Original Article

Latent Tuberculosis Infection among Household Contacts of Tuberculosis Patients, Healthcare Workers, and Tuberculosis Patients Using QuantiFERON-tuberculosis Gold Plus and Tuberculin Skin Test in a Tertiary Care Hospital Setting Bhubaneswar, Odisha – A Cross-sectional Study

Braja Sundar Barik[1,2], Chinmay Divyadarshi Kar[1], Shritam Das[1], Tahziba Hussain[1], Sasmita Nayak[2], Arun Kumar Sahu[3], Sooman Sundaray[3], Sanghamitra Pati[1]

[1]Division of NCDs, ICMR-Regional Medical Research Centre, Bhubaneswar, Odisha, India, [2]Department of Biotechnology, School of Biotechnology, KIIT University, Bhubaneswar, Odisha, India, [3]Department of TB and Chest Diseases, Capital Hospital, Bhubaneswar, Odisha, India

Abstract

Introduction: Contacts of tuberculosis (TB) patients have an increased risk of latent TB infection (LTBI). Currently, it is diagnosed using one of the two methods: Tuberculin skin test (TST) or QuantiFERON-TB Gold Plus. This study aims to estimate the concordance of TST and QFT-TB Gold Plus and associated factors among 73 healthcare workers (HCWs) and 172 household contacts (HHCs) who came in contact with active TB patients. This study was conducted from January to June 2023. **Methods:** Prevalence and agreement were calculated. A regression analysis was performed to assess the predictors of discordance factors. **Results:** The prevalence of latent TB was 20.40% (n = 50), defined as a positive result on either test. The overall agreement among participants was 62.04%, with a kappa coefficient of 0.26 (0.16–0.36, 95% confidence interval [CI]) (McNemar, $P < 0.001$). A higher risk of LTBI was associated with BCG vaccination history, odd ratio 1.63, (95% CI 0.78–3.43) for TST and 0.51 (95% CI 0.22–1.15) for QFT, but this was not significant. Moreover, in our study, only the body mass index of 18.5–25 kg/m^2 yielded an odds ratio of 2.33 (95%CI 0.77–6.47) for TST and 1.72 (95% CI 0.48–6.05) for QFT, was significant. Compared with QFT-TB Gold Plus, the sensitivity and specificity of TST were 80.65 (68.63–89.58) and 55.74 (48.22–63.06). **Conclusion:** TST exhibited a profound level of agreement with the QFT-Gold Plus assay but showed a higher rate of positivity due to some associated factors among HCWs, HHCs, and TB patients.

Keywords: Bhubaneswar, comparison, interferon-gamma release assays, latent tuberculosis infection, QuantiFERON-TB gold plus assay, tuberculin skin test

Introduction

Of all communicable diseases, tuberculosis (TB) caused by *Mycobacterium tuberculosis (M. tb)* is the primary reason for morbidity and mortality. The incidence of TB has increased from 10.6 million cases globally in 2022, and from 10 million cases in 2020 to 10.3 million cases in 2021. Each year, over 10 million individuals are infected with TB and approximately, 1 million die from it.[1] The estimated TB incidence in India in 2022 is 2.77 million, accounting for approximately 28% of the global TB burden ranking among the top three countries globally.[1,2] Even though TB is spread by the air, not everyone who is exposed to it gets infected. Nearly 95% of people have a unique T-cell pathophysiology, which causes the infection to be latent and leave some viable bacilli

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jgid

DOI: 10.4103/jgid.jgid_78_24

Address for correspondence: Dr. Tahziba Hussain, Division of NCDs, ICMR-Regional Medical Research Centre, Chandrasekharpur, Nandankanan Road, Bhubaneswar - 751 023, Odisha, India.
E-mail: tahziba_hussain@hotmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Barik BS, Kar CD, Das S, Hussain T, Nayak S, Sahu AK, *et al*. Latent tuberculosis infection among household contacts of tuberculosis patients, healthcare workers, and tuberculosis patients using quantiFERON-tuberculosis gold plus and tuberculin skin test in a tertiary care hospital setting Bhubaneswar, Odisha – A cross-sectional study. J Global Infect Dis 2025;17:52-9.

Received: 03 April 2024 **Revised:** 11 July 2024
Accepted: 07 February 2025 **Published:** 31 March 2025

that can reactivate and cause active TB disease. Individuals who have contracted TB can be categorized as asymptomatic, noninfectious state, similar to latent TB infection (LTBI), or as having active TB, which is transmissible and depicted by signs and symptoms. LTBI is the immune response to *M. tb* antigen stimulation in the absence of clinically active TB. In this context, treating LTBI becomes critical.[3,4] In order to stop the global TB epidemic by 2035, the World Health Organization (WHO) adopted the end TB strategy in 2014. It establishes interim targets for 2020, 2025, and 2030 which suggest that for every lakh people, there should be <10 cases of TB. Despite the WHO's 2035 global target of ending TB, the Indian government has declared that it wants to achieve this goal by 2025. According to a 2019 mathematical modeling study, there were 1.7 billion LTBI worldwide and the global prevalence was 24.8%. In healthy individuals, the life-time risk of developing TB is 5%–10%.[5-7] It is crucial to diagnose and treat LTBI in order to achieve the end TB strategy goal in a high prevalent country like India. Diagnosing and treating LTBI to stop clinically active TB disease is an essential component of end TB strategy.[6,7] Tuberculin skin test (TST) and interferon-gamma release assays (IGRA) or Quantiferon (QFT-TB) Gold Plus assay are the two most commonly used methods for diagnosing LTBI. TST has low sensitivity in immunocompromised individuals and low specificity (as a result of environmental nontuberculous mycobacteria [NTM] or prior BCG vaccination), whereas IGRA outcomes are affected by a distinctiveness. Due to the presence of antigens in purified protein derivative (PPD) in collective by numerous species of mycobacteria, TST lacks sufficient specificity for diagnosis.[8-10] Test that identify existence of immune responses to specific antigens to *M. tb*, *in vitro*, are called IGRAs. These consist of the TB 7.7, Culture Filtrate Protein 10 (CFP-10), and Early Secretory Antigenic Target-6 (ESAT-6). The majority of NTM and BCG strains lack the antigens found in IGRAs, in contrast to the TST. In a number of countries, IGRA has been used as a TST substitute or diagnostic test for LTBI in the event of a positive TST result. While IGRA is more sensitive than TST for *M. tb* infection, its sensitivity is known to be lowered by a number of factors, including homozygosity for HLA-DRB1 * 0701, body mass index (BMI) <18 kg/m^2 and advanced age. Currently, QFT-TB Gold Plus, a newer version of IGRA is commercially used. QFT-TB Gold Plus includes Nil, TB1, TB2, and Mitogen tubes. The TB1 is specific for response of CD4 T-cell and contains peptides of ESAT-6 and CFP-10; TB2 contains peptides of ESAT-6 and CFP-10 to find out responses of CD4 and CD8 T-cell and mitogen is the positive control.[11-13] Using whole proteins rather than peptides improves the sensitivity of the assay because the proteins may contain multiple epitopes that stimulate T cells more potently and possibly result in higher interferon gamma (IFN-γ) values when they are broken down into different small peptides. While these tests provide significant operational benefits, the doctor administering them faces a number of difficulties. These concerns, include: (1) low or variable sensitivity, including discordance with TST; (2) poor reproducibility; (3) restricted interpretive criteria; (4) lower efficacy in children; and (5) unknown prognostic value.[14,15] The WHO states that approximately 25%–28% of the global population harbors LTBI According to TST surveys. Studies conducted across India have measured the frequency of TB infection within groups at high-risk for the disease, such as healthcare workers (HCWs), refugees, patients with diabetes and rheumatoid arthritis as well as household contacts (HHCs). Healthcare professionals face the risk of contracting TB at work through nosocomial infection. It is critical to comprehend the current burden of TB infection at the population level in a country like India where the disease is endemic.[16-19] Individuals who live in the same household as an active TB patient called HHCs are also exposed to the active case, including deprivation, unfavorable environmental factors, history of TB, incomplete nutrition and limited access to healthcare. As a result, they are more likely to pass away from the illness. Creating methods to test these individuals at high risk for TB infection could aid in determining who requires chemoprophylaxis. Hence, a result showing positive is not always linked to infection by *M. tb*; it could be a result from reactions due to cross immunity in those who had received BCG vaccination or who were weakened by NTM.[20,21] Despite the fact that IGRA test is authorized for the identification of LTBI, we assessed the performance of TST in comparison to QFT-TB Gold Plus and the common factors associated such as BCG vaccination, BMI, and previous TB history in both HHCs, HCWs due to the difficulties associated with the diagnosis of this illness.

Methods

Research quality and ethics statement

The detailed protocol of the study was reviewed and authorized by Institutional Human Ethics Committee of ICMR-Regional Medical Research Centre, Bhubaneswar, Odisha (ICMR-RMRC/IHEC-2022/112, Dt-2/3/2022). Written informed consent was obtained from all the study participants.

Methodology

This study was carried out in the department of Pulmonary Medicine, Capital Hospital Bhubaneswar, Odisha. We sequentially enrolled the 172-HHCs of the active TB cases, 73 healthcare workers and 29 NTEP registered clinically active pulmonary TB patients who sought treatment at the hospital (26 drug sensitive cases and 3 multidrug-resistant cases), between January and September, 2023. Among the 29 index cases, six patients were hospitalized due to their critical health status. The diagnosis of active TB was made through the positive results from the Microscopy, Chest X-ray, Xpert MTB/RIF tests, TrueNAT MTB/RIF, and culture. Those who were 18 years of age or older, without any clinical symptoms of TB, and who had contact with the index cases at home or in the hospital for at least the previous 3 months were included in the study. Staff members at the hospital documented the HHCs list from the index cases on their initial visit. Informed consent was obtained from each participant who agreed to enroll. A questionnaire was used to review the history of TB incidence,

BCG vaccination history, BMI among HCWs and HHCs. Participants below 18 years, pregnant woman, breast feeding woman, skin condition which interferes the TST reading and who had vaccinated with any kind of live vaccine within 6 months were excluded from the study. TST was performed using 0.1 mL of (PPD RT23) that was injected intradermally into the volar surface of hand. The induration was observed after 48–72 h following the injection and the results of TST were analyzed as depict in Figure 1. An induration of >10 mm was considered to be positive. The assay was carried out in compliance with the manufacturer's guidelines. QFT-Plus test kit comprises of four heparinized vacuutainer (Qiagen, Germany) tubes: Nil, TB1, TB2, and Mitogen used to collect whole blood. The blood samples were mixed thoroughly and were kept in an incubator for 16–24 h at 37°C. The tubes were centrifuged at 2500 rpm for 15 min and plasma was preserved at − 20°C till IGRA assays were conducted. We used an Erba Lisa Scan EM (Transasia, Bio-medical, UAE) to perform QFT-Plus ELISA assays. The TB1/TB2-nil of ≥0.35 (IU/mL) and nil values ≥25% characterize as positive result; whereas, TB1/TB2-nil <0.35 IU/mL nil values <25% when mitogen ≥0.5 IU/mL was defined as a negative result. These criteria by manufacturer were followed for the interpretation of the results as positive, negative, and indeterminate. Additional data showed that IGRA readings of 0.2 IU/mL to 0.7 IU/mL were treated as borderline. Hence, the results were elucidated as ≥0.7 IU/mL-positive, ≤0.35 – <0.7 IU/mL-borderline-positive, ≤0.2 – <0.35 IU/mL-borderline-negative, and <0.2 IU/mL-negative. If TB1 and TB2 tubes showed >0.7 IU/mL and IFN-γ were ≥10 IU/mL. Re-sampling was done.

Diagnostic measurement

In order to rule out active TB, HCWs, and HHCs (positive QFT-TST) with productive coughs underwent AFB microscopy, Xpert MTB/RIF, and chest X-rays.

Statistical analysis

The concordance between TST and IGRA was measured qualitatively using Cohen's kappa value as poor, fair, moderate, good, and very good agreement, respectively. Data were

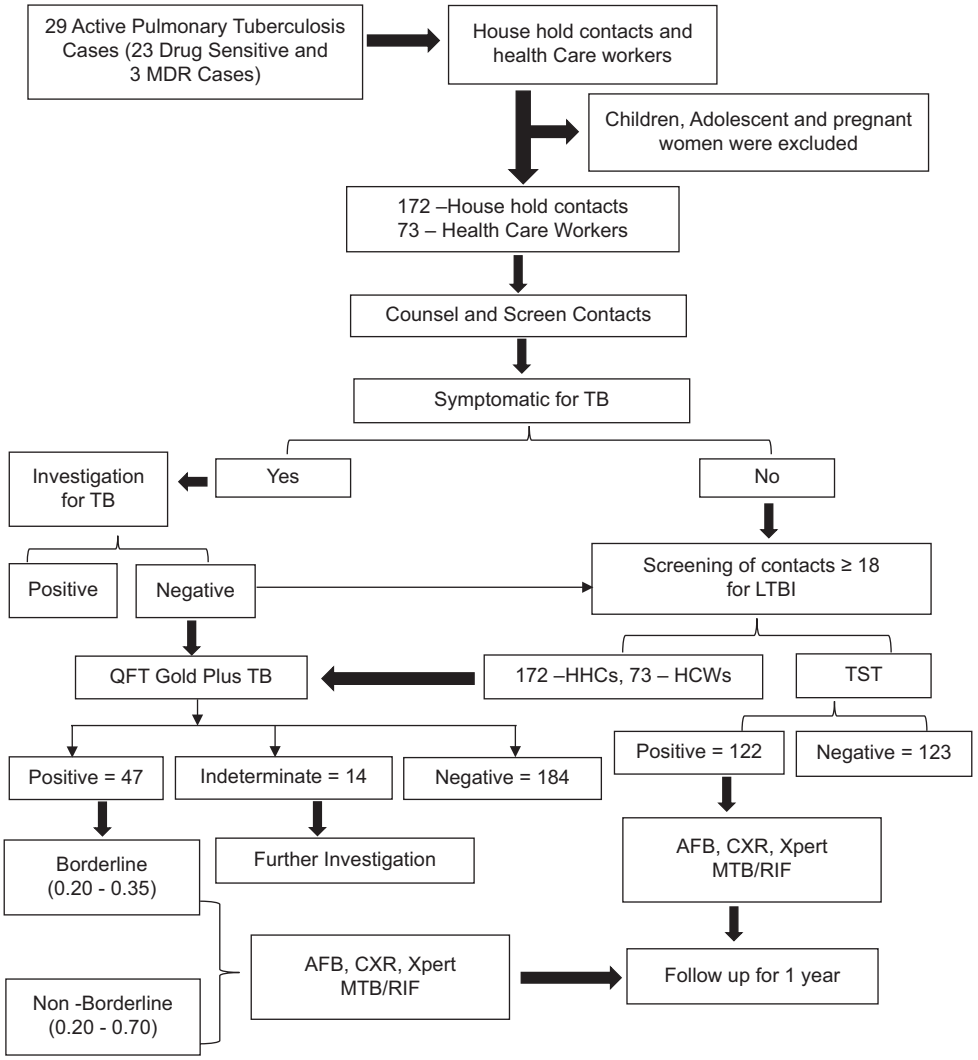

Figure 1: The flow chart oablef methodology. LTBI: Latent tuberculosis infection, HHCs: household contacts, HCWs: Healthcare workers, TST: Tuberculin skin test

analyzed using the STATA version 16.0 (STATA Corporation, Texas, USA). To determine the base line characteristics and factors associated with LTBI, descriptive statistics was used. The prevalence of LTBI was calculated with 95% confidence interval (CI) using TST and QFT-TB Gold Plus. Regression analysis was done to estimate the odd ratio at 95% CI to analyze the variables associated with the LTBI. The concordance between TST and QFT-TB Gold Plus was assessed using kappa coefficient.

Results

Two hundred and forty-five participants who had close contact with 29 index cases were enrolled in this study. The TST and QFT was performed on the same day to avoid the false positive of QFT due to possible boosting effect of tuberculin. Participant with indeterminate QFT results were re-tested. Among 245 participants, 136 (55.51) belonged to the 18–40 years of age group, and 68 (51.65) of them tested positive for TST and 32 (51.65) for QFT [Table 1]. Out of 132 (53.88) male participants, 67 (51.15) tested positive for TST and 34 (54.84) tested positive for QFT. In contrast, 113 female participants showed 64 (48.85) positive results for TST and 28 (45.16) positive results for QFT. The individuals with BMI indices between 18.5 and 25 kg/m^2 exhibited the highest positive results for TST-100 (76.34) and QFT-45 (72.58). Positive TST result is significantly influenced by the history of BCG vaccination. The most favorable outcome is shown by the male with a BCG vaccination history of 71 (54.20). Among 245 contacts 172 (62.2) were house hold contacts of active TB patients and 73 (29.8) were healthcare workers. Among HHCs 107 (62.2) were positive for TST and 55 (31.9) were positive for QFT, while 24 (32.8) were positive for TST and 7 (9.5) were positive for QFT among HCWs.

Among all the participants, 50 (20.40%) were positive for TST and QFT; whereas 102 (41.63%) showed negative results. Table 2 shows the concordance between TST and QFT. Overall, the accordance of TST and QuantiFERON TB Gold Plus was 62.04%. The overall/positive/negative rates among health care workers (HCWs) was 71.42%, 71.12%, and 71.23%, respectively whereas among HHCs, the overall/positive/negative rates were 58.13%, 81.81%, and 47.00%, respectively. Among the total participants, the sensitivity of TST was 80.65% (95% CI 68.63–89.58) and specificity was 55.74% (95% CI 48.22–63.06), whereas, in HCWs and HHCs, the sensitivity was 71.43% (95% CI 29.04–96.33) and 81.82% (95% CI 69.10–90.92) and the specificity was 71.21% (95% CI 58.75–81.70) and 47.01% (95% CI 37.72–56.45) compared to QFT–TB Gold Plus as gold standard.

Among 73 HCWs, 5 individuals tested positive for both TST and QFT, 19 individual tested positive for TST but negative for QFT, 2 individual tested TST negative and IGRA positive, 47 individual tested negative for both. Whereas, among 173 HHCs, 45 individuals tested positive for TST and IGRA both, 62 individual tested positive for TST but Negative for IGRA, 10 individuals tested negative for TST and positive for IGRA and 55 individual tested negative for both. The overall value of Cohen's kappa coefficient (k-value) was 0.26 (0.16–0.36, 95% CI), 0.20 (95% CI 0.01–0.40) for HCWs, and 0.23 (95%

Table 1: The sociodemographic variables attributable to tuberculin skin test and QFT results

Variables	Total number of sample, *n* (%)	TST		QFT	
		Positive, *n* (%)	Negative, *n* (%)	Positive, *n* (%)	Negative, *n* (%)
Age (years)					
18–40	136 (55.51)	68 (51.91)	68 (59.65)	32 (51.65)	104 (56.83)
41–63	97 (33.59)	56 (42.75)	41 (35.96)	27 (43.55)	70 (38.25)
64–86	12 (4.90)	7 (5.34)	5 (4.39)	3 (4.84)	9 (4.92)
Gender					
Male	132 (53.88)	67 (51.15)	65 (57.02)	34 (54.84)	98 (53.55)
Female	113 (46.12)	64 (48.85)	49 (42.98)	28 (45.16)	85 (46.45)
BMI (kg/m^2)					
<18.5	47 (19.18)	24 (18.32)	23 (20.18)	13 (20.97)	34 (18.58)
18.5–25	176 (71.84)	100 (76.34)	76 (66.17)	45 (72.58)	131 (71.58)
>25	22 (8.98)	7 (5.34)	15 (13.16)	4 (6.45)	18 (9.84)
BCG vaccination history					
Yes	122 (49.80)	71 (54.20)	51 (44.74)	24 (38.71)	98 (53.55)
No	86 (35.10)	43 (32.82)	43 (37.72)	26 (41.94)	60 (32.79)
Unknown	37 (15.10)	17 (12.98)	20 (17.54)	12 (19.35)	25 (13.66)
TB past history					
Yes	13 (5.31)	10 (7.63)	3 (2.63)	5 (8.06)	8 (4.37)
No	232 (94.69)	121 (92.37)	111 (97.37)	57 (91.9)	175 (95.63)
Contacts					
HHCs	172 (70.2)	107 (62.21)	65 (37.79)	55 (31.98)	117 (68.02)
HCWs	73 (29.8)	24 (32.88)	49 (67.12)	7 (9.59)	66 (90.41)

TST: Tuberculin skin test, BMI: Body mass index, TB: Tuberculosis, QFT: Quantiferon

Table 2: Concordance between standard tuberculin skin test and QFT-tuberculosis gold plus (interferon-gamma release assays) assay

Attributes	QFT-gold plus result				Percentage agreement (95% CI)			Sensitivity (%)	Specificity (%)
TST result	Positive	Negative	Total	*P*	Overall percentage agreement	Positive percentage agreement	Negative percentage agreement		
Total									
Positive	50	81	131	24.63, 0.00001	62.04 (54.65–81.24)	80.64 (85.46–99.48)	55.73 (57.30–71.56)	80.65 (68.63–89.58)	55.74 (48.22–63.06)
Negative	12	102	114						
Total	62	183	245						
HCWs									
Positive	5	19	23	5.214, 0.0224	71.42 (64.92–84.43)	71.21 (47.82–100)	71.23 (60.90–83.24)	71.43 (29.04–96.33)	71.21 (58.75–81.70)
Negative	2	47	50						
Total	7	66	73						
HHCs									
Positive	45	62	107	13.22, 0.0002	58.13 (59.76–78.32)	81.81 (83.84–99.42)	47.00 (50.36–68.78)	81.82 (69.10–90.92)	47.01 (37.72–56.45)
Negative	10	55	65						
Total	55	117	172						
TB patients									
Positive	27	2	29	Not available	93.10 (81.90–99.78)	100 (49.23–100)	Not available	Not available	Not available
Negative	0	0	0						
Total	27	2	29						

HCWs: Healthcare workers, HHCs: Household contacts, TB: Tuberculosis, TST: Tuberculin skin test, CI: Confidence interval, QFT: Quantiferon

CI 0.11–0.34) for HHCs as depict in Table 3, and it was subsequently classified as fair for each.

The univariate analysis in Table 4 shows the risk factors associated with LTBI, age stratified in to 18–40 years, 41–63 years (1.35 [95%CI 0.80–2.30]) for TST and (1.25 [95%CI 0.69–2.27]) for QFT, 64–86 years (1.42 [95% CI 0.42–4.62]) and (1.08 [95% CI 0.27–4.24]) for QFT were associated with positive TST and QFT results. The male gender was a risk for both TST and QFT. Other variables that attributed the positive TST and QFT were BMI index of 18.5–25 kg/m^2 (2.23 [95% CI 0.77–6.47]) for TST and (1.72 [95% CI 0.48–6.05]) for QFT, having BCG vaccination history (1.17 [95% CI 0.78–3.43]) for TST and past history of TB (3.05 [95% CI 0.82–11.39]) for TST and (1.91 [95% CI 0.60–6.10]) for QFT. Among contacts, the HHCs were more prone to affected with LTBI than HCWs with an odd ratio of (3.45 [95% CI 1.88–6.35]) for TST and (4.46 [95% CI 1.88–10.55]) for QFT**.** In multivariate analysis, only the BMI index of 18.5–25 kg/m^2 (3.47 [95% CI 1.19–10.09]) for TST and (1.29 [95% CI 0.37–4.48]) for QFT, respectively.

Discussion

One hidden aspect of the greater TB epidemic affecting the entire world is LTBI. LTBI patients may eventually develop into the active form of TB, so getting a proper diagnosis and effective treatment is crucial to maintaining TB control.[22] Since, it is easy to use and offers proof of an anti-mycobacterial cellular immune response, *in vivo*, TST acted as the most widely used technique for the identification of LTBI. The BCG vaccine recipients, however, have the inconvenience of testing positive. Greater specificity has been added by the continued use of IGRAs and the new QTF-Plus version appears as a potential tool for separating active TB from LTBI. Studies of IGRA and TST from high-TB burden countries were used by the guidelines group of WHO to develop the WHO-LTBI management standard.[23-25] In general, our study showed a concordance rate of 62.04% between the TST and QFT-Gold Plus. The cause of indeterminate results is unclear, however, there are a number of possible causes, such as volume of the blood collected, mixing of blood, order of tubes, incubation hour, and delay in analyzing.[25-27] Our findings showed that the percentage of LTBI determined by IGRA and TST was 50/245 (HCWs and HHCs-20.40%). The percentage of positive IGRA among HCW was 5/73 (6.8%) and among HHCs was 45/172 (26.16%). We evaluated IGRA and TST outcomes to calculate the proportion of LTBI in the group of individual with presumptive LTBI and recommended examining despite the absence of a gold standard for LTBI diagnosis. Our findings contradict lower and higher rates of TST+/IGRA+ and TST-/IGRA-reported in earlier studies involving HCWs and HHCs. Our findings indicate a greater likelihood of LTBI among those recommended to be screened under our settings, necessitating precautionary action to tackle TB. In certain circumstances, the LTBI diagnosis is only taken into consideration in the event the two tests are positive. Our findings are consistent with earlier research, showing that the LTBI made up a larger percentage compared to using IGRA when using TST. A larger portion of TST+/IGRA-among contradictory outcomes is the result of this. IGRAs have reportedly been shown to have greater specificity than TSTs. Compared to IGRA, the TST is more sensitive. The chosen cutoff affects the sensitivity and specificity of TST.[25,28,29] For *M. tb* infection, a smaller cutoff will lead to a reduced specificity and greater sensitivity. General correlation between the TST and IGRA results is low, primarily

Table 3: The comparison between the QFT-tuberculosis gold plus and tuberculin skin test result in diagnosing latent tuberculosis infection

	TST			Kappa value (95% CI)
	Positive	Negative	Total (%) 95% CI	
QFT-TB gold plus				
Positive	50	81	131 (53.5%) 47.02–59.81	0.26 (0.16–0.36)
Negative	12	102	114 (46.5%) 40.19–52.98	
Total (%) 95% CI	62 (25.3) 20.09–31.32	183 (74.7) 68.68–79.91	245	
HHCs				
Positive	45	62	107 (62.2) 54.4–69.3	0.23 (0.11–0.34)
Negative	10	55	65 (37.8) 30.6–45.5	
Total (%) 95% CI	55 (31.9) 25.2–39.5	117 (68.1) 60.4–70.8	172	
HCWs				
Positive	5	19	24 (32.8) 22.6–44.9	0.20 (0.01–0.40)
Negative	2	47	49 (67.2) 55–77.4	
Total (%) 95% CI	7 (9.6) 4.2–19.3	66 (90.4) 80.6–95.7	73	

P (McNemar test)=<0.001, *K*=0.26 (0.16–0.36) for overall sample, *K*=0.23 (0.11–0.34) for HHCs, *K*=0.20 (0.01–0.40) for HCWs. HCWs: Healthcare workers, HHCs: Household contacts, TB: Tuberculosis, CI: Confidence interval, TST: Tuberculin skin test, QFT: Quantiferon

Table 4: The positivity and independent variables associated with latent tuberculosis infection

Variables	Univariate analysis				Multivariate analysis			
	TST		QFT		TST		QFT	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Age (years)								
18–40	Reference		Reference		Reference		Reference	
41–63	1.365 (0.80–2.30)	0.244	1.253 (0.69–2.27)	0.457	1.67 (0.88–3.16)	0.111	1.24 (0.61–2.49)	0.546
64–86	1.4 (0.42–4.62)	0.581	1.083 (0.27–4.24)	0.909	2.12 (0.40–11.06)	0.372	1.28 (0.21–7.50)	0.782
Gender								
Male	Reference		Reference		Reference		Reference	
Female	1.267 (0.76–2.09)	0.358	0.949 (0.53–1.69)	0.861	1.00 (0.47–2.11)	0.999	0.84 (0.36–1.97)	0.701
BMI (kg/m^2)								
<18.5	2.236 (0.77–6.47)	0.138	1.720 (0.48–6.05)	0.398	1.62 (0.50–5.30)	0.417	1.30 (0.32–5.20)	0.702
18.5–25	2.819 (1.05–7.25)	0.032	1.545 (0.49–4.08)	0.452	3.47 (1.19–10.09)	0.022	1.298 (0.37–4.48)	0.679
>25	Reference		Reference		Reference		Reference	
BCG vaccination history								
Yes	1.637 (0.78–3.43)	0.191	0.510 (0.22–1.15)	0.108	1.88 (0.75–4.70)	0.172	0.47 (0.18–1.24)	0.131
No	1.176 (0.54–2.54)	0.680	0.902 (0.39–2.06)	0.809	1.25 (0.50–3.15)	0.624	0.91 (0.35–2.36)	0.855
Unknown	Reference		Reference		Reference		Reference	
TB past history								
Yes	3.057 (0.82–11.39)	0.096	1.918 (0.60–6.10)	0.269	3.33 (0.81–13.70)	0.095	1.72 (0.49–6.04)	0.396
No	Reference		Reference		Reference		Reference	
Contacts								
HHCs	3.36 (1.88–5.98)	0.000	4.43 (1.90–10.29)	0.0001	3.45 (1.88–6.35)	0.000	4.46 (1.88–10.55)	0.001
HCWs	Reference		Reference		Reference		Reference	

HCWs: Healthcare workers, HHCs: Household contacts, TST: Tuberculin skin test, BMI: Body mass index, TB: Tuberculosis, OR: Odd ratio, CI: Confidence interval, BCG: Bacillus calmette guerin, QFT: Quantiferon

due to positive TST results in BCG-vaccinated individuals. Several national guidelines recommend an IGRA for confirmation of a suspected infection and initial TST screening to be able to increase the test specificity of the result.[8,10,28,29] Addressing the barriers associated with the testing of TST and IGRA among contacts in field settings includes identifying and reaching all contacts of active TB patients and reading after TST administration can be challenging due to logistical obstacles such as remote locations, limited transportation, difficulty in tracking contacts, laboratory facilities, sample collection, transport, storage (cold chain), processing and lack of awareness about the importance of follow-up visit. Cultural preconceptions, the stigma attached to TB, lack of health literacy, language barrier, efficient communication techniques, and mistrust of medical professionals can all have an impact on the contacts' willingness to participate in screening programs.

Limitation

Our study has some strengths and few limitations. A large number of patients were tested for TST and IGRA at the same time. Whereas few participants were reluctant to participate in this study, some of them denied to take TST due to the difficulty of returning to the hospital after 48–72 h for review of the outcomes. Due to very high cost of QFT Gold Plus (IGRA), it was not possible to do the LTBI tests among all the HCWs and HHCs who had close contact with the active TB patients. Another limitation is the small sample size because the IGRA tests were not widely used, which made it difficult to interpret the results.

Conclusion

TST and IGRA present varied advantages and specific challenges when screening contacts of active TB patients, when used in together, they can enhance diagnostic precision and support more successful global TB control and prevention initiatives. However, their usefulness is impacted by a number of risk factors, including BCG vaccination status, prior TB history, BMI, and access to healthcare. To optimize TB screening and control efforts in diverse populations, it is imperative to address these factors through customized strategies and integrated healthcare approaches. TST may have restrictions on its specificity and logistical needs, but it is still a useful tool in situations where resources are few.

Research quality and ethics statement

This study was approved by Institutional Human Ethics Committee of ICMR-Regional Medical Research Centre, Bhubaneswar, Odisha (ICMR-RMRC/IHEC-2022/112, Dt-2/3/2022). The authors followed applicable EQUATOR Network (https://www.equator-network.org/) guidelines during the conduct of this research project.

Acknowledgments

The authors would like to acknowledge the STO, Odisha, for facilitating study. We also acknowledge the support of TBHV, ANM, ASHAs, and other healthcare workers.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Global Tuberculosis Report. WHO; 2023. p. 1-75.
2. Chauhan A, Parmar M, Dash GC, Solanki H, Chauhan S, Sharma J, *et al*. The prevalence of tuberculosis infection in India: A systematic review and meta-analysis. Indian J Med Res 2023;157:135-51.
3. Lee SH. Tuberculosis infection and latent tuberculosis. Tuberc Respir Dis (Seoul) 2016;79:201-6.
4. Cohen A, Mathiasen VD, Schön T, Wejse C. The global prevalence of latent tuberculosis: a systematic review and meta-analysis. Eur Respir J 2019;54:1900655. doi: 10.1183/13993003.00655-2019.
5. Kiazyk S, Ball TB. Latent tuberculosis infection: An overview. Can Commun Dis Rep 2017;43:62-6.
6. Uplekar M, Raviglione M. WHO's end TB strategy: From stopping to ending the global TB epidemic. Indian J Tuberc 2015;62:196-9.
7. Hannah A, Dick M. Identifying gaps in the quality of latent tuberculosis infection care. J Clin Tuberc Other Mycobact Dis 2020;18:100142.
8. World Health Organization. Latent Tuberculosis Infection: Updated and Consolidated Guidelines for Programmatic Management. World Health Organization; 2018. p. 1-20.
9. Paton NI, Borand L, Benedicto J, Kyi MM, Mahmud AM, Norazmi MN, *et al.* Diagnosis and management of latent tuberculosis infection in Asia: Review of current status and challenges. Int J Infect Dis 2019;87:21-9.
10. Lee SH. Diagnosis and treatment of latent tuberculosis infection. Tuberc Respir Dis (Seoul) 2015;78:56-63.
11. Chandrasekaran P, Mave V, Thiruvengadam K, Gupte N, Shivakumar SV, Hanna LE, *et al.* Tuberculin skin test and QuantiFERON-gold in tube assay for diagnosis of latent TB infection among household contacts of pulmonary TB patients in high TB burden setting. PLoS One 2018;13:e0199360.
12. Ndzi EN, Nkenfou CN, Gwom LC, Fainguem N, Fokam J, Pefura Y. The pros and cons of the QuantiFERON test for the diagnosis of tuberculosis, prediction of disease progression, and treatment monitoring. Int J Mycobacteriol 2016;5:177-84.
13. Pieterman ED, Liqui Lung FG, Verbon A, Bax HI, Ang CW, Berkhout J, *et al*. A multicentre verification study of the QuantiFERON(®)-TB Gold Plus assay. Tuberculosis (Edinb) 2018;108:136-42.
14. Sotgiu G, Saderi L, Petruccioli E, Aliberti S, Piana A, Petrone L, *et al.* QuantiFERON TB Gold Plus for the diagnosis of tuberculosis: A systematic review and meta-analysis. J Infect 2019;79:444-53.
15. Trajman A, Steffen RE, Menzies D. Interferon-gamma release assays versus tuberculin skin testing for the diagnosis of latent tuberculosis infection: An overview of the evidence. Pulm Med 2013;2013:601737.
16. 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.
17. 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.
18. Lee SJ, Lee SH, Kim YE, Cho YJ, Jeong YY, Kim HC, *et al.* Risk factors for latent tuberculosis infection in close contacts of active tuberculosis patients in South Korea: A prospective cohort study. BMC Infect Dis 2014;14:566.
19. Janagond AB, Ganesan V, Vijay Kumar GS, Ramesh A, Anand P, Mariappan M. Screening of health-care workers for latent tuberculosis infection in a Tertiary Care Hospital. Int J Mycobacteriol 2017;6:253-7.
20. Krishnamoorthy Y, Ezhumalai K, Murali S, Rajaa S, Jose M, Sathishkumar A, *et al.* Prevalence and risk factors associated with latent tuberculosis infection among household contacts of smear positive pulmonary tuberculosis patients in South India. Trop Med Int Health 2021;26:1645-51.

21. Karbito K, Susanto H, Adi MS, Sulistiyani S, Handayani OW, Sofro MA. Latent tuberculosis infection in family members in household contact with active tuberculosis patients in Semarang City, Central Java, Indonesia. J Public Health Afr 2022;13:2157.
22. Muñoz L, Stagg HR, Abubakar I. Diagnosis and management of latent tuberculosis infection. Cold Spring Harb Perspect Med 2015;5:a017830.
23. Çavuşoğlu C, Yaşar-Duman M, Sezai Taşbakan M, Işıkgöz-Taşbakan M, Nurullah Orman M. Evaluation of the performance of QuantiFERON®-TB Gold plus test in active tuberculosis patients. J Clin Tuberc Other Mycobact Dis 2021;23:100223.
24. Venkatappa TK, Punnoose R, Katz DJ, Higgins MP, Banaei N, Graviss EA, *et al.* Comparing QuantiFERON-TB Gold Plus with other tests to diagnose *Mycobacterium tuberculosis* Infection. J Clin Microbiol 2019;57:e00985-19.
25. Oh CE, Ortiz-Brizuela E, Bastos ML, Menzies D. Comparing the diagnostic performance of QuantiFERON-TB Gold Plus to other tests of latent tuberculosis infection: A systematic review and meta-analysis. Clin Infect Dis 2021;73:e1116-25.
26. Zhang Y, Zhou G, Shi W, Shi W, Hu M, Kong D, *et al.* Comparing the diagnostic performance of QuantiFERON-TB Gold Plus with QFT-GIT, T-SPOT.TB and TST: A systematic review and meta-analysis. BMC Infect Dis 2023;23:40.
27. Primaturia C, Reniarti L, Nataprawira HMN. Comparison between the Interferon γ Release Assay-QuantiFERON Gold Plus (QFT-Plus)-and Tuberculin Skin Test (TST) in the Detection of Tuberculosis Infection in Immunocompromised Children. Pulm Med 2020;10: 2020:7159485. doi: 10.1155/2020/7159485.
28. Auguste P, Tsertsvadze A, Pink J, Court R, McCarthy N, Sutcliffe P, *et al.* Comparing interferon-gamma release assays with tuberculin skin test for identifying latent tuberculosis infection that progresses to active tuberculosis: Systematic review and meta-analysis. BMC Infect Dis 2017;17:200.
29. Nienhaus A, Schablon A, Diel R. Interferon-gamma release assay for the diagnosis of latent TB infection – Analysis of discordant results, when compared to the tuberculin skin test. PLoS One 2008;3:e2665.