Mantoux Says Yes, But Does Interferon-Gamma Release Assay (IGRA) Agree? Confirming Latent Tuberculosis Infection (LTBI) in Rural Malaysia

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Introduction

Interferon-Gamma Release Assay (IGRA) is a blood test that enhances the diagnostic accuracy of latent tuberculosis infection (LTBI), especially in individuals with prior Bacillus Calmette–Guérin (BCG) vaccination. Compared to the tuberculin skin test (TST), IGRA offers superior specificity by reducing false-positive results associated with BCG vaccination or exposure to non-tuberculous mycobacteria. IGRA supports more accurate LTBI diagnosis and enables targeted treatment in BCG-vaccinated populations. Targeted population screening can be conducted through the Intensified Case Finding (ICF) initiative to facilitate early detection of active tuberculosis (TB) and LTBI cases.

Case Report

This study was performed to evaluate the utility of IGRA in confirming LTBI among Mantoux-positive individuals during a community-based tuberculosis screening initiative among a predominantly BCG-vaccinated population in Gua Musang, Malaysia, in November 2024. A cross-sectional study was conducted using data extracted from the records of an Intensified Case-Finding (ICF) initiative conducted in Kampung Pulai, Gua Musang, on 4th of November 2024. Descriptive analysis was conducted using Microsoft Excel.

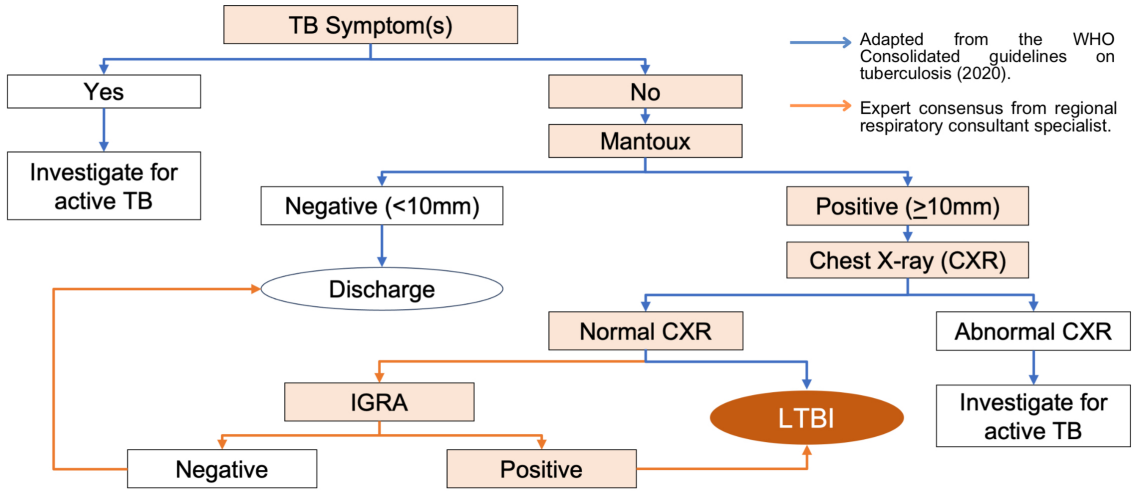

Figure 1. Diagnostic algorithm for active TB and LTBI screening during the ICF initiative in Kampung Pulai

A total of 88 individuals from a population of 1,500 in Kampung Pulai, Gua Musang, were screened for active tuberculosis (TB) and latent TB infection (LTBI). Of these, 81 were asymptomatic and underwent Mantoux testing. Sixteen individuals tested Mantoux-positive, all of whom subsequently underwent chest radiography, which revealed no abnormalities. Three Mantoux-positive individuals

were initiated on LTBI treatment without interferon-gamma release assay (IGRA) confirmation, prior to consultation with the respiratory physician. Following discussion with the respiratory physician, IGRA testing was performed for the remaining 13 Mantoux-positive individuals, of whom five tested IGRA-positive, confirming LTBI.

Table 1. Sociodemographic, clinical characteristic and outcome among population screened during ICF initiative in Kampung Pulai, November 2024

Variable	Screened (n=88)	Mantoux positive (n=16)	IGRA positive (n=5)
	n (%)	n (%)	n (%)
Age group			
18-64 years	71 (80.7)	12 (75.0)	4 (80.0)
≥ 65 years	17 (19.3)	4 (25.0)	1 (20.0)
Gender			
Male	52 (59.1)	9 (56.2)	3 (60.0)
Female	36 (40.9)	7 (43.8)	2 (40.0)
Race			
Malay	5 (5.7)	2 (12.5)	1 (20.0)
Chinese	82 (93.2)	14 (87.5)	4 (80.0)
Others	1 (1.1)	- (-)	- (-)
TB symptom(s)			
Yes	7 (8.0)	- (-)	- (-)
No	81 (92.0)	16 (100.0)	5 (100.0)
BCG scar			
Present	82 (93.2)	15 (93.8)	5 (100.0)
Absent	6 (6.8)	1 (6.2)	- (-)
TB close contact			
Yes	2 (2.3)	- (-)	- (-)
No	86 (97.7)	16 (100.0)	5 (100.0)

Incorporating IGRA may improve diagnostic clarity in LTBI management. Among the Mantoux-positive, asymptomatic individuals with normal chest X-ray, only 38.5% tested IGRA-positive, highlighting the potential for overdiagnosis if relying on TST alone. Notably, 93.2% of screened individuals had BCG scars, which may contribute to false-positive TST results. The observed TST–IGRA discordance aligns with previous studies (1,2,3). While IGRA may enhance diagnostic precision, implementation challenges remain due to cost, limited test availability, and logistical constraints particularly in rural community. A targeted testing strategy using IGRA selectively for Mantoux-positive individuals may help balance diagnostic value with resource constraints.

Conclusion

As a conclusion, a TST-first, followed by IGRA-confirm strategy may be effective in confirming LTBI diagnosis in a high BCG-vaccinated population. For recommendations, IGRA can be a confirmatory test for Mantoux-positive, asymptomatic individuals with normal chest X-ray in population-based LTBI screening. Further assessment of the feasibility and cost-effectiveness of the TST-first, followed by IGRA-confirm strategy for diagnosing LTBI is needed to guide broader implementation.

Keywords: LTBI, IGRA, Mantoux test, tuberculosis screening, Gua Musang

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