et d'un test positif QFT-3G (OR 2,26 ; IC95% 1,27–4,01) ; un âge >30 ans est associé à un risque accru de QFT-3G positif (OR 2,91 ; IC95% 1,32–6,43).

**DISCUSSION :** Chez les HCW de Géorgie, on a trouvé une prévalence élevée de la LTBI et l'association d'une durée plus longue de travail avec un accroissement du risque. Ces données éclairent la nécessité de mesures efficaces de lutte contre l'infection tuberculeuse et constituent une information de base importante pour la mise en oeuvre de mesures de contrôle de l'infection tuberculeuse.

## RESUMEN

**MARCO DE REFERENCIA :** Pese a que la tuberculosis (TB) constituye un importante problema de salud pública en Georgia, pocas han sido las medidas de control de la infección tuberculosa introducidas en los establecimientos de atención de salud.

**OBJETIVO :** Evaluar la prevalencia y los factores de riesgo de infección tuberculosa latente (LTBI) en los profesionales de la salud (HCW) en Georgia mediante dos pruebas diagnósticas, la reacción cutánea a la tuberculina (TST) y una prueba de liberación de interferón-gamma, el QuantiFERON®-TB en tubo (QFT-3G).

**MÉTODO :** Estudio transversal llevado a cabo entre junio y agosto de 2006 en HCW del Programa Nacional de Tuberculosis de Georgia.

**RESULTADOS :** Participaron en el estudio 265 HCW ; 177 (67%) presentaron una reacción positiva a la TST y 159 (60%) una prueba QFT-3G positiva. Doscientos tres participantes (77%) tuvieron un resultado positivo

por lo menos a una de las pruebas y en 50% ambas pruebas fueron positivas. Se observó una concordancia moderadamente buena entre ambas pruebas (74%, índice  $\kappa = 0,43$  ; IC95% 0,33–0,55). En el análisis multifactorial se encontró que una permanencia en el trabajo durante >5 años se asociaba con una mayor probabilidad de reacción positiva a la TST (OR = 5,09 ; IC95% 2,77–9,33) y a la prueba QFT-3G (OR = 2,26 ; IC95% 1,27–4,01) ; la edad >30 años se asoció con un riesgo aumentado de una prueba QFT-3G positiva (OR = 2,91 ; IC95% 1,32–6,43).

**DISCUSIÓN :** Se encontró una alta prevalencia de LTBI en los HCW de Georgia y la mayor permanencia en este empleo se asoció con un mayor riesgo. Estos datos ponen de manifiesto la necesidad de medidas eficaces de control de la infección tuberculosa y aportan una importante información de referencia para el momento en que se instauren dichas medidas.