Comparison of the QuantiFERON®-TB Gold assay and tuberculin skin test to detect latent tuberculosis infection among target groups in Trinidad & Tobago

Shirematee Baboolal,[1] *Dottin Ramoutar,*[2] *and Patrick Eberechi Akpaka*[1]

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ABSTRACT

Objective. *To compare the QuantiFERON®-TB Gold (QFT-G) assay and tuberculin skin test (TST) in screening/diagnosis of latent tuberculosis infection (LTBI) among individuals in Trinidad & Tobago at high risk for TB.*

Methods. *A total of 560 individuals (TB patient contacts, HIV patients, health care workers, prison inmates, and TB patients [controls]) were recruited for the study. Blood was drawn and processed using the QFT-G assay, followed by immediate administration of TST solution on subjects' forearm. Data were analyzed with Epi Info™ 3.5.1 software. Results were compared across the target groups using the chi-square test* ($P < 0.05$).

Results. *The QFT-G assay detected LTBI in 51% of the subjects (with most positive results occurring among the control group) whereas the TST detected it in 39.4%* ($P = 0.001$). *Overall, the QFT-G assay detected LTBI more frequently than the TST among all subjects except the control group, where detection favored the TST. The QFT-G assay produced indeterminate and nonreactive results in some HIV patients but required less turnaround time than the TST (23.3 h versus 70.2 h;* $P < 0.0001$). *The TST cost less per subject than the QFT-G assay (US $3.70 versus US $18.60;* $P = 0.0008$).

Conclusions. *The QFT-G assay cost more but had a higher detection rate among most target groups and required less turnaround time than the TST. However, its sensitivity was lower among immunocompromised subjects. Therefore, the QFT-G assay should be used with caution for LBTI screening/diagnosis in resource-poor, high–HIV prevalence settings such as Trinidad & Tobago.*

Key words Latent tuberculosis, tuberculin test; enzyme-linked immunosorbent assay; Trinidad and Tobago.

In May 2005, QuantiFERON®-TB Gold (QFT-G), a new in vitro test manufactured by Cellestis Limited (Carnegie, Victoria, Australia), was approved by the U.S. Food and Drug Administration (FDA) as an aid in the diagnosis of *Mycobacterium tuberculosis*, including both latent tuberculosis infection (LTBI) and tuberculosis (TB) disease. Following this approval, the U.S. Centers for Disease Prevention and Control (CDC) set some guidelines for its use (1).

The QFT-G assay is a whole-blood enzyme-linked immunosorbent assay (ELISA)-based test. It detects in vitro cell-mediated immune responses to TB infection by quantifying the amount of interferon gamma (IFN-γ) released in the plasma of whole blood incubated overnight with mixtures of overlapping peptides spanning the sequence of the

[1] Department of Para-Clinical Sciences, Faculty of Medical Sciences, The University of the West Indies, St. Augustine, Trinidad & Tobago. Send correspondence to: Patrick Eberechi Akpaka, Patrick.Akpaka@sta.uwi.edu

[2] Caura Chest Hospital, Caura, Trinidad & Tobago.

early secretory antigenic target 6-kDa (ESAT-6) protein and the culture filtrate protein 10kDa (CFP-10). These antigens are the products of a genomic region (RD1) present in all *M. tuberculosis* and pathogenic *M. bovis* strains but absent in all Bacille Calmette-Guérin (BCG) vaccine strains and nearly all nontuberculosis mycobacteria (NTM) of clinical relevance. The tuberculin skin test (TST), on the other hand, measures immune response or cell-mediated hypersensitivity to tuberculin purified protein derivative (PPD), a polyvalent antigenic mixture of proteins derived from *M. tuberculosis* cultures. The PPD antigen used in the TST is also present in NTM and in the BCG vaccine strain.

An important factor in successful elimination of TB is accurate and timely detection of LTBI. This not only allows for the early use of appropriate antituberculosis drugs, thus enhancing effective TB treatment and eradication, but also helps reduce transmission and prevent progression to overt disease. The cost of TB treatment is enormous as it must be administered over several months and may be complicated by other factors, such as coinfection of the target population with HIV/AIDS. HIV infection is the greatest risk factor for progression of LTBI to active TB, and HIV-positive individuals are much more likely to develop the disease during their lifetime than those who are HIV-negative (50% risk versus 5%–10% risk respectively).

In Trinidad & Tobago, as in most Caribbean and developing countries, the TST has been used to support screening and diagnosis of TB and LTBI for more than 50 years. According to the country's annual National Tuberculosis Planning (NTP) report, between 2004 and 2006 more than 14 033 TSTs (an average of 4 677 per year) were administered nationwide (NTP Report, 2006). Of these, 1 312 were not read (indicating some national resources are squandered in TST screening for TB contacts and other high-risk groups). In contrast to the UK National Institute of Health and Clinical Excellence recommendation of dual testing strategy (use of the IFN-γ release assay on TST-positive individuals) (2), the CDC has advocated that the QFT-G assay be used in place of rather than in addition to the TST (1). The present study was undertaken to evaluate and compare the more conventional TST versus the newer QFT-G method in screening for LTBI in various groups at high risk for TB to determine which method is best suited for use in a resource-limited, high–HIV prevalence country such as Trinidad & Tobago in terms of cost, turnaround time, and reliability. Part of this study was presented at the 14th International Congress on Infectious Diseases (Hyatt Hotel, Miami, Florida, USA, 9–12 March 2010) (3).

MATERIALS AND METHODS

Study design, sites, and subjects

The current research was an observational, cross-sectional study conducted at three sites on the twin islands of Trinidad and Tobago from February through October 2007. Two of the study sites were outpatient respiratory care clinics ("chest clinics") located in the north and south of the country respectively; the third site was Caura Chest Hospital (CCH), a 66-bed ambulatory tertiary health facility established specifically for TB patients.

Based on the 2006 NTP report, the minimum required sample size for the study was 508 subjects (10% of all individuals in the country deemed at risk of being infected with TB). The study sample pool comprised 560 individuals from the following high-risk groups: 1) TB contacts (mainly family members and friends of individuals being treated for TB infection) (n = 200); 2) health care workers (n = 45), including three doctors, 30 nurses, five ancillary staff, and seven clerical staff from CCH and two chest clinics where TB patients were either admitted or followed up; 3) HIV-positive patients followed up at the chest clinics (n = 70); 4) TB patients admitted to or receiving treatment at CCH, or receiving follow-up care at the chest clinics, with laboratory confirmation of TB diagnosis based on positive sputum smear and culture (the control group) (n = 180); and 5) prison inmates from Trinidad & Tobago's maximum security prison (n = 65). The screening for this latter group, which was conducted by the National Tuberculosis Control Programme (NTCP), was approved by the Ministry of National Security in order to obtain more data about a suspected TB outbreak at the facility. Based on subsequent testing, 15 of the 560 individuals in the study sample were determined to be coinfected with HIV. At the time of the research, all HIV and TB patients were receiving highly active antiretroviral treatment (HAART) and anti-tuberculosis therapy. All 560 individuals gave oral consent to participate in the research and received pre-counseling prior to the study. None of the study subjects were below the age of 18 (eliminating the need for parental consent) and none were pregnant.

The study was approved by the Ethics Committee of the Faculty of Medical Sciences at The University of the West Indies (St. Augustine, Trinidad). The head of the NTCP, which is based at CCH, granted the authors permission to use the hospital facility for their study.

Specimen collection

A 5-mL whole-blood specimen was drawn in heparinized tubes from all 560 subjects for testing with the QFT-G assay, which was immediately followed by administration of the TST via an intradermal injection at the lateral upper part of subjects' right forearm. Subjects were instructed not to scratch the area (even if it itched) and to return to the hospital or chest clinics 72 hours after the injection for a reading of the indurations.

QFT-G assay

All blood samples were tested at one laboratory (located 0.5 h–1.5 h from CCH and the two chest clinics), where they were processed and evaluated for the presence of IFN-γ according to manufacturer's instructions. In the laboratory, 1-mL aliquots of heparinized whole blood were incubated for 16–24 hours at 37 ºC with three drops of saline (nil), phytohemaglutinin (mitogen), ESAT-6 protein, and CFP-10 in Costar 24-well microtiter plates. After incubation, plasma samples were harvested and stored at –20 ºC until ELISA analysis of their IFN-γ content.

The IFN-γ levels of the 50-µL plasma samples were determined using the ELISA reagents and protocol provided in the QFT-G assay kit. The QFT-G assay was performed in batches of 20 to 22 by a medical laboratory technician. The 50-µL plasma samples were added to diluted conjugate in flat-bottom microtiter wells and incubated for 2 hours at room temperature. Eight dilutions of IFN-γ

standard (ranging from 0.0 IU/mL to 10.0 IU/mL) were included in each plate. After washing the samples six times, a substrate was added to achieve color development directly proportional to the amount of IFN-γ present in each specimen. Optical densities were interpreted using assay-specific software provided by the manufacturer. IFN-γ assay results were interpreted as described in the QFT-G product package insert. An IFN-γ level ≥ 0.35 IU/mL (TB antigens minus negative control) was considered a positive result. When an IFN-γ concentration was indeterminate, the process was repeated to minimize human and laboratory errors. Results with mitogen minus negative control ≥ 0.5 IU/mL and/or TB antigens minus negative control ≥ 0.35 IU/mL were considered determinate. Values > 10 IU/mL were treated as 10 IU/mL due to the possibility of ELISA measurement inaccuracies above the 10-IU/mL resolution level.

Mantoux TST

The TSTs were performed and read by highly experienced and competent certified, trained nurses at CCH and the chest clinics. Study participants were injected with 0.1 mL (5 tuberculin units [TU]) of Tubersol® (Connaught Laboratories, Willowdale, Ontario, Canada) using the Mantoux method (4) immediately after the blood samples for the QFT-G were drawn by the phlebotomists. The diameters of the resulting wheal reactions were measured 72 hours after puncture. All results obtained were recorded as either positive (if ≥ 10 mm) or negative (< 10 mm) for indurations.

Both the QFT-G assay and the TST were administered to all study participants. The certified nurses who read the TSTs were also the TST administrators and therefore were not blinded to the distribution of the results across the different target groups. The laboratory technician who performed the QFT-G assay was blinded to the TST results.

Turnaround time

TST. The turnaround time (TAT) for the TST was defined as the time the tuberculin was placed on the forearm of the subject to the time the reading was made by the certified nurse. Time spent by the subjects traveling to CCH or the chest clinics and waiting to undergo the test was excluded from this calculation. The following components were included in overall TAT but were not disaggregated to address their variability: time required for administration of the intradermal injection (5 min or more, depending on whether or not the subject was afraid of the needle stick); and time required to perform the reading during the subject's return visit (5–10 min, depending on how long it took the certified nurse to explain the results).

QFT-G. For the QFT-G assay, TAT was defined as the time venous blood was drawn to the completion of the laboratory processes. As in the calculations of time spent for completion of the TST, TAT for the QFT-G assay did not include subject travel time to CCH and the chest clinics or time spent waiting for test administration and did not disaggregate variable time components. For this test those components included the time required to deliver the blood sample to the laboratory (which ranged from 15–30 min to as much as 2 h, with heavy traffic), and the time required to draw blood (5–15 min, depending on whether the subject was afraid of the needle stick and/or if the phlebotomist experienced difficulty in locating a vein appropriate for venipuncture). Although it took less than 24 hours to complete each individual QFT-G assay, the readings were done in batches, to reduce the hands-on time required by the laboratory technician, which increased the average TAT way beyond the 24-hour time frame. To adjust for this anomaly, the time that the partially processed blood samples were stored (at –20 ºC) awaiting the completion of the other assays in the test batch was subtracted from the overall TAT.

Cost per test

The cost per test was based solely on the direct cost of materials used. For example, the cost of delivering blood samples to the laboratory from CCH and the chest clinics was not included. Labor costs were not included either, as various categories of staff (phlebotomists, drivers, nurses, and laboratory technicians) had provided services on a volunteer basis. For expendable laboratory supplies such as reagents, the cost was calculated based on the amount of material required for each assay.

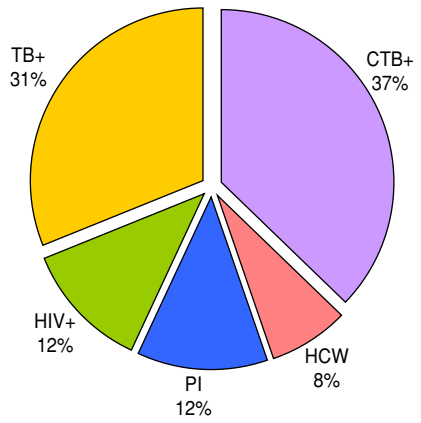
Statistical analysis

Data were analyzed with Epi Info™ 3.5.1 software (CDC, Atlanta, Georgia, United States). The chi-square test and Fisher's exact test were used, as appropriate, to compare data from the different target groups. The data were descriptive and were reported as comparisons of frequency distributions. A P value < 0.05 was considered significant.

RESULTS

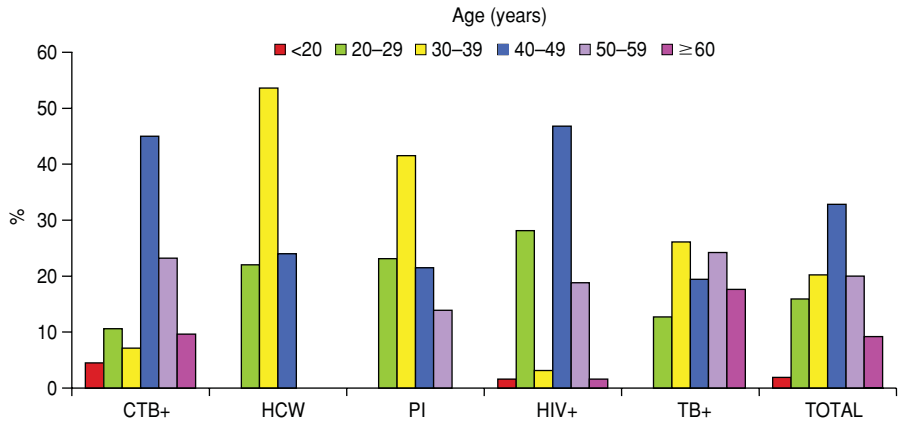
All 560 subjects recruited for the study had blood samples drawn and received both the TST and the QFT-G assay. Two subjects from the TB contacts group and four of the health care workers failed to return for the test reading and were therefore excluded from the study. Six study subjects from the HIV-positive group had indeterminate results, even after repeating the procedure, so were also excluded. The 15 subjects from the TB-infected [control] group found to be coinfected with HIV had indeterminate and nonreactive results and therefore were also excluded from the study. Therefore, the study analysis was based on a final sample of 533 individuals from the original subject pool. Distribution by high-risk group is shown in Figure 1. Most of the subjects were male (73.5%) and between the ages of 40 and 49 years (32.8%) (Figure 2).

FIGURE 1. Distribution of study sample for cross-sectional comparison of QuantiFERON®-TB Gold assay and tuberculin skin test in diagnosis/screening for latent tuberculosis (TB) infection, by high-risk group, Trinidad & Tobago, February–October 2007



CTB+ = contacts of TB patients; HCW = health care workers; PI = prison inmates; HIV+ = HIV patients; TB+ = TB patients (controls)

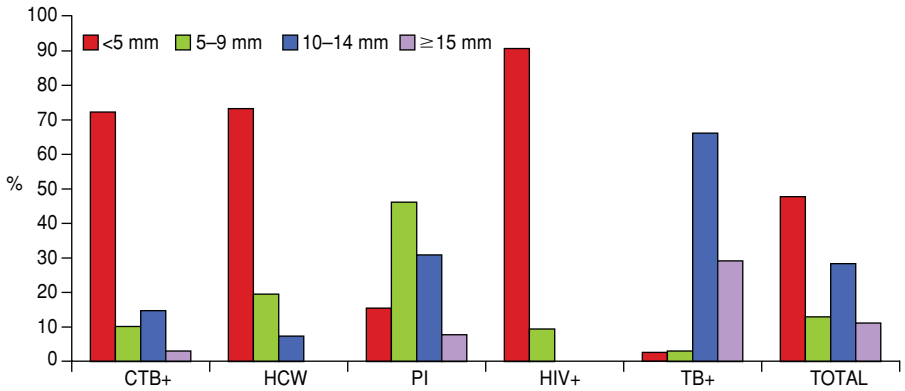
FIGURE 2. Age distribution of study sample for cross-sectional comparison of QuantiFERON®-TB Gold assay and tuberculin skin test in diagnosis/screening for latent tuberculosis (TB) infection, by high-risk group, Trinidad & Tobago, February–October 2007



CTB+ = contacts of TB patients; HCW = health care workers; PI = prison inmates; HIV+ = HIV patients; TB+ = TB patients (controls)

The TST results are summarized in Figure 3 by high-risk group. Surprisingly, only 1.8% (3/165) of the TB patient (control group) readings were < 5 mm and only 3% (5/165) were 5–9 mm. As expected, 95.2% of the TB patients had a wheal reaction ≥ 10 mm. None of the HIV subjects had a reaction ≥ 10 mm but most of them (90.6%) had a reaction < 5 mm; the rest (9.4%) had a reaction measuring 5–9 mm. Among the health care workers, there were no TST readings ≥ 15 mm, but most (73.2%) were < 5 mm. In Trinidad & Tobago, a TST reading > 10 mm among uncompromised individuals is considered a positive result. For individuals with HIV or any other underlying disease condition, such as malignancy, the positive cutoff threshold drops to 5–9 mm. Therefore, the 9.4% of HIV-positive subjects in the current study with readings at that level were considered to have positive TST results. Cutoff thresholds for interpretation of actual TST results (which are not considered biologically meaningful) range from 5 mm to 15 mm, depending on the type of high-risk group being surveyed and the level of TB prevalence in the study setting. The positive cutoff values used in the current study are relatively high but did not affect the final study results due to the clustered distribution of the induration values described above.

FIGURE 3. Tuberculin skin test (TST) readings among study sample for cross-sectional comparison of QuantiFERON®-TB Gold assay and TST in diagnosis/screening for latent tuberculosis (TB) infection, by high-risk group, Trinidad & Tobago, February–October 2007



CTB+ = contacts of TB patients; HCW = health care workers; PI = prison inmates; HIV+ = HIV patients; TB+ = TB patients (controls)

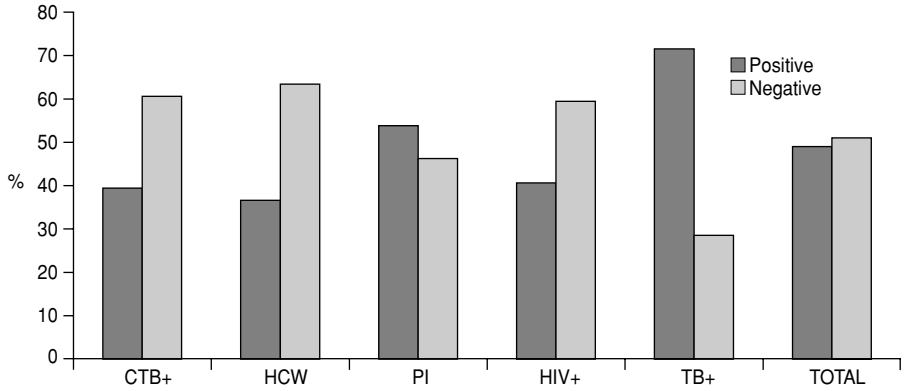
As shown in Figure 4, 71% of the TB-positive subjects, 40.6% of the HIV-positive subjects, 36.6% of the health care workers, and 53.8% of the prison inmates had positive results for the QFT-G assay. A comparison of the results from the QFT-G assay and those from the TST is shown in Table 1.

Based on the study results, the QFT-G assay detected a significantly higher proportion of LTBI-infected individuals than the TST in all high-risk groups except TB patients (the study controls), among whom the TST appeared to be more effective. These differences were statistically significant among all target groups studied for each testing method.

There was no significant age difference between the TST-positive subjects and those with positive results for the QFT-G assay, who ranged from 20 to 61 years and 21 to 59 years respectively (with a mean age of 33.1 versus 34.5 years; $P > 0.05$). As mentioned above, the majority of the subjects were males. Most of the HIV- and TB-positive subjects (68.8% and 69.7% respectively) were in the 30–59 year age group. The average number of hours required to complete the TST was 70.1 hours versus 23.4 hours for the QFT-G assay ($P < 0.0001$). The average cost to perform each TST was US $3.70 (for a total cost of US $2 065), whereas US $18.60 was required to carry out the QFT-G assay (total cost of US $10 440.00). These differences were significant (US $3.70 versus US $18.60; $P = 0.0008$) and favored use of the TST method for LBTI detection.

When the results of both tests were combined, the rate of LTBI detection increased to 88.4%. In the prison inmate group, concomitant results for both tests were available for all 65 subjects. Of these, 38.5% (15/65) tested positive based on the TST and 53.8% (35/65) tested positive based on the QFT-G assay. The rate of concordance between the two tests for this target group was 49.2% (32/65) for negative results, 15.3% (10/65) for positive results, and overall agreement of 75%. For all discordant results, subjects were more likely to be TST-positive and QFT-G–negative (92.9%) versus TST-negative and QFT-G–positive (7.1%). Overall, 39.4% of all subjects had a positive TST result and 51% had a positive QFT-G assay result. The significant differences obtained for TAT favored the QFT-G assay, whereas the cost of materials required to perform the tests favored the TST.

FIGURE 4. QuantiFERON®-TB Gold assay (QFT-G) results among study sample for cross-sectional comparison of QFT-G and tuberculin skin test in diagnosis/screening for latent tuberculosis (TB) infection, by high-risk group, Trinidad & Tobago, February–October 2007



CTB+ = contacts of TB patients; HCW = health care workers; PI = prison inmates; HIV+ = HIV patients; TB+ = TB patients (controls)

DISCUSSION

Unlike the TST and IFN-γ analysis, most diagnostic assays for detecting *M. tuberculosis* infection are based on either isolation or identification of the bacteria, which makes them inapplicable for diagnosis of latent infection. The development of IFN-γ tests to detect T-cells specific for *M. tuberculosis* antigens addressed this important issue. The current study was carried out among individuals from various groups with a high risk of developing TB due to exposure to or contact with TB patients, lack of isolation facilities, or weak infection control. In the current study, the two selected testing methods (QFT-G and TST) detected LTBI among the various target groups at different rates.

Among the TB patient [control] group, the rate of TB detection by the QFT-G assay (71.5%) was significantly higher than that of the TST. This rate of detection was similar to that observed by Lee et al., who reported a sensitivity of 70% among 87 patients diagnosed with TB (5), and higher than both the 64.4% rate of detection observed by Kobashi et al. in Japan (6) and the rate observed by Dewan et al., who reported a sensitivity of 60% in culture-confirmed cases (7). However, the 71.5% rate was lower than that reported by both Kang et al. (81% sensitivity in 54 patients) and Mori et al. (89% sensitivity among 118 patients) (8, 9). More recently, Kobashi et al. demonstrated significant differences in the quantitative responses of IFN-γ to *M. tuberculosis* between patients with active TB disease and those with LTBI (10).

Combining the results for the QFT-G assay and the TST in the current study increased the overall sensitivity for detection of LBTI among the culture-confirmed TB-infected control group. This confirms and reinforces recommendations that negative results should not be used alone to exclude active TB but should be interpreted in conjunction with other clinical and diagnostic findings (11). It also underscores the fact that the QFT-G assay has a limited role in the evaluation of patients with culture-confirmed TB. The authors of the current study agree with Kobashi et al.'s conclusion that it would be difficult to use the QFT-G assay to completely discriminate active TB disease from LTBI (10).

In the current study, 40.6% of all HIV patients included in the analysis had a positive result for the QFT-G assay. This was in huge contrast to the earlier study by Kobashi et al. (6), in which all HIV patients produced QFT-G–positive results. The indeterminate or nonreactive results observed in some of the HIV-positive subjects in the current study also contrast with those found by Ferrara et al. (11). In the current study, the QFT-G assays were run several times to minimize the effect of laboratory and procedural errors. However, the indeterminate and nonreactive results persisted, with test results continuing to produce low mitogen levels. Although all indeterminate or nonreactive results were excluded from the final analysis, the QFT-G assay results should be interpreted with caution, bearing in mind the high prevalence of HIV in Trinidad & Tobago and the Caribbean region. There are several possible explanations for a high rate of indeterminate and nonreactive results, including the presence of lymphocytopenia and/or inflammatory and immunosuppressive conditions, as well as hypoalbuminemia, which suggests poor nutritional status (12), and there is a high probability that some of these conditions could have existed among the subjects of the current study. Lymphocytopenia (especially the CD4 strain) has been shown to depend on the elaboration of inflammatory cytokines by T-cells previously sensitized to *M. tuberculosis*–specific antigens in QFT-G assays. In the blood, mononuclear cells from peripheral blood are stimulated in vitro, and the production of IFN-γ from sensitized T-lymphocytes by *M. tuberculosis*—specific antigen is measured by ELISA in the QFT-G (13).

In the current study, however, only 57.9% of TST-positive subjects had a positive QFT-G result. More than half of this group consisted of prison inmates with a

TABLE 1. Comparison of QuantiFERON®-TB Gold (QFT-G) assay and tuberculin skin test (TST) in diagnosis/screening for latent tuberculosis (TB) infection among high-risk groups (number and frequency of cases detected, and average cost and turnaround time per test), Trinidad & Tobago, February–October 2007

Target group	No. subjects tested	No. cases detected (%)		*P*
		TST	QFT-G	
Contacts of TB patients[a]	198	35 (17.7)	78 (39.4)	< 0.001
Health care workers	41	3 (7.3)	15 (36.6)	< 0.003
Prison inmates	65	15 (23.0)	35 (53.8)	< 0.006
HIV patients	64	12 (18.8)	26 (40.6)	< 0.0006
TB patients (controls)	165	157 (87.2)	118 (71.5)	< 0.008
Total	533	210 (39.4)	272 (51.0)	0.08
Cost per test[b]		$3.70	$18.60	< 0.0008
Turnaround time[c]		70.2	23.3	< 0.0001

[a] Individuals exposed to active TB (mainly friends and family of TB-infected patients).
[b] In 2009 US dollars ($1 = 6.30 TTD).
[c] Average number of hours from administration of the intradermal injection on subjects' forearms to the certified nurses' readings of the wheal reaction at puncture.

documented TST > 10 mm. In Trinidad & Tobago, TST is likely to be a very good indicator of latent infection in recently exposed individuals because 1) most individuals under the age of 20 years did not receive the BCG vaccination, which was discontinued during the early 1990s, and 2) BCG vaccination has been observed to significantly increase the likelihood of a positive TST in subjects without LTBI.

Multiple outbreaks of TB, including those involving the multi-drug-resistant strain (MDR-TB), have been reported in prisons and jails, especially among HIV-infected inmates, a population regarded as having moderate risk of acquiring TB (14). The results of the current study from this moderate-risk population show that prevalence of LTBI was 38.5% and 53.8% based on the TST and the QFT-G assay respectively. These values were quite high compared to those observed in correctional facilities in the United States, where prevalence was less than 10%. However, the QFT-G values obtained in the current study were in line with the current rate of TB in Trinidad & Tobago, which is estimated to be about 17 per 100 000 population (15).

It has been suggested that annual TB screening of prison inmates using the TST may account for the increase in the number of TST-positive results, due to the "boosting" effect caused by repeat use of the test. However, this type of screening is not carried out among prison inmates in Trinidad & Tobago. Therefore, the high rate of TST-positive results in the current study was attributed mainly to exposure to the disease.

The prevalence of LTBI among health care workers using the TST in the current study was a mere 7.3%. This value was very low compared to those reported by studies in Portugal (33%) and Germany (10%) (16, 17). The low value found in the current study may have been due to a smaller sample size and the use of a higher positive cutoff. Like the studies in Portugal and Germany, the current study showed that the QFT-G assay was more useful than the TST in identifying LTBI among health care workers. As this target group may be exposed to TB more frequently than the local population, screening of staff exposed to the disease is frequently recommended to identify infected individuals and treat them adequately and promptly. Because the QFT-G assay was more sensitive than the TST in detecting LTBI, the authors of the current study strongly support its use in screening health care workers in Trinidad & Tobago.

The TST may also be less desirable due to complications in interpreting its results caused by the above-mentioned boosting effect (from repeat testing) as well as conversions and reversions (changes in results from negative at baseline to positive and vice versa, respectively). In a study on health care workers in India, Pai et al. suggested that individuals with recent exposure to TB usually presented with large increases (≥ 10 mm) in TST indurations that were always accompanied by substantial increases in IFN-γ (18). This finding was in line with the results of the current study.

The QFT-G assay also fared better than the TST in terms of TAT. In terms of cost, however, the TST appears best suited for the resource-strapped environment of Trinidad & Tobago, assuming the calculation of this variable is based mainly on the cost of the materials required to perform the test (versus the cost of labor and other inputs). This argument is partly supported by Pooran et al., who concluded in a recent report that screening for LTBI using TST alone was the most cost-effective testing strategy but ultimately incurred the highest cost due to test inaccuracies (19). Another factor that may make the TST less cost-effective over time is high replacement costs, since the Mantoux test solution is often not accessible in developing countries and would have to be replaced with the relatively labor-intensive IFN-γ release assay. Minimizing cost for TB testing has become increasingly important because prevalence of the disease has fallen dramatically in developed countries and more than 90% of all cases worldwide occur in resource-strapped developing countries (20). However, as pointed out by both Diel et al. and Marra et al., use of the IFN-γ release assay alone or in combination with the TST for screening close TB contacts prior to LTBI treatment is highly cost-effective in reducing the TB disease burden (21, 22).

Study limitations

An inherent limitation of the current study or any analysis designed to compare cost and TAT against an imperfect, conventional test such as the TST is that no gold standard has been established for resolution of discordant results. Another limitation of this study is its small sample size and limited number of heterogeneous subjects, which constrain generalization of the results to a larger population.

Conclusions

Despite these limitations, similar to other reports (6, 19), the current comparison of TST and QFT-G assay results supports the conclusion that the QFT-G assay provides more accurate results than the TST in detecting LTBI, and has a faster turnaround. However, the QFT-G assay appears to be more expensive and produces indeterminate and nonreactive results for immunocompromised individuals such as HIV patients. Therefore, caution must be exercised when screening or diagnosing LTBI based on QFT-G assay results in a resource-poor, high–HIV prevalence setting such as Trinidad & Tobago.

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RESUMEN

Comparación entre la prueba QuantiFERON®-TB Gold y la prueba cutánea de la tuberculina para detectar la infección tuberculosa latente en grupos destinatarios en Trinidad y Tabago

Objetivo. Comparar la prueba QuantiFERON®-TB Gold (QFT-G) con la prueba cutánea de la tuberculina (PPD) para el tamizaje y diagnóstico de la infección tuberculosa latente (ITBL) en personas con alto riesgo de tuberculosis en Trinidad y Tabago.
Métodos. Para el estudio, se reclutó un total de 560 individuos (personas en contacto con pacientes de tuberculosis, pacientes con VIH, trabajadores de la salud, presidiarios y pacientes de tuberculosis [grupo testigo]). Las muestras de sangre se extrajeron y procesaron utilizando la prueba QFT-G, seguida de la aplicación inmediata de la solución de PPD en el antebrazo de las personas. Los datos se analizaron con el software Epi Info™ 3.5.1. Los resultados obtenidos en los grupos destinatarios se compararon utilizando la prueba de la ji al cuadrado ($P < 0,05$).
Resultados. La prueba QFT-G detectó la infección tuberculosa latente en 51% de los individuos (la mayoría de los resultados positivos se presentaron en el grupo testigo) mientras que la prueba PPD la detectó en 39,4% ($P = 0,001$). En términos generales, la prueba QFT-G detectó la infección tuberculosa latente con mayor frecuencia que la PPD en todos los individuos, excepto en aquellos del grupo testigo, donde el índice de detección favoreció a la PPD. La prueba QFT-G produjo resultados indeterminados y no reactivos en algunos pacientes con VIH, pero requirió menos tiempo de respuesta que la PPD (23,3 h contra 70,2 h; $P < 0.0001$). La prueba PPD tuvo un costo menor por individuo que la QFT-G (US$3,70 en comparación con US$18,60; $P = 0.0008$).
Conclusiones. La prueba QFT-G tuvo un costo más elevado, pero la tasa de detección fue más alta en la mayoría de los grupos destinatarios y el tiempo de respuesta fue más rápido en comparación con la PPD. Sin embargo, la sensibilidad de la prueba QFT-G fue inferior entre los individuos inmunodeficientes. Por consiguiente, se deben tomar las precauciones necesarias para utilizar la prueba QFT-G en el tamizaje y diagnóstico de ITBL en entornos de escasos recursos y alta prevalencia de VIH como Trinidad y Tabago.

Palabras clave Tuberculosis latente; prueba de tuberculina; prueba ELISA; Trinidad y Tabago.