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Comparative evaluation of QuantiFERON-TB gold in-tube plus for *Mycobacterium tuberculosis* infection among adolescents in China

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Summary

To our knowledge, this is the first head-to-head study to evaluate QuantiFERON-TB Gold Plus, QuantiFERON-TB Gold In-Tube, ESAT6-CFP10, and tuberculin skin test among adolescents. Our study highlights the value of QFT-Plus in detecting *Mtb* infection among high school freshmen when compared to QFT-GIT.

Abstract

Background No head-to-head studies have simultaneously compared the performances of QuantiFERON-TB Gold In-Tube (QFT-GIT), QuantiFERON-TB Gold Plus (QFT-Plus), ESAT6-CFP10 (EC) skin test, and Tuberculin skin test (TST) in adolescents. This study aimed to conduct a comparative assessment of QFT-GIT and QFT-Plus for detecting *Mycobacterium tuberculosis*(*Mtb*) infection in high school freshmen.

Methods We concurrently administered QFT-GIT, QFT-Plus, EC skin test, and TST to first-year high school students. Blood samples were obtained for the QFT-GIT and QFT-Plus assays before the administration of the EC skin test and TST. The diagnostic values were compared. Discrepancies between the tests were quantified using Cohen's kappa coefficient.

Results A total of 787 freshmen were recruited in this study. Among 787 subjects, EC was positive in 0.8%, TST in 5.3%, QFT-GIT in 1.1%, and QFT-Plus in 3.2%. Overall agreements for QFT-GIT vs. QFT-Plus, QFT-Plus TB1, and QFT-Plus TB2 were 95.7% (95% CI, 94.0–97.0), 97.3% (95% CI, 95.9–98.3), and 95.9% (95% CI, 94.3–97.2), respectively. Cohen's kappa values were 0.485 (95% CI, 0.319–0.621), 0.593 (95% CI, 0.413–0.744), and 0.451 (95% CI, 0.274-0.600). Consistency rates for QFT-GIT, QFT-Plus, EC skin test, and TST were 96.6% (95% CI, 95.0, 97.0), 92.1% (95% CI, 89.0, 94.0), 94.5% (95% CI, 92.6, 96.1), and 91.2% (95% CI, 88.8, 93.1) with Cohen's kappa values of 0.19 (95% CI, -0.01, 0.38), 0.07 (95% CI, -0.02, 0.19), 0.08 (95% CI, -0.01, 0.23), and 0.12 (95% CI, 0.01, 0.21).

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Conclusion The QFT-GIT and QFT-Plus assays exhibited a high level of agreement but demonstrated a moderate correlation. IFN-γ levels measured by both QFT-GIT and QFT-Plus were comparable. Notably, Our study suggests QFT-Plus may detect a higher rate of *Mtb* infection among high school freshmen compared to QFT-GIT, EC skin test, and TST, though this requires cautious interpretation due to the absence of a gold standard for *Mtb* infection diagnosis.

Keywords Tuberculosis, QuantiFERON-TB gold plus, QuantiFERON-TB gold In-Tube, ESAT6-CFP10, *Mycobacterium tuberculosis* infection

Background

Approximately one-quarter of the world's population have been infected with *Mycobacterium tuberculosis*(*Mtb*), and 5–10% of them will develop active tuberculosis throughout their lives [1]. Screening for and providing preventive treatment to individuals at high risk of *Mtb* infection, such as individials in close contact with confirmed tuberculosis cases, has proven to be an effective strategy towards achieving the End TB Strategy by 2035 [2].

The Tuberculin skin test (TST) and interferon-γ release assay (IGRA) stand as the most widely employed methods for detecting *Mtb* infection [1]. However, challenges arise due to false positive attributed to cross-reactivity with *Mycobacterium* bovis bacillus Calmette-Guérin (BCG) vaccination and *Nontuberculous Mycobacterium*(NTM), limiting their utility. In contrast, IGRAs such as the QuantiFERON-TB Gold In-Tube (QFT-GIT) assay (Qiagen, Hilden, Germany) utilizing an enzyme-linked immunosorbent assay (ELISA) and the T-SPOT.TB assay (Oxford Immunotec, Abingdon, UK) employing an enzyme-linked immunosorbent spot (ELISPOT) assay demonstrated improved performance without cross-reactivity [3]. Nevertheless, a drawback lies in their relatively poor sensitivity for detecting *Mtb* infection in children and immunocompromised individuals [4, 5]. On June 8, 2017, the United States Food and Drug Administration (FDA) approved QuantiFERON-TB Gold Plus (QFT-Plus), a fourth-generation test, as a replacement for QuantiFERON-TB Gold In-Tube (QFT-GIT). QFT-Plus, a new-generation iteration of QFT-GIT, has become widely used for the diagnose of *Mtb* infection. In QFT-Plus, unlike QFT-GIT, the TB antigen 1 (TB1) tube is formulated with peptides derived from the 6-kDa early secretory antigenic target (ESAT-6) and the 10-kDa culture filtrate protein (CFP-10), excluding TB7.7, to specifically stimulate CD4 + T-helper lymphocytes. Meanwhile, the TB antigen 2 (TB2) tube is designed to elicit responses from both CD4 + T-helper lymphocytes and CD8 + cytotoxic T lymphocytes [6]. CD8 + cytotoxic T cells have emerged as a crucial element in the host's immune response to and regulation of *Mtb*, making it a more sensitive test to find *Mtb* infection. Thus far, it has demonstrated similar performance characteristics to the QFT-GIT and QFT-Plus among adults [7–9]; however, no direct comparative study assessing QFT-GIT and QFT-Plus for diagnosing *Mtb* infection among children in China has been conducted. In 2022, newer *Mtb* antigen-based skin tests were suggested as alternative methods for detecting *Mtb* infection [10], including a novel ESAT6-CFP10 (EC) skin test [11]. Furthermore, a recent meta-analysis has indicated that *M. tuberculosis* antigen-based skin tests are performed on par with interferon-γ release assay or TST to detect latent tuberculosis infection [12]. However, no studies have been conducted to assess the performance of the EC skin test in children. Additionally, no head-to-head studies have simultaneously compared the performances of different generations of QFT, EC skin test, and TST in children.

To address this question, we conducted a comparative study on high school freshmen in eastern China to compare the diagnostic performance of TST, the EC skin test, QFT-GIT, and QFT-Plus for detecting *Mtb* infection.

Methods

Study population and design

The study was conducted as a part of admission screening for grade ten freshmen in China in September 2022. Based on the Guidelines for Tuberculosis Prevention and Control in Schools in China, all freshmen and junior students in boarding schools must be screened for *Mtb* infection before school admission. For individuals experiencing fever (body temperature above 37.5℃), acute infectious diseases (such as measles, pertussis, influenza, pneumonia), acute conjunctivitis, acute otitis media, systemic skin diseases, allergies, and other conditions where the physician determines that skin testing is temporarily unsuitable, only the QFTs will be conducted during this session. Among participants, the EC skin test, QFT-GIT and QFT-Plus assays, and a TST were used to evaluate *Mtb* infection. The EC skin test is a recombinant reagent developed by Zhifei Longcom Biologic Pharmacy Company, China, and is approved by the National Medical Products Administration as a standard test for diagnosing *Mtb* infection, which is extensively utilized throughout China.

Procedures

All eligible students were inquiried about medical and allergy history, including acute infectious diseases (e.g., measles, pertussis, influenza, pneumonia, acute conjunctivitis and acute otitis media), history of multiple

drug allergies, allergic reactions, or psychosomatic disorders, and systemic skin conditions. Blood samples were obtained for the QFT-GIT and QFT-Plus assays before the administration of the EC skin test and TST. Subsequently, individuals underwent the TST on the volar surface of the left forearm and the EC skin test on the right forearm. Both the TST and EC skin tests were carried out utilizing the Mantoux method. TST and EC skin test results were assessed 48 to 72 h after administration, following established guidelines. The TST responses were evaluated with cutoff points of 10 mm [13], while the EC test used a cutoff of 5 mm [14]. The individuals responsible for interpreting the skin indurations were unaware of the QFT results. Different readers were assigned for the EC skin test and the TST. They independently measured the diameters of induration of TST or induration and redness of EC without access to the results of the other test.

We applied standard positive thresholds for the QFT, EC skin test, and TST. Results were considered positive for QFT-GIT and QFT-Plus assays if the IFN-γ concentration in the *Mtb* antigen tube (TB for QFT-GIT and either TB1 or TB2 for QFT-Plus) exceeded the IFN-γ concentration in the nil tube by at least 0.35 IU/ml and was at least 25% of the value in the nil tube. Results were deemed indeterminate if the IFN-γ concentration in the nil tube exceeded 8.0 IU/ml or if the IFN-γ concentration in the mitogen tube was less than 0.5 IU/ml. A positive TST result was established when the induration reaction measured 10 mm or more, while a positive EC skin test result was indicated by an induration reaction measuring 5 mm or greater.

Table 1 Characteristics of enrolled adolescents ($n=787$)

Characteristic	All
Median Age, yrs(IQR)($n=787$)	15.6 (15.3–15.9)
Sex	
Female	400 (50.8)
Male	387 (49.2)
Bacillus Calmette-Guérin scar($n=775$)	
No	240 (30.5)
Yes	535 (68.0)
Suspected symptoms($n=775$)	
No	604 (77.9)
Yes	171 (22.1)
Smokers in families($n=775$)	
No	597 (77.0)
Yes	178 (23.0)
EAST6-CFP-10 skin test($n=713$)	
Negative	707 (99.2)
Positive	6 (0.8)
Tuberculin skin test($n=775$)	
Negative	675 (94.7)
Positive	38 (5.3)
QuantiFERON-TB Gold In-Tube	
Negative	761 (96.7)
Positive	9 (1.1)
Indeterminate	17 (2.2)
QuantiFERON-TB Gold Plus	
Negative	744 (94.7)
Positive	26 (3.3)
Indeterminate	16 (2.0)

QFT-GIT and QFT-plus assays

The QFT-GIT and QFT-Plus assays (Qiagen, Hilden, Germany) were conducted in accordance with the manufacturer's instructions. Within four hours of collecting whole-blood samples in lithium heparin tubes, one milliliter of whole blood was transferred into a *Mtb* antigen tube for the QFT-GIT test and into *Mtb* antigen tubes (TB1 and TB2) for the QFT-Plus test, alongside separate tubes for nil and mitogen controls. These five tubes were promptly placed in a 37 °C incubator for 16–24 h. Quantitative measurement of IFN-γ was simultaneously performed for both assays using a DS-2 automated ELISA processor.

Statistical analysis

Our statistical analyses encompassed a combination of 2×2 contingency tables for categorical variables and the presentation of continuous variables using means and standard deviations (SD). Depending on appropriateness, we chose either the Fisher exact test or the Chi-square test to compare the two tests. Paired-Samples T-tests were employed to compare quantitative data. Additionally, we assessed the agreement between binary events in QFT-GIT and QFT-Plus using Cohen's kappa (k) coefficient. The kappa coefficients were categorized as follows: poor ($k\le0.20$), fair ($0.20<k\le0.40$), moderate ($0.40<k\le0.60$), good ($0.60<k\le0.80$), and very good ($0.80<k\le1.00$). We used bivariate correlation analysis to compare quantitative IFN-γ levels between QFT-GIT and QFT-Plus.

Result

A total of 787 freshmen were enrolled in this study, with 713 (90.6%) undergoing both EC skin tests and TST. All participants received QFT-GIT, except for one (0.1%) who did not experience QFT-Plus due to insufficient blood. Among all individuals, 400 (50.8%) were females. Five hundred thirty-five (68.0%) had BCG scars. Nearly one quarter (22.1%) had suspected symptoms (like persistent cough, chest pain, fever, night sweats) (Table 1).

In total, 6 students (0.8%) tested positive for EC, 38 (5.3%) were positive using the TST, 9 (1.1%) were QFT-GIT positive, and 25 (3.2%) through the QFT-Plus. Indeterminate results were observed in 17 students (2.2%) by QFT-GIT and 16 (2.0%) by QFT-Plus. Among the 25 positive QFT-Plus results, a noteworthy 44.0% (11 cases)

tested positive for TB1, and an impressive 100.0% (25 cases) tested positive for TB2 (Appendix Table 1). Out of the 9 patients who had positive results from the QFT-GIT test, 2 individuals (22.2%) showed positive results for both TB1 and TB2. However, 3 students exclusively tested positive for TB1 ($TB1^+TB2^-$, 33.3%), 1 individuals for TB2 ($TB1^-TB2^+$, 11.1%) and 3 students had negative results of TB1 and TB2.

Table 2 illustrates the levels of agreement between QFT-GIT and QFT-Plus. The overall agreements between QFT-GIT and QFT-Plus, QFT-Plus TB1, and QFT-Plus TB2 were 95.7% (95% CI, 94.0–97.0), 97.3% (95% CI, 95.9–98.3), and 95.9% (95% CI, 94.3–97.2), respectively. Cohen's kappa values for these agreements were 0.49 (95% CI, 0.32–0.62), 0.59 (95% CI, 0.41–0.74) and 0.45 (95% CI, 0.27–0.60), respectively. The consistency rates between QFT-Plus and the two skin tests are relatively high, at 94.5% (95%CI: 92.6–96.1)for the EC skin test and 91.2%(95%CI: 88.8, 93.1) for the TST. However, the Cohen's kappa values (0.082 for EC and 0.123 for TST) indicate minimal agreement (Appendix Table 2).

The differences in absolute quantitative IFN-γ levels between the QFT-GIT TB antigen tube and the QFT-Plus TB1 and TB2 antigen tubes ranged from − 4.18 to 4.33 IU/ml, -4.29–1.97 IU/ml and − 4.28–4.28 IU/ml, respectively. Notably, the quantitative IFN-γ level observed in the QFT-GIT test exceeded that of both the QFT-Plus TB1 test ($P = 0.084$) and the QFT-Plus TB2 test ($P = 0.550$). However, no statistically significant difference was observed in the quantitative IFN-γ levels between the QFT-GIT, QFT-Plus TB1, and QFT-Plus TB2 tests, as illustrated in Fig. 1. Additionally, there was a weak correlation observed among the IFN-γ levels in the QFT-GIT TB antigen tube and both QFT-Plus TB1 and TB2 tubes, with Pearson's correlation coefficients of 0.036 ($P = 0.308$) and 0.039 ($P = 0.005$) (Fig. 2).

IFN-γ responses in the three samples with QFT-GIT^+QFT-$Plus^-$ results ranged from 0.04 to 0.14 IU/ml (median, 0.12 IU/ml), and for the 20 samples with QFT-GIT^-QFT-$Plus^+$ results, the IFN-γ responses ranged from 0.02 to 1.99 IU/ml (median, 0.13 IU/ml) for TB1 and from 0.03 to 4.31 IU/ml (median, 0.57 IU/ml) for TB2. Notably, approximately 4.3%, 26.1%, and 52.3% of the discordant results (excluding the indeterminate results) fell within the range of IFN-γ response levels between 0.30 and 1.00 IU/ml for QFT-GIT, QFT-Plus TB1, and TB2. This included 3 out of 23 samples with QFT-GIT^+QFT-$Plus^-$ results and 20 out of 23 samples with QFT-GIT^--QFT^-Plus^+ results. Among the 20 samples with QFT-GIT^--QFT-$Plus^+$ results, 14 yielded reactive results in TB2, 5 showed reactivity in TB1 alone, and 1 exhibited in both TB1 and TB2 (Table 3).

Discussion

In this study, we conducted a comparative analysis of QFT-GIT, QFT-Plus assays, EC skin tests, and TST to diagnose *Mtb* infection among high school freshmen. We observed a substantial level of concordance between these four tests, with agreement rates reaching approximately 90%. While the levels of IFN-γ produced did not display any noteworthy distinctions between the QFT-GIT and QFT-Plus assays, it is worth noting that the QFT-Plus test exhibited a significantly higher rate of positive results than the QFT-GIT test. This outcome suggests that QFT-Plus has the potential to identify a more significant number of *Mtb* infections within these specific populations compared to the QFT-GIT assay, EC skin test and TST.

The concordance between QFT-GIT and QFT-Plus has been reported as follows in various patient populations: 96.6% in individuals at risk for TB and healthcare workers [15], 93.7% in immunocompromised patients [8], 91.1% in immunocompetent patients [16], 86.8% in clinical

Table 2 Agreement of diagnostic results for QuantiFERON-TB gold In-Tube and QuantiFERON-TB Gold Plus

Test	QFT-GIT result				
	Negative	Positive	Indeterminate	Consistency (95% CI)	Kappa Value (95% CI)
QFT-Plus result					
Negative	735	3	6	95.7 (94.0, 97.0)	0.485 (0.319, 0.621)
Positive	20	6	0		
Indeterminate	5	0	11		
QFT-Plus TB1					
Negative	749	4	6	97.3 (95.9, 98.3)	0.593 (0.413, 0.744)
Positive	6	5	0		
Indeterminate	5	0	11		
QFT-Plus TB2					
Negative	740	6	6	95.9 (94.3, 97.2)	0.451 (0.274, 0.600)
Positive	15	3	0		
Indeterminate	5	0	11		

Abbreviation: QFT-GIT, QuantiFERON-TB Gold In-Tube; QFT-Plus, QuantiFERON-TB Gold Plus

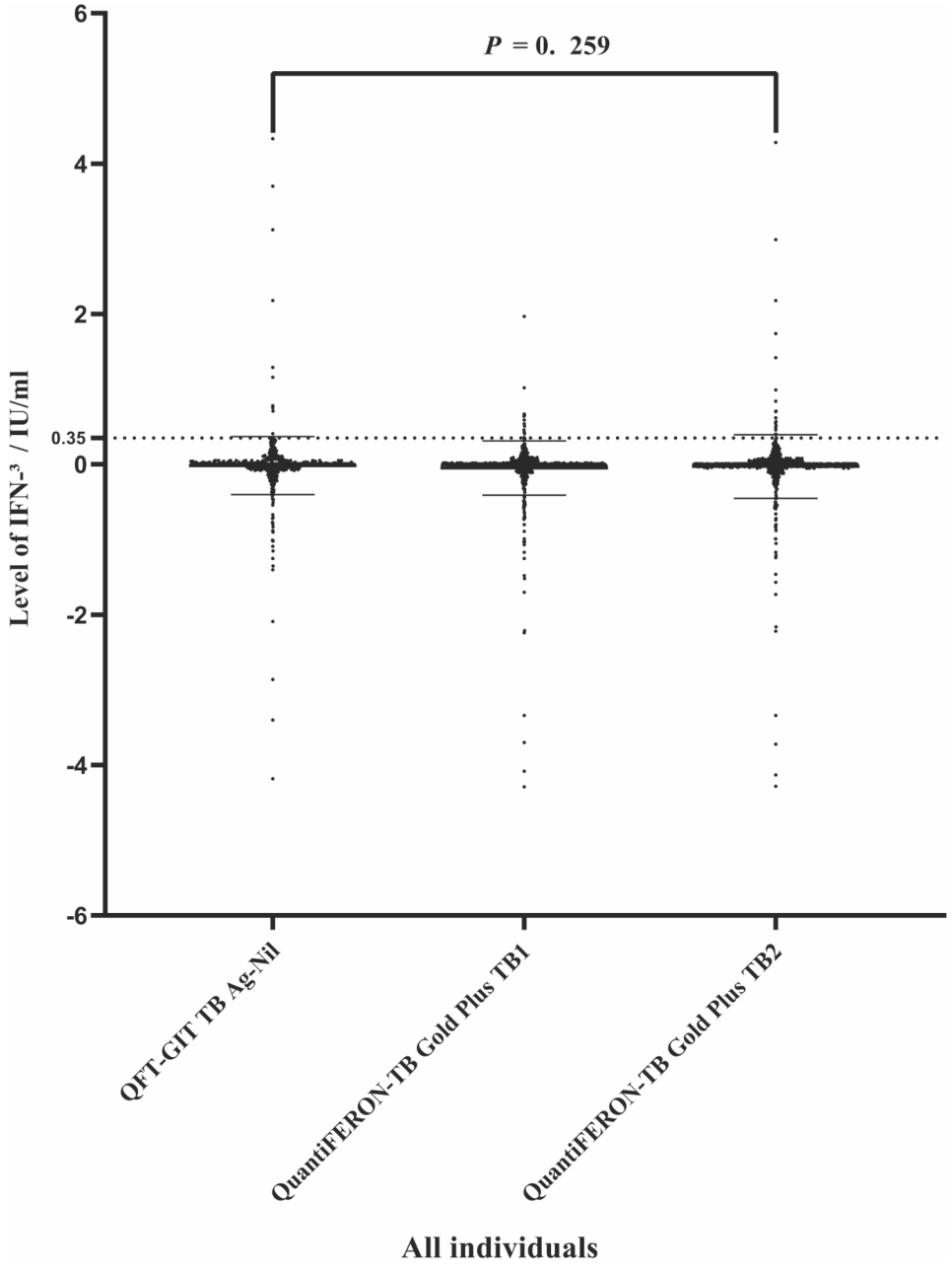

Fig. 1 Quantitative IFN-γ responses to QuantiFERON-TB Gold In-Tube, QuantiFERON-TB Gold Plus antigen TB1, and TB2

specimens [17] and 100% in children tuberculosis disease and 96% in children household contacts [18]. A recent meta-analysis demonstrated a strong agreement between QFT-Plus and QFT-GIT, yielding a combined Cohen's kappa statistic of 0.83 [19]. Some studies suggested that QFT-Plus performs equivalently to the QFT-GIT predicate for assessing active tuberculosis and *Mtb* infection [15, 20]. QFT-Plus could potentially offer more excellent utility in detecting *Mtb* infection among elderly and immunocompromised patients when dealing with limited sample sizes [21, 22]. In contrast to previous studies, our research focused on a relatively large sample of high school freshmen, revealing an agreement rate of 95.7%. These findings align with earlier research in this field. We also observed comparable agreement rates between QFT-Plus and EC skin tests, as well as TST. The agreement between QFT-Plus and QFT-GIT in our study was higher than that reported in other studies. For instance, a study conducted among household contacts in Vietnam reported an agreement rate of 65.3% [23] and another study among contacts in the US reported an agreement rate of 77% [24], likely because *Mtb* infection rates in freshmen were lower. No head-to-head studies have been conducted to directly compare the QFT-Plus with the

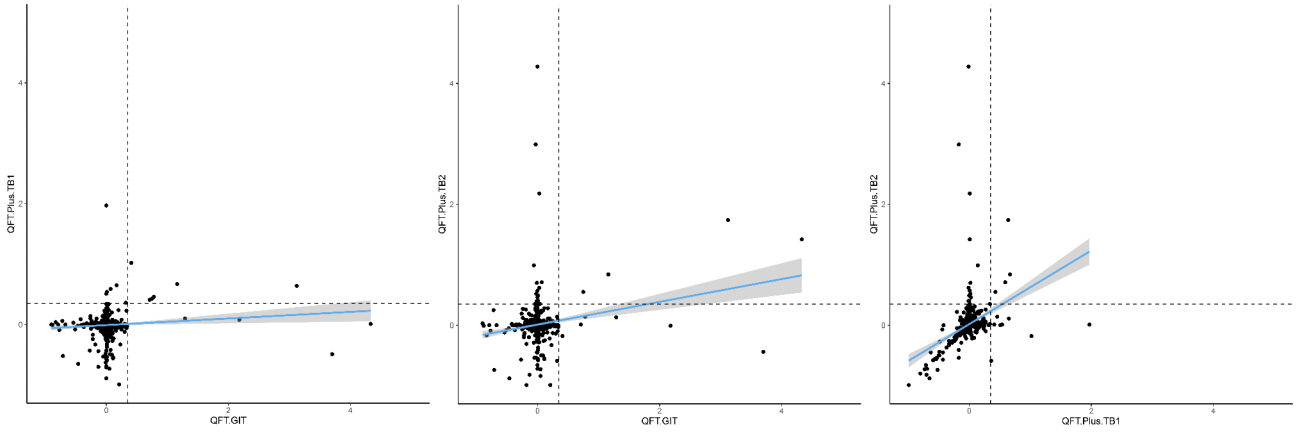

Fig. 2 Linear regression analysis in QuantiFERON-TB Gold In-Tube, QuantiFERON-TB Gold Plus TB1 and TB2 among all subjects

Table 3 Distribution of IFN-γ values in discordant results between QFT-GIT and QFT-Plus

QFT results	No cases (%)	QFT-GIT			QFT-Plus, TB1			QFT-Plus, TB2		
		Range	IQR	Median	Range	IQR	Median	Range	IQR	Median
QFT-GIT + QFT-Plus-	3 (0.4)	1.29–3.70	-	2.18	0.04–0.14	-	0.12	0.03–0.17	-	0.09
QFT-GIT-QFT-Plus+	20 (2.5)	-0.06-0.32	-0.01-0.03	0	0.02–1.99	0.04–0.63	0.13	0.03–4.31	0.22–0.94	0.57
QFT-GIT[I]QFT-Plus-	6 (0.8)	-0.02-0.00	-0.02-0.00	-0.005	0.03–0.14	0.03–0.08	0.05	0.03-037	-0.02-0	0.06
QFT-GIT-QFT-Plus[I]	5 (0.6)	-0.06-0.29	-0.03-0.18	0	0.04–0.62	0.05–0.39	0.05	0.03–0.46	0.04–0.30	0.05

Abbreviation: QFT-GIT, QuantiFERON-TB Gold In-Tube; QFT-Plus, QuantiFERON-TB Gold Plus; IFN-γ, interferon gamma; I, indeterminate; IQR, interquartile range

EC skin test. Furthermore, the low Cohen's kappa values observed between QFT-Plus and the EC skin test, as well as TST, indicate minimal agreement, likely due to the low prevalence of *Mtb* infection among adolescents. Notably, the number of individuals with positive TST results was lower than those with positive QFT-Plus results. This difference might be indicative of the enhanced sensitivity of QFT-Plus in detecting LTBI, especially in individuals with prior BCG vaccination or other factors that may affect TST performance. This finding aligns with previous research, which reported TST positivity rates of 5.6% and QFT-Plus positivity rates of 15.5% in immunocompromised children [25]. These results highlight that QFT-Plus demonstrates greater sensitivity in detecting LTBI compared to TST in this vulnerable population.

Significantly, a systematic review and meta-analysis indicated that QFT-Plus exhibited a 1.3% higher sensitivity compared to QFT-GIT. However, additional assessment is needed to evaluate the sensitivity of QFT-Plus in immunocompromised individuals [19]. In our study, the QFT-Plus assay produced a notably higher rate of positive results among patients when compared to the QFT-GIT assay, primarily attributable to TB2. Compared to TB1, TB2 demonstrated an augmentation in CD8 + T cell responses, a phenomenon associated with active tuberculosis and *Mtb* infection [6, 26]. Although finding more *Mtb* infection individuals, most of the amount of concentration in TB2 minus concentration in nil tube was between 0.35 and 1.00. Previous studies investigating the reproducibility of the QFT-GIT have identified various factors, including preanalytical, analytical, manufacturing, and biological factors, that can contribute to assay variability of up to ± 0.60 IU/ml around the cutoff point. This variability can lead to false-positive QFT results and conversion/reversion events [27–29]. Variability and reproducibility challenges around a singular binary cutoff point can give rise to difficulties in interpreting results, especially in the case of low-risk patients or healthcare workers with IFN-γ values near the assay cutoff, posing challenges for result interpretation [27, 30]. This limitation has been recognized and tackled in the latest guidelines from the American Thoracic Society, Infectious Diseases Society of America, and the Centers for Disease Control and Prevention for tuberculosis diagnosis. According to these guidelines, testing for *Mtb* infection should not be conducted in individuals with a low likelihood of *Mtb* infection.

Moreover, the guidelines acknowledge that such testing may still occur, and they recommend retesting low-risk individuals who initially test positive with IGRA. In this context, a subsequent negative result should precede the initial positive result [31]. Given the low-risk profile of high school freshmen, further research is warranted to establish whether TB2 can reliably detect actual cases of *Mtb* infection.

Numerous studies have reported significantly elevated levels of IFN-γ in TB2 tubes compared to both TB and TB1 tubes, and likewise, significantly higher IFN-γ levels

were observed in TB1 tubes compared to TB tubes [17]. Several other studies have also noted substantially elevated median levels of IFN-γ in QFT-GIT compared to QFT-Plus, positing that this discrepancy may be attributed to excluding the TB7.7 peptide [32]. In our study, the IFN-γ levels were highest in the QFT-GIT tube, while there were no significant differences in IFN-γ levels among the TB, TB1, and TB2 tubes.

Ultimately, we noted a limited correlation between the quantitative IFN-γ values obtained from the QFT-GIT TB antigen tube and those from both the TB1 and TB2 QFT-Plus antigen tubes, a finding that deviated from previous studies. The exact reason behind this phenomenon remained elusive [15, 33]. One potential explanation for this discrepancy could be that the absence of the TB7.7 antigen from the QFT-Plus appears to have a significant impact on assay performance. This finding contradicts the conclusions drawn in three prior studies [15, 34, 35]. Another potential reason could be that the high school freshmen were part of a low-risk group. In such cases, there may be challenges related to variability and reproducibility when using a singular binary cutoff point for the QFT-Plus assay.

Our study has several limitations. Firstly, we did not perform concurrent T-SPOT. TB could have served as a reference standard to evaluate the precision of the QFT-GIT and QFT-Plus assays. However, we did an EC skin test and TST instead of T-SPOT.TB. Secondly, we did not elucidate how the QFT-Plus assay could enhance the diagnosis of *Mtb* infection among high school freshmen as there is no gold standard of *Mtb* infection. Thirdly, it is important to note that the presence of a visible BCG scar may not fully reflect an individual's vaccination status. Some participants without a scar may still have received the BCG vaccine, and others with a scar may have received the vaccine many years prior, potentially affecting its impact on TST results.

Conclusions

In conclusion, our study revealed that the QFT-GIT and QFT-Plus assays exhibited a high level of agreement but demonstrated a moderate correlation. The IFN-γ levels measured by both QFT-GIT and QFT-Plus were comparable. Notably, our study highlights the potential of QFT-Plus in detecting a higher rate of *M*tb infection among high school freshmen compared to QFT-GIT, EC skin test and TST.

Abbreviations

Mtb	Mycobacterium tuberculosis
TST	Tuberculin skin test
IGRA	Interferon-γ release assay
BCG	Bovis bacillus Calmette-Guérin
NTM	Nontuberculous mycobacterium
QFT-GIT	QuantiFERON-TB gold in-tube assay
ELISA	Enzyme-linked immunosorbent assay
ELISPOT	Enzyme-linked immunosorbent spot
QFT-Plus	QuantiFERON-TB gold plus
EC	ESAT6-CFP10
SD	Standard deviations
k	Kappa

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-21954-7 .

Supplementary Material 1

Acknowledgements

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Author contributions

Jianming Wang, Peng Lu and Leonardo Martinez conceived the study, analyzed the data and drafted the manuscript. Hao Xue and Qiao Liu participated in the study design. Peng Lu, Jingjing Xu, Hao Xue, Jingjing Xu Qiao Liu, Xiaoyan Ding and Hui Ding implemented the field investigation. Peng Lu and Leonardo Martinez drafted the manuscript. All authors contributed to the study and have read and approved the final manuscript.

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Data availability

The datasets used during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study underwent a comprehensive review and obtained ethical approval from the Jiangsu Provincial Center for Disease Control and Prevention ethics committee. Informed consent in written form was obtained from all eligible subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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