



University of
St Andrews

TB or not TB? What is the best methodology for latent tuberculosis infection detection in HIV-infected individuals – TST or IGRA?: A Critical Review.

ZAKWAN. Muhammad ¹, DHALIWAL. Winnie ¹

¹University of St. Andrews, Scotland

Background

- TB is caused by *Mycobacterium tuberculosis* (MTB) and represents a major public health problem.
- Achieving global targets for TB elimination remains challenging due to its nature of infection, which usually remains latent in individuals and can reactivate later in life.
- An estimated quarter of the world's population potentially harbours a latent TB infection (LTBI).
- The risk of LTBI reactivation is amplified multifold in individuals with HIV, making them extremely potent reservoirs of TB transmission.
- Effective LTBI detection within HIV-infected individuals is vital to prompt immediate preventive treatment and forms a key component of TB prevention and elimination.
- There are two diagnostic tools used to detect LTBI, called the tuberculin skin test (TST) and interferon-gamma release assay (IGRA).

Aims and Methods

The objective of this review was to compare the performance of TST and IGRA in detecting LTBI in HIV-infected individuals in terms of:

- Diagnostic efficacy
- Operational limitations
- Cost-effectiveness

A systematic search of available literature across four databases was performed, and of the initial 338 citations generated, 12 papers were selected, analyzed and critically appraised.

LTBI Diagnostic Tools



TST

- Intradermal injection of MTB extracts into forearm
- Takes 2-3 days until a visible skin reaction appears on injection site
- The diameter of the swelling is measured and interpreted



IGRA

- Serological test, only requiring a single blood draw
- Sample gets taken to the lab for processing and interpretation
- Convenient – results are available after 24 hours

Results and Discussion

Diagnostic Efficacy of TST and IGRA

Sensitivity

- Dependent on the patient's CD4 T cell count.
- IGRA was able to detect LTBI in a larger proportion of HIV-infected individuals, making it more sensitive compared to TST.
- However, both tests have limited utility amidst severe immunosuppression

Specificity

IGRA is more specific than TST because of the absence of cross-reactivity (present in TST) with antigens within two sources:

- BCG vaccination
- Non-tuberculous mycobacterial (NTM) infection

Operational Limitations of TST and IGRA

TST	IGRA
Requires two clinic visits	Only needs a single blood draw
Takes 48-72 hours	Results available in 24 hours
Subjective interpretation	Objective interpretation
	Requires specialized training

Cost-effectiveness of TST and IGRA

The decision as to which test is best used is must also address test cost and available resources and constraints within the patient's setting. Different papers had different recommendations, catering for patient-specific and environmental factors.

Conclusion

- IGRA has comparatively higher utility in HIV-infected individuals than TST
- Both tests are not perfect, especially amidst severe immunosuppression
- Further research needed to find better alternatives in LTBI detection within these high-risk individuals, ultimately to reduce the burden of global TB

Acknowledgment

1. Winnie Dhaliwal (University of St Andrews, Scotland)
2. The School of Medicine, University of St Andrews, Scotland

Author's Info

Email: mzakwanzakariya@gmail.com
Tel: +6012-2627900

References

1. Wolf T, Goetsch U, Oremek G, Bickel M, Khaykin P, Haberl A, et al. Tuberculosis skin test, but not interferon-gamma-releasing assays is affected by BCG vaccination in HIV patients. *The Journal of Infection*. 2013;66(4):378-80.
2. Kuisen GM, Dalla-Costa LM, Rossini A, Raboni SM. Interferon-gamma release assay versus tuberculin skin test for latent tuberculosis infection among HIV patients in Brazil. *The Brazilian journal of infectious diseases : an official publication of the Brazilian Society of Infectious Diseases*. 2019;20(1):69-75.
3. Klautau GB, da Mota NVF, Sales MJC, Burattini MN, Rodrigues DS. Interferon-gamma release assay as a sensitive diagnostic tool of latent tuberculosis infection in patients with HIV: a cross-sectional study. *BMC Infectious Diseases*. 2018;18(1):585.
4. James PM, Carneiro FA, Kadishali RL. The performance of quantiferon-TB gold in-tube (QFT-IT) test compared to tuberculin skin test (TST) in detecting latent tuberculosis infection (LTBI) in the presence of HIV coinfection in a high TB-burden area with BCG vaccinated population. *Journal of the International Association of Providers of AIDS Care*. 2014;13(1):47-55.
5. Yang CH, Chan PC, Liao ST, Cheng SH, Wong WW, Huang LM, et al. Strategy to Better Select HIV-Infected Individuals for Latent TB Treatment in BCG-Vaccinated Population. *PLoS one*. 2013;8(8):9.
6. Pappalardo R, Esposito V, Onofrio M, Pappalardo G, Vignati R, Siringiovanni V, et al. Interferon gamma release assays and tuberculin skin test performance in different settings of HIV immunodeficiency. *In vivo (Athens, Greece)*. 2015;29(1):137-40.
7. de Oliveira SMOVL, Trainini A, Paniago AMM, Mota-Castro ARC, Ruffino-Netto A, Maciel ELN, et al. Frequency of indeterminate results from an interferon-gamma release assay among HIV-infected individuals. *Journal brasileiro de pneumologia : publicacao oficial da Sociedade Brasileira de Pneumologia e Tisiologia*. 2017;43(3):215-8.
8. Khawcharoenporn T, Apisanthanarak A, Phetsuksiri B, Rudeeaneksin J, Srisungngam S, Mundy LM. Tuberculin skin test and QuantiFERON-TB Gold In-tube Test for latent tuberculosis in Thai HIV-infected adults. *Respirology (Carlton, Vic)*. 2015;20(2):240-7.
9. Chkhartishvili N, Kempker RR, Dvili N, Abashidze L, Sharavtze L, Gabunia P, et al. Poor agreement between interferon-gamma release assays and the tuberculin skin test among HIV-infected individuals in the country of Georgia. *BMC Infectious Diseases*. 2013;13:513.
10. Souza JM, Evangelista MDN, Trainini A. Added value of QuantiFERON TB-gold in-tube for detecting latent tuberculosis infection among persons living with HIV/AIDS. *BioMed research international*. 2014;2014:294963.
11. Leung CC, Chan K, Yam WC, Lee MP, Chan CK, Wong KH, et al. Poor agreement between diagnostic tests for latent tuberculosis infection among HIV-infected persons in Hong Kong. *Respirology (Carlton, Vic)*. 2016;21(7):1322-9.
12. Adams S, Ehrlich R, Baatjes R, Dendukuri N, Wang Z, Dheda K. Predictors of discordant latent tuberculosis infection test results amongst South African health care workers. *BMC Infectious Diseases*. 2019;19(1):131.