

Accuracy of Two Novel Tuberculosis-specific Skin Tests in Diagnosing Tuberculosis Infection

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Background

Accurate diagnosis of latent tuberculosis infection (LTBI) is essential for targeting tuberculosis preventive treatment (TPT), a key strategy in the global effort to end TB. The Tuberculin Skin Test (TST) using purified protein derivative (PPD) is widely used but may yield false positives in Bacillus Calmette–Guérin (BCG)-vaccinated individuals. Interferon Gamma Release Assays (IGRAs) offer improved specificity but are costly and require laboratory infrastructure. To address these limitations, the World Health Organization recently endorsed tuberculosis antigen-based skin tests (TBSTs) that detect ESAT-6 and CFP-10 antigens, including C-TST (Anhui Zhifei Longcom, China) and Cy-Tb (Serum Institute of India, India), as alternatives. However, data from high-burden, BCG-vaccinated settings remain limited.

Methods

We conducted a cross-sectional study at Siriraj Hospital and the Central Chest Institute of Thailand, comparing reactions to PPD, Cy-Tb, C-TST, and IGRA among three groups: (1) microbiologically confirmed TB cases, (2) individuals at low risk, and (3) individuals at high risk of TB infection. Positive test criteria were defined as induration ≥10 mm for PPD and ≥5 mm for Cy-Tb and C-TST. This study is funded by the Health Systems Research Institute (HSRI).

Results

This is a preliminary analysis. As of July 31, 2025, 124 of 305 participants had been enrolled (10 in Group 1, 100 in Group 2, 14 in Group 3). Using IGRA as the reference, sensitivity for Cy-Tb and C-TST exceeded PPD (63.9%, 69.4%, and 50.0%, respectively), with high specificity (100%, 98.9%, and 94.3%). Concordance between C-TST and Cy-Tb was excellent (Kappa = 0.924). Among positive reactions, large indurations ≥15 mm were commonly observed particularly with Cy-Tb and C-TST (87.0% for Cy-Tb, 88.5% for C-TST, 46.4% for PPD).

Table 1: Baseline Characteristics of Participants Stratified by Group

Characteristic	Overall N = 124	Confirmed TB N = 10	Low Risk N = 100	High Risk N = 14
Age (year) Median (Q1,Q3)	41 (33, 47)	42 (34, 47)	41 (32, 49)	41 (33, 43)
Gender:				
Male	44 (35.5%)	4 (40%)	35 (35%)	5 (35.7%)
Female	80 (64.5%)	6 (60%)	65 (65%)	9 (64.3%)
BMI (kg/m²) Median (Q1,Q3)	25 (23, 28)	23 (21, 25)	26 (23, 28)	24 (23, 25)

Table 2: Diagnostic Accuracy in Diagnosing Tuberculosis

Test Name	Sensitivity (95% CI)	Specificity (95% CI)	Likelihood ratio of a positive test (95% CI)	Likelihood ratio of a negative test (95% CI)
Using IGRA as a gold standard (n=124)				
PPD (10 mm)	50.0% (32.9–67.1)	94.3% (87.2–98.1)	8.80 (3.54–21.90)	0.53 (0.38–0.74)
Cy-Tb (5 mm)	63.9% (46.2–79.2)	100.0% (95.9–100.0)	ND	0.36 (0.23–0.56)
C-TST (5 mm)	69.4% (51.9–83.7)	98.9% (93.8–100.0)	61.11 (8.60–434.20)	0.31 (0.19–0.51)

ND= not determined due to zero denominator.

Conclusions

Preliminary findings suggest that TBSTs (C-TST and Cy-Tb) offer IGRA-comparable performance, outperform PPD, and offer clearer, more interpretable results.

