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Latent Tuberculosis Infection Diagnostics: Comparative Performance of TST, IGRAs, and Cy-Tb: Reg No: 302

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Abstract

Background: Traditional methods such as Tuberculin Skin Test (TST) demonstrates reduced specificity due to BCG vaccination and environmental mycobacteria cross-reactivity. Interferon-Gamma Release Assays (IGRAs) improve specificity but require complex laboratory infrastructure. The Cy-Tb skin test has emerged as an affordable, and field-friendly diagnostic alternative. **Objective**: This review synthesizes current evidence comparing LTBI diagnostics, focusing on procedures, diagnostic accuracy, safety, and programmatic relevance of Cy-Tb relative to TST and IGRA, with emphasis on high TB burden settings. **Methods:** Comprehensive searches were conducted in Medline and Scopus databases using terms such as “latent tuberculosis infection,” “Cy-Tb skin test,” “tuberculin skin test,” “interferon-gamma release assay,” and “diagnostic accuracy.” 35 studies published between 2015-2025 were included. **Results:** Sensitivity for Cy-Tb ranged from 70% to 80%, and specificity ranged from 98% to 99% (Ruhwald M et al., South Africa and Muniyandi M et al., India). TST sensitivity ranged from 60% to 77%, while specificity from 55% to 65% in BCG vaccinated populations. (Chandrasekaran P et al., India). For IGRAs, sensitivity ranged from 75% to 85%, and specificity from 95% to 98%. (Chandrasekaran P et al., India and Pai M et al., Canada) The concordance between Cy-Tb and IGRA exceeds 90%, demonstrating strong diagnostic agreement (Aggerbeck H et al., 2018). Cy-Tb is associated mainly with mild, transient local injection site. TST can cause local skin reactions and rare systemic hypersensitivity, while IGRAs carry minimal risk (Hamada et al., China). **Conclusion:** Cy-Tb offer improved specificity and comparable sensitivity to IGRAs with simplicity and cost-effectiveness suitable for large-scale implementation in high-burden settings. Scalable and accessible LTBI diagnostics with favourable safety profiles, like Cy-Tb, are critical to accelerating TB elimination efforts globally.

Keywords

Latent Tuberculosis Infection, Cy-Tb Test, Tuberculin Skin Test, Interferon-Gamma Release Assay, TB Preventive Therapy, Cost-Effectiveness, High-Burden Settings