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Detection of latent tuberculosis infection in household contacts of drug-resistant tuberculosis patients using interferon-gamma release assay: a study at Universitas Indonesia Hospital

Muhammad Faris Indratmo[1], Diah Handayani[2,4], Ardiana Kusumaningrum[3,4], Febriana Catur Iswanti[5*], Mohamad Sadikin[5]

[1]Master's Programme in Biomedical Sciences, Faculty of Medicine, Universitas Indonesia
[2]Department of Pulmonology, Faculty of Medicine, Universitas Indonesia
[3]Department of Clinical Microbiology, Faculty of Medicine, Universitas Indonesia
[4]Universitas Indonesia Hospital
[5]Department of Biochemistry & Molecular Biology, Faculty of Medicine, Universitas Indonesia
[*]Corresponding author: Department of Biochemistry and Molecular Biology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia. Email: febriana.iswanti@ui.ac.id

ABSTRACT

Background: Drug-resistant tuberculosis (DR-TB) poses significant public health challenges in Indonesia. Household contacts of DR-TB patients face elevated risk of *Mycobacterium tuberculosis* infection, which may remain latent and asymptomatic.

Objective: This study aimed to assess the prevalence of latent tuberculosis infection (LTBI) among household contacts of DR-TB patients using interferon-gamma release assay (IGRA).

Methods: This cross-sectional study was conducted at Universitas Indonesia Hospital from February to May 2023. Eighteen asymptomatic household contacts from six confirmed DR-TB index cases were enrolled. Participants underwent clinical evaluation, chest radiography, and LTBI screening using the QuantiFERON-TB Gold Plus (QFT-Plus) assay.

Results: Among 18 participants (mean age 33.3 years; 55.6% female), 8 (44.4%) tested positive for LTBI, while 10 (55.6%) tested negative. The highest IGRA positivity rates were observed in adolescents aged 12–16 years (66.7%) and young adults aged 17–25 years (60.0%). All participants were clinically asymptomatic with normal chest radiographs.

Conclusion: This study demonstrates substantial LTBI prevalence among household contacts of DR-TB patients. The findings underscore the importance of systematic contact tracing, IGRA-based screening, and timely tuberculosis preventive therapy to reduce disease transmission and progression in high-risk populations.

Keywords: household contacts, drug-resistant tuberculosis, interferon-gamma release assay, latent tuberculosis infection, contact tracing

Introduction

Tuberculosis (TB) continues to pose a significant public health challenge in Indonesia. TB ranks among the top ten causes of mortality globally and remains the leading cause of death from infectious diseases. According to the World Health Organization (WHO), TB affects approximately 10 million individuals worldwide each year. Despite being both preventable and curable, the disease is responsible for an estimated 1.5 million deaths annually. The WHO, in collaboration with the Government of Indonesia, has committed to the goal of eliminating TB by 2030. In 2020, global reports indicated 132,222 cases of drug-resistant tuberculosis (DR-TB), with Indonesia accounting for 7,921 confirmed cases [1,2].

Drug-resistant tuberculosis is a form of tuberculosis caused by *Mycobacterium tuberculosis* that is resistant to at least isoniazid and rifampicin, the two main first-line anti-tuberculosis drugs. Some cases also show resistance to fluoroquinolones and second-line injectable agents, known as extensively drug-resistant tuberculosis (XDR-TB). DR-TB treatment is prolonged, lasting 9–20 months, and often involves second-line drugs that are less effective, more toxic, and more expensive. These challenges contribute to higher rates of treatment failure, increased side effects, and greater risk of disease transmission [1].

Mycobacterium tuberculosis is transmitted via airborne particles rather than through surface contact. Transmission occurs when an individual inhales droplet nuclei containing *M. tuberculosis*. These droplet nuclei pass through the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs. The risk of infection depends on several factors, including the infectiousness of the source case, the proximity and duration of exposure, the concentration of inhaled droplets, and the immune status of the exposed individual [3,4].

During the initial phase of infection, *M. tuberculosis* is internalized by phagocytic immune cells and begins to replicate intracellularly. Infected immune cells may traverse the alveolar barrier, potentially leading to systemic dissemination. In most individuals, an effective cell-mediated immune response develops within 2–8 weeks. Activated T lymphocytes, macrophages, and other immune cells form granulomas that encapsulate necrotic tissue, thereby limiting the replication and spread of the bacilli. Within these caseous granulomas, most *M. tuberculosis* organisms are killed, effectively halting disease progression. However, in some individuals, the bacteria are not completely eradicated. *M. tuberculosis* possesses mechanisms to evade host immune responses, allowing the bacilli to persist in a dormant, non-replicating state within the host. This condition is referred to as latent tuberculosis infection (LTBI) [5,6].

Household contacts of DR-TB patients represent a high-risk group for TB transmission due to close and prolonged exposure. Although these individuals may not exhibit symptoms, they can harbor LTBI, a condition in which *M. tuberculosis* persists in a dormant state without causing active disease. If not identified and treated, LTBI may progress to active TB, particularly under conditions of immunosuppression or other risk factors, thereby continuing the chain of transmission [7]. A cross-sectional study in Semarang found that 63.8% of household contacts of TB patients tested positive for LTBI using interferon-gamma release assay (IGRA), underscoring the silent but substantial reservoir of infection within communities [8]. Studies using the tuberculin skin test (TST) in household contacts have reported positivity rates ranging from 20–60%, depending on exposure and population background. However, the TST has limited sensitivity (70–80%) and specificity (60–80%), and its accuracy is affected by prior Bacille Calmette–Guérin (BCG) vaccination and environmental mycobacteria. In contrast, IGRAs such as the QuantiFERON-TB Gold Plus (QFT-Plus) test demonstrate higher specificity (>95%) and are unaffected by BCG vaccination, making them more reliable for detecting LTBI in endemic regions like Indonesia [9].

The challenge of controlling TB, especially DR-TB, lies not only in treating active cases but also in detecting and managing LTBI among high-risk populations. In this context, effective contact investigation and screening strategies are essential. Active tuberculosis is typically diagnosed through sputum smear microscopy, culture, or molecular tests, combined with clinical and radiographic findings. In contrast, LTBI requires immunological testing, either by TST or IGRA. The TST shows variable sensitivity and specificity, while IGRA offers superior specificity because it measures interferon-gamma release in response to *M. tuberculosis*-specific antigens (ESAT-6 and CFP-10), which are absent in BCG strains and most environmental mycobacteria, thereby reducing the incidence of false positives [9,10,13].

Given the high burden of DR-TB in Indonesia and the substantial risk of LTBI among household contacts, implementing accurate diagnostic tools is

critical to identify latent infections and interrupt the transmission chain. This study aims to evaluate the prevalence of LTBI among household contacts of DR-TB patients using the QFT-Plus assay, thereby supporting the development of more targeted TB control interventions and contributing to national TB elimination goals.

Methods

Study design and setting

This cross-sectional study was conducted at Universitas Indonesia Hospital, Depok, Indonesia, from February to May 2023. The study was designed to assess the prevalence of latent tuberculosis infection (LTBI) among household contacts of patients with confirmed drug-resistant tuberculosis (DR-TB).

Subject recruitment

Study participants were household contacts of newly diagnosed DR-TB patients (diagnosed within the preceding three months). Household contacts were defined as individuals who had lived in the same residence as a DR-TB index case for at least 250 hours of cumulative exposure [11]. The diagnosis of DR-TB in index cases was confirmed using molecular rapid testing (polymerase chain reaction-based assay) that detected resistance to rifampicin and/or isoniazid.

Exclusion criteria included individuals with known immunocompromising conditions, such as diabetes mellitus or human immunodeficiency virus (HIV) infection. These conditions were excluded because they significantly alter immune responses and may confound IGRA interpretation, potentially leading to false-negative results due to impaired T-cell function. Additionally, individuals with a prior history of active TB treatment or current symptoms suggestive of active TB (persistent cough, fever, night sweats, weight loss) were excluded from the study.

All participants provided written informed consent prior to enrollment. For participants under 18 years of age, written consent was obtained from parents or legal guardians, along with assent from the minor when appropriate. At the time of recruitment, the LTBI status of participants was unknown. Laboratory personnel conducting the QuantiFERON-TB Gold Plus (QFT-Plus) assays were blinded to the participants' clinical background and relationship to index cases to minimize potential bias in test processing and interpretation.

Clinical evaluation

Close contacts underwent clinical evaluation, including laboratory testing and chest X-ray examination.

IGRA testing procedures

Detection of LTBI was performed using the QuantiFERON-TB Gold Plus assay kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions. A 5 mL peripheral blood sample was collected from the antecubital vein using standard venipuncture technique. Blood was immediately distributed into four QFT-Plus Blood Collection Tubes: Nil (negative control), TB1 (CD4+ T-cell stimulation), TB2 (CD4+ and CD8+ T-cell stimulation), and Mitogen (positive control), with 1 mL allocated to each tube.

The tubes were gently inverted 10 times to ensure proper mixing and were incubated upright at 37°C for 20 hours. Following incubation, the tubes were centrifuged at 2,000–3,000 rpm for 15 minutes. Plasma was then carefully harvested and stored at 2–8°C until assay performance, which occurred within 48 hours of collection.

The QFT-Plus assay is based on the enzyme-linked immunosorbent assay (ELISA) principle, which quantifies interferon-gamma (IFN-γ) released by sensitized T lymphocytes following stimulation with *M. tuberculosis*-specific antigens (ESAT-6 and CFP-10). Results were interpreted according to the manufacturer's criteria: positive (TB antigen response minus Nil ≥0.35 IU/mL and ≥25% of Nil value), negative (TB antigen response minus Nil <0.35 IU/mL or <25% of Nil value, and Mitogen minus Nil ≥0.5 IU/mL), or indeterminate (failed

quality control criteria). All assays were performed in duplicate to ensure reliability.

Data collection

Collected data included demographic characteristics (gender and age) and results of the IGRA examination in close contacts of drug-resistant tuberculosis (DR-TB) patients.

Data analysis

Collected data were processed and analyzed using Microsoft Excel 2016 (Microsoft Corp., USA), SPSS version 26 (IBM Corp., USA), and QuantiFERON-TB Gold Plus Analysis Software version 2.62 (Qiagen, Germany).

Descriptive statistics were used to summarize participant characteristics and IGRA results. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Due to the preliminary nature and small sample size of this study, inferential statistical testing was not performed.

Ethical approval

This study received ethical clearance from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia, under approval number KET.987/UN2.F1/ETIK/PPM.00.02/2022. All procedures were conducted in accordance with the Declaration of Helsinki and Indonesian national research ethics guidelines.

Results

Study participant characteristics

A total of 18 household contacts from 6 confirmed DR-TB index cases were enrolled in this study. All participants were asymptomatic and showed no clinical or radiological evidence of active TB at the time of enrollment, as determined by physical examination, laboratory blood tests, and chest radiography. The demographic and clinical characteristics of the study participants are presented in Table 1.

Table 1. Demographic and clinical characteristics of household contacts (n=18)

Characteristics of close contacts	n	%
Gender		
Male	8	44.4
Female	10	55.6
Age		
5-11	1	5.6
12-16	3	16.7
17-25	5	27.8
26-35	0	0
36-45	4	22.2
46-55	1	5.6
56-65	4	22.2
Relationship to index case		
Spouse	9	50
Child	6	33.3
Parent	2	11.1
Sibling	1	5.6
Clinical Status		
Asymptomatic	18	100
Chest X-ray radiograph findings		
No abnormalities	18	100

Participant ages ranged from 8 to 64 years, with a mean age of 33.3 ± 4.26 years. The most frequently represented age group was 17–25 years (n=5, 27.8%), followed by the 36–45 years and 56–65 years groups (n=4 each, 22.2%). The gender distribution included 8 males (44.4%) and 10 females (55.6%). Half of the household contacts were spouses of the DR-TB index cases (n=9, 50.0%), followed by children (n=6, 33.3%), parents (n=2, 11.1%), and siblings (n=1, 5.6%).

IGRA test results

All 18 blood samples were successfully processed. The distribution of IGRA results is summarized in Table 2. All tests yielded valid results with no indeterminate outcomes.

Among the 18 participants tested, 8 (44.4%) were positive for LTBI by IGRA, while 10 (55.6%) tested negative. When stratified by gender, IGRA positivity was 37.5% (3/8) among males and

Table 2. IGRA test results stratified by demographic characteristics

Close Contact Group	IGRA Positive n (%)	IGRA Negative n (%)	Total n (100%)
Total	**8 (44.4)**	**10 (55.6)**	**18 (100)**
Sex			
Male	3 (37.5)	5 (62.5)	8 (100)
Female	5 (50)	5 (50)	8 (100)
Age group (years)			
5-11	0	1 (100)	1 (100)
12-16	2 (66.7)	1 (33.3)	3 (100)
17-25	3 (60)	2 (40)	5 (100)
26-35	0	0	
36-45	1 (25)	3 (75)	4 (100)
46-55	1 (50)	1 (50)	2 (100)
56-65	1 (33.3)	2 (66.7)	3 (100)
Relationship to index case			
Spouse	4 (44.4)	5 (55.6)	9 (100)
Child	3 (50)	3 (50)	6 (100)
Parent	0	2 (100)	2 (100)
Sibling	1 (100)	0	1 (100)

50.0% (5/10) among females. Among the age groups examined, the highest IGRA positivity rates were observed in participants aged 12–16 years (66.7%, 2/3) and 17–25 years (60.0%, 3/5). When examined by relationship to the index case, children showed 50.0% positivity (3/6), spouses 44.4% (4/9), while both parents tested negative and the single sibling tested positive.

Discussion

This study found that 44.4% (8/18) of household contacts of DR-TB patients tested positive for LTBI using IGRA, despite being asymptomatic and showing no radiological abnormalities. These findings demonstrate that household contacts of DR-TB patients face substantial risk of *Mycobacterium tuberculosis* exposure and infection, even in the absence of clinical manifestations.

The observed LTBI prevalence is consistent with Reichler et al., who found that 45.7% (1,390/3,040) of close contacts were diagnosed with LTBI through IGRA testing [14]. However, our findings show higher prevalence compared to Erawati et al., who reported 23% (46/195) LTBI prevalence among close contacts of TB patients in an Indonesian cohort [15]. This difference may reflect the heightened transmission risk associated with drug-resistant strains or variations in household exposure intensity and duration.

IGRA examination has become a key method for detecting LTBI, particularly in high-risk populations. The assay measures interferon-gamma (IFN-γ) released by sensitized T lymphocytes in response to specific *Mtb* antigens, namely Early Secreted Antigenic Target 6 (ESAT-6) and Culture Filtrate Protein 10 (CFP-10), which are absent from Bacille Calmette-Guérin (BCG) strains and most non-tuberculous mycobacteria [12]. IFN-γ is primarily produced by CD4+ and CD8+ T cells, as well as natural killer (NK) cells. This cytokine plays a pivotal role in activating macrophages to produce reactive oxygen species (ROS), enhancing their ability to eliminate intracellular *Mtb*. CD4+ T cells recognize *Mtb* antigens and secrete IFN-γ, which is essential for macrophage activation and control of *Mtb* proliferation within granulomas [13]. This makes IGRA not only a useful diagnostic tool

but also a reflection of the host's immunological response to latent infection.

Examination of demographic characteristics in this study reveals patterns that warrant consideration. The majority of LTBI-positive subjects were adolescents and young adults aged 12–25 years, with positivity rates of 66.7% and 60.0% respectively in these age groups. Reichler et al. also noted that LTBI prevalence was highest among adult contacts compared to children, potentially due to cumulative exposure duration and immune system differences [14].

Regarding gender distribution, although more women than men were included in this study (55.6% vs. 44.4%), IGRA positivity rates were similar between females (50.0%) and males (37.5%). Previous studies, including one by Alatas et al., found no statistically significant difference in LTBI prevalence between male and female contacts [16]. However, cultural and behavioral factors such as caregiving roles often undertaken by women could influence exposure levels and deserve further investigation in larger cohorts.

The strong association between household contact and LTBI is well established. Reichler et al. reported that household contacts had significantly higher risk of infection compared to non-household contacts due to prolonged and repeated exposure in confined environments [14]. In Indonesia, where household density can be high and ventilation often inadequate, the risk of airborne transmission is further amplified [17]. This environmental factor, combined with limited access to TB preventive therapy, reinforces the importance of early detection and preventive intervention among high-risk populations.

Although all individuals in this study were asymptomatic with normal clinical and radiological findings, IGRA results indicate that they may harbor *Mtb* infection. Globally, approximately one-quarter of the population is estimated to be infected with LTBI [18]. The duration of latency is highly variable, and even individuals who appear healthy can carry this risk for many years.

Studies report that 5%–15% of individuals with LTBI may progress to active tuberculosis, particularly within the first 2–5 years after initial infection [19,20]. This transition, known as reactivation, underscores the clinical significance of LTBI as a major reservoir for future active TB cases [21]. The detection of LTBI in household contacts of DR-TB patients therefore represents a critical step in TB control strategies, especially in high-burden countries like Indonesia.

The risk of tuberculosis reactivation among individuals with LTBI can be significantly reduced through appropriate Tuberculosis Preventive Therapy (TPT). When a new case of DR-TB is diagnosed, household contacts, especially those confirmed with LTBI, should be promptly screened and considered for TPT to prevent progression to active disease. Evidence suggests that TPT can reduce TB reactivation risk by approximately 60%–90%, particularly when using isoniazid or rifapentine-based regimens [22].

The findings of this study support the need for routine IGRA screening among close contacts of DR-TB patients, followed by timely initiation of preventive therapy for those who test positive for LTBI. From a public health perspective, these findings highlight the importance of strengthening TB control strategies through integrated contact tracing, IGRA-based screening, and targeted preventive therapy for household contacts of DR-TB patients. Such interventions are especially crucial in high-burden settings like Indonesia, where household transmission remains a major contributor to new TB cases. Strengthening early detection and management of LTBI among high-risk populations can significantly reduce the reservoir of latent infections and help curb TB incidence in the long term.

The distinction between close contacts who develop LTBI and those who remain uninfected despite similar exposure to *Mtb* may be partially attributed to differences in innate immune responses, particularly in macrophage phagocytic capacity and lysosomal function. A study by Iswanti et al. (2024) reported that monocyte-derived macrophages from patients with active drug-resistant TB exhibited significantly elevated levels of β-glucuronidase and acid phosphatase activity, along with increased

oxidative burst capacity, when compared to healthy controls [23]. This immunological profile may influence whether exposure to *M. tuberculosis* results in latent infection or progresses to active disease, underscoring the importance of host immune regulation in TB latency.

Notably, the study also identified a strong negative correlation between lysosomal enzyme activity and phagocytosis, suggesting that while lysosomal activation is enhanced in active TB, it may reflect a compensatory or dysregulated immune response that is ultimately ineffective in eliminating *Mtb* [23]. In contrast, the LTBI group in the present study demonstrated a more balanced immune profile, characterized by adequate phagocytic activity and lysosomal enzyme production capable of containing *Mtb* without leading to active disease. Meanwhile, uninfected contacts may show lower levels of immune activation, which could indicate either insufficient exposure or the presence of more efficient early immune mechanisms that prevent the establishment of infection altogether.

This study has several limitations. The small sample size (n=18) limits the generalizability of findings and precludes meaningful statistical comparisons between subgroups. The cross-sectional design prevents assessment of causal relationships and does not allow for longitudinal follow-up to determine which LTBI-positive individuals progress to active TB. Potential selection bias exists as all participants were recruited from a single hospital, which may not represent the broader population of DR-TB household contacts.

Additionally, the absence of detailed immunological profiling in the close contact group limits our understanding of the mechanisms underlying differential susceptibility to *Mtb* infection. Future studies should focus on characterizing the cellular immune landscape in household contacts, including macrophage polarization and cytokine production profiles, to provide deeper insights into host resistance mechanisms and factors influencing LTBI persistence or progression. Research should also explore predictive biomarkers of reactivation and evaluate the immunological effectiveness of TPT in close contacts of DR-TB patients. Larger multicenter studies with longitudinal follow-up are needed to confirm these preliminary findings and assess the long-term outcomes of LTBI-positive household contacts. Such data will be instrumental in optimizing LTBI management and refining strategies for TB prevention at both clinical and population levels.

Conclusion

This study provides evidence that household contacts of patients with drug-resistant tuberculosis are at significant risk of exposure to *Mycobacterium tuberculosis*, even in the absence of clinical symptoms or radiological abnormalities. The detection of LTBI in 44.4% of household contacts underscores the importance of proactive screening using specific diagnostic tools such as IGRA.

The findings highlight the urgent need to implement comprehensive contact tracing and Tuberculosis Preventive Therapy programs targeting close contacts of DR-TB patients. Early identification and preventive treatment of LTBI in this high-risk population are essential strategies to reduce the risk of TB reactivation and transmission within the community.

From a public health perspective, these findings reinforce the importance of strengthening TB control policies, particularly in high-burden countries like Indonesia. Clinically, the study supports integrating routine IGRA testing into the standard of care for DR-TB contact management, which could inform timely and targeted intervention decisions, ultimately improving patient outcomes and reducing future TB incidence.

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Declaration of interest

The authors declare that none of them has any conflict of interest with any private, public or academic party related to the information contained in this manuscript

Author contributions

MFI: writing – original draft, investigation, data curation.; DH: validation, project administration, methodology; AK: resources, methodology FCI: conceptualization, funding acquisition, writing-review & editing. MS: conceptualization, supervision.

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References

1. World Health Organization. Global Tuberculosis Report 2020. Geneva: WHO; 2020. Available from : https://www.who.int/publications/i/item/9789240013131 (11 Jul 2023)
2. Kementerian Kesehatan Republik Indonesia. TB MDR. Available from : https://tbindonesia.or.id/pustaka-TB/informasi/teknis/tb-mdr/ (07 July 2023)
3. Maison DP. Tuberculosis pathophysiology and anti-VEGF intervention. J Clin Tuberc Other Mycobact Dis. 2022 Jan 19;27:100300. https://doi.org/10.1016/j.jctube.2022.100300
4. Ather B, Mirza TM, Edemekong PF. Airborne Precautions. [Updated 2023 Mar 13]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK531468/ (29 Aug 2023)
5. Ryndak MB, Laal S. Mycobacterium tuberculosis Primary Infection and Dissemination: A Critical Role for Alveolar Epithelial Cells. Front Cell Infect Microbiol. 2019 Aug 21;9:299. https://doi.org/10.3389/fcimb.2019.00299
6. Heemskerk D, Caws M, Marais B, et al. Tuberculosis in Adults and Children. London: Springer; 2015. Chapter 2, Pathogenesis. Available from: https://www.ncbi.nlm.nih.gov/books/NBK344406/ (10 Sep 2023)
7. Fox GJ, Barry SE, Britton WJ, Marks GB. Contact investigation for tuberculosis: a systematic review and meta-analysis. Eur Respir J. 2013;41(1):140-156. https://doi.org/10.1183/09031936.00070812
8. Sari IP, Febrianti N, Nuryastuti A. Deteksi infeksi TB laten pada kontak serumah pasien TB paru menggunakan uji QuantiFERON-TB Gold In-Tube. Jurnal Kedokteran Diponegoro. 2022;11(1):33-40.
9. Al-Motairi A, Booy R, Rashid H. Interferon-gamma release assays for the diagnosis of latent tuberculosis infection: a systematic review. J Infect Public Health. 2020;13(2):161-170.
10. Yancey JR, Melchert VE. QuantiFERON-TB Gold+ for the Diagnosis of Mycobacterium tuberculosis Infection. Am Fam Physician. 2021 Feb 1;103(3):177-178.
11. Reichler MR, Khan A, Yuan Y, Chen B, McAuley J, Mangura B, Sterling TR; Tuberculosis Epidemiologic Studies Consortium Task Order 2 Team. Duration of Exposure Among Close Contacts of Patients With Infectious Tuberculosis and Risk of Latent Tuberculosis Infection. Clin Infect Dis. 2020 Oct 23;71(7):1627-1634. https://doi.org/10.1093/cid/ciz1044
12. Pai M, Denkinger CM, Kik SV, Rangaka MX, Zwerling A, Oxlade O, Metcalfe JZ, Cattamanchi A, Dowdy DW, Dheda K, Banaei N. Gamma interferon release assays for detection of Mycobacterium tuberculosis infection. Clin Microbiol Rev. 2014 Jan;27(1):3-20. https://doi.org/10.1128/CMR.00034-13
13. European Centre for Disease Prevention and Control. Use of interferon-gamma release assays in support of TB diagnosis. Stockholm: ECDC; 2011.
14. Reichler MR, Khan A, Sterling TR, Zhao H, Moran J, McAuley J, et al. Evaluation of Investigations Conducted to Identify the Infectious Source of Primary Multidrug-Resistant Tuberculosis Cases - United States, 2011-2016. Clin Infect Dis. 2020;70(9):1944-52. https://doi.org/10.1093/cid/ciz581
15. Erawati D, Kusumawati RL, Santoso S, Mustofa M. The Use of IGRA for Detecting Latent TB Infection Among Household Contacts of Tuberculosis Patients in Indonesia. Jurnal Respirologi Indonesia. 2022;42(3):178-84.
16. Alatas F, Sahiratmadja E, Nasution DA, et al. Gender and Latent Tuberculosis Infection: A Cross-sectional Study Among Household Contacts in Indonesia. Asian Pac J Trop Med. 2018;11(5):340-5. https://doi.org/10.4103/1995-7645.233179
17. World Health Organization. Global Tuberculosis Report 2023. Geneva: WHO; 2023. Available from: https://www.who.int/publications/i/item/9789240076729

18. Houben RM, Dodd PJ. The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling. PLoS Med. 2016;13: e1002152. https://doi.org/10.1371/journal.pmed.1002152
19. Centers For Disease Control and Prevention. The Difference Between Latent TB Infection and TB Disease. Available from: https://www.cdc.gov/tb/publications/factsheets/general/ltbiandactivetb.htm. (25 Oct 2023)
20. Kiazyk S, Ball TB. Latent tuberculosis infection: An overview. Can Commun Dis Rep. 2017 Mar 2;43(3-4):62-66. https://doi.org/10.14745/ccdr.v43i34a01
21. Shea KM, Kammerer JS, Winston CA, Navin TR, Horsburgh CR Jr. Estimated rate of reactivation of latent tuberculosis infection in the United States, overall and by population subgroup.Am J Epidemiol. 2014;179:216-25. https://doi.org/10.1093/aje/kwt246
22. Centers of Desease Control and Prevention. Latent Tuberculosis Infection : A Guideline For Primary Health Care Providers. Atlanta. U.S. Department of Health and Human Services; 2020.
23. Iswanti FC, Handayani KM, Kusumaningrum A, Yamazaki T, Handayani D, Sadikin M. Lysosomal enzymes and the oxygen burst capability of monocyte-derived macrophages in active drug-resistant tuberculosis patients in relation to cell attachment. Tuberculosis (Edinb). 2024 May;146:102498. https://doi.org/10.1016/j.tube.2024.102498