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RESEARCH ARTICLE

Screening for Latent Tuberculosis Infection using Interferon-Gamma Release Assay Test among Healthcare Workers

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Abstract

Healthcare workers (HCWs) represent a significant demographic for screening latent tuberculosis infection (LTBI) due to their potential exposure to infectious patients. Tests based on immunology detection, such as the tuberculin skin test (TST) and the interferon-gamma release assay (IGRA), have been pivotal in diagnosing LTBI. The objective of this study was to evaluate the efficacy of the IGRA test in detecting LTBI compared to the TST among HCWs in an infectious disease hospital. In a cross-sectional study conducted in August 2019 at the Sulianti Saroso Infectious Disease Hospital, we examined 84 HCWs selected through consecutive sampling. Participants were assessed using questionnaires, and the IGRA and TST tests were performed. The findings revealed that 42 (50%) HCWs tested positive for LTBI based on the IGRA test. Most were female, aged 36–45 years, had direct exposure to TB patients, and had been in the healthcare profession for over a decade. The concordance between the TST and IGRA test, as indicated by a κ value, was 0.234. Furthermore, a significant correlation was observed between the incidence of LTBI and the duration of the healthcare profession (p=0.016). In conclusion, our research suggests that both TST and IGRA tests can effectively detect LTBI. The IGRA test had a higher positivity rate among HCWs with over ten years of service.

Keywords: Interferon-gamma release assay, latent tuberculosis infection

Introduction

Indonesia ranks third in global tuberculosis (TB) burden, following India and China.[1] Prioritizing TB management is imperative.[2] Early diagnosis and treatment of pulmonary TB are paramount to curtail TB transmission.[1,3] The risk of TB infection among healthcare workers (HCWs) consistently surpasses that of the general population across the globe.[4] Systematic reviews have revealed that the median estimated annual TB incidence among HCWs in regions with high TB incidence is 1,180/100,000 persons (IQR 91–3,222), in stark contrast to 311/100,000 persons (IQR 168–405) in the general population.[5] In light of this, the CDC guidelines advocate for a comprehensive TB screening program tailored for all HCWs.[4]

Mycobacterium tuberculosis infection can often be contained by the immune system, causing the bacterium to become dormant, leading to latent infection.[4] Latent tuberculosis infection (LTBI) can progress to an active infection or undergo reactivation. Hence, pinpointing and treating LTBI is crucial to minimize the emergence of new active infections within hospital environments.[6,7] Diagnosing LTBI presents a challenge, given the indeterminate bacterial count and the inherent difficulties of direct examination. Consequently, immunological assessments, such as the tuberculin test and the Interferon-gamma release assay (IGRA), have become the cornerstone for LTBI diagnosis.[8,9] This study seeks to evaluate the efficacy of the IGRA test in diagnosing LTBI, juxtaposed against the tuberculin test, among HCWs at the Sulianti Saroso Infectious Disease Hospital.

Methods

A cross-sectional investigation was undertaken at the Sulianti Saroso Infectious Disease Hospital (SSIDH), recognized as a center of excellence in managing infectious diseases, particularly tuberculosis. Eligible participants for the study were healthcare workers who underwent a medical evaluation in 2018, encompassing a tuberculin test and chest X-ray results. Moreover, participation was contingent upon their consent to undergo the interferon-gamma (IFN-γ) release assay (IGRA). We omitted those currently undergoing TB treatment or diagnosed with an active TB infection. The sample size was

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ascertained using the Lameshow formula, and 84 HCWs were accrued through a consecutive sampling technique.

Data accumulated from August to September 2019, the primary information using a designated questionnaire and the IGRA test. We extracted Secondary data from both the laboratory and radiology departments. Categorical variables were presented in percentages and frequencies, with a comparative analysis facilitated by either the chi-square or Fisher's exact test. To gauge the consistency between the two diagnostic methods, we employed the Kappa Test. Our study was sanctioned by the Health Research Ethics Committee of the Sulianti Saroso Infectious Disease Hospital, as evidenced by Ethical Clearance Number 17/38/XXXVI.10/VI/2019—informed written consent procured from all participants.

Results

Our study encapsulated 84 participants who satisfied the inclusion prerequisites. This cohort included both medical and non-medical professionals. The age bracket of these participants ranged from 19 to 56 years, with an average age of 34.58±8.16 years. Their tenure at the SSIDH spanned from 1 to 29 years, averaging 9.32±6.93 years. Table 1 delineates the detailed characteristics of the participants.

Table 1 Characteristic of Participants

Variables	n=84	%
Gender		
Male	22	26.2
Female	62	73.8
Education		
High school	8	9.5
College study	45	53.6
Undergraduate school	26	31.0
Graduate school	5	6.0
Duration of healthcare profession (years)		
≥10	40	47.6
<10	44	52.4

We amassed data, juxtaposing the IGRA and tuberculin test results (as depicted in Table 2). From the pool of 84 participants, 42 (50%) were flagged positive for LTBI using the IGRA test, whereas the tuberculin skin test (TST) only identified 14 as positive. In evaluating the concordance between the two testing methodologies, we derived a κ statistic of 0.234. Despite the modest κ value, it underscores that both the TST and IGRA tests can be deployed as viable detection tools for LTBI.

We delved into the risk factors associated with positive IGRA results (as detailed in Table 3). Our study substantiated that one's tenure in the healthcare profession emerged as the sole determinant correlated with a positive IGRA outcome ($p<0.05$). Contrarily, the bivariate analysis didn't discern any statistically significant disparity between LTBI and potential risk determinants such as age, gender, educational background, presence of a BCG scar, past instances of TB contact outside the hospital environment, or the utilization of respiratory protection like the N95 mask.

Discussion

In our study, the proportion of LTBI in HCWs at the infectious disease hospital was 50%. The precise prevalence of latent tuberculosis infection in Indonesia is challenging, potentially indicating a gap in awareness regarding the importance of screening and testing for LTBI in HCWs. Furthermore, specific guidelines need to be added on which groups should be targeted for these procedures in countries with high TB incidence countries. The World Health Organization (WHO) has suggested that screening for LTBI should primarily focus on adults in contact with TB patients.[8] Previous research has shown that the prevalence of LTBI among HCWs varies widely, ranging from 9% to 86%.[9–12] In high TB incidence countries, HCWs are at an increased risk of LTBI due to their repeated exposure

Table 2 Comparison between IGRA and Tuberculin Test

IGRA	Tuberculin Test			κ Score	p
	Positive	Negative	Total		
Positive	24	18	42	0.234	0.028
Negative	14	28	42		

Table 3 Risk Factors Related to Positive IGRA Result

Variables	IGRA Result			p
	Positive n=42 (%)	Negative n=42 (%)	Total n=84 (%)	
Age (years)				
≥35	27 (58.7)	19 (41.3)	46 (100)	0.125
<35	15 (39.5)	23 (60.5)	38 (100)	
Gender				
Male	11 (50)	11 (50)	22 (100)	1.000
Female	31 (50)	31 (50)	62 (100)	
Education				
High school	3 (37.5)	5 (62.5)	8 (100)	0.294
College study	20 (44.4)	25 (55.6)	45 (100)	
Undergraduate school	17 (65.4)	9 (34.6)	26 (100)	
Graduate school	2 (40)	3 (60)	5 (100)	
Duration of healthcare profession (years)				
≥10	26 (65)	14 (35)	40 (100)	0.016
<10	16 (36.4)	28 (63.6)	44 (100)	
BCG scar				
No	9 (39.1)	14 (60.9)	23 (100)	0.328
Yes	33 (54.1)	28 (45.9)	61 (100)	
History of contact				
Yes	28 (50.9)	27 (49.1)	55 (100)	1.000
No	14 (48.3)	15 (51.7)	29 (100)	
Use of respirator masks				
No*	27 (46.6)	31 (53.4)	58 (100)	0.479
Yes	15 (57.7)	11 (42.3)	26 (100)	

Note: *use of surgical masks

to TB cases and inconsistent implementation of control practices.[9] Compared to household exposures, HCWs are subjected to more frequent, albeit shorter, risk periods. Moreover, there's the concern that infected HCWs could become transmission vectors to patients in healthcare environments.[4]

LTBI is a persistent immune response to stimulation without clinically evident active TB. Clinicians should employ a combination of anamnesis, physical examinations, and chest X-rays to rule out active *Mycobacterium tuberculosis* infections. According to WHO guidelines, no single test is the gold standard for diagnosing LTBI.[8] Studies from the USA indicate that conversions (from negative to positive) and reversions (from positive to negative) were more frequently detected using the IGRA test as compared to the tuberculin skin test.[8,13] IGRA boasts several advantages, including needing a single sample (thus requiring only one patient visit), reduced cross-reactivity with non-tuberculosis bacteria and BCG vaccinations, rapid results, objectivity in measurements, and the lack of boosting.[14,15] IGRAs are pricier and more technically intricate than the TST.[8] We did not derive a definitive conclusion in our study, as the agreement between the TST and IGRA was a mere 0.234. Rafiza et al.,[16] in their Malaysian study, found results mirroring ours and linked these findings to the mandatory BCG vaccinations in their nation. Indonesia's vaccination program mandates BCG vaccinations for newborns. Cross-reactivity with other members of the *Mycobacterium* family could lead to false-positive TST results.[13,16]

Our study found no difference in the proportion of LTBI between older and younger HCWs. While some past research indicated that HCWs over 50 were a risk factor,[6,10,13,15] other studies found that health workers aged 30–39 were more susceptible.[7,16] This suggests that

age might be interlinked with other factors like contact history and employment duration.[13,15]

In our research, the only significant factor related to a positive IGRA test was the duration of the healthcare profession. Contrary to HCWs with an employment duration under ten years, our study indicated a higher positivity rate among those with over ten years of service (p=0,016). It aligns with findings from prior studies.[9,16] Both Apriani et al.[9] and Rafiza et al.,[16] in their systematic reviews, highlighted work duration as an independent occupational risk factor for LTBI, as measured by the IGRA test. They also noted other factors like the history of contact with TB patients and the average daily time of direct patient contact in previous years. Joshi et al.[13] documented a threefold rise in the prevalence of LTBI with employment exceeding ten years. Joshi et al.[13] highlighted that attending physicians were more susceptible than medical students and that an individual's risk of infection increased with their time in healthcare. It suggests that both age and years in healthcare mirror cumulative exposure to *M. tuberculosis*.

Our findings showed that consistent use of respirator masks (N95 masks) wasn't a standalone factor in preventing LTBI. However, in Thailand, a hospital's multi-pronged administrative control measures resulted in a significant decline (from 9.3% to 2.2%) in the annual incidence of LTBI among its HCWs. A similar administrative control study in Brazil across two hospitals underscored the importance of respiratory masks in successfully reducing the incidence of LTBI.[14] These cases emphasize the significance of employing personal protective equipment and maintaining strict administrative controls to thwart LTBI among HCWs.[13,14] Contrastingly, our data indicated that 57.7% of participants who wore a respirator mask tested positive on the IGRA test, suggesting the need for the correct and snug fit of the mask.

Our study does have limitations—the sample size needed to be more significant to represent the entire HCW community in the hospital. Additionally, potential biases exist in classifying risk factors, given that many HCWs had histories of working in various departments before their current roles. Also, the IGRA test and tuberculin test were performed separately. Given that we sourced Tuberculin test data from earlier medical check-up reports, and with TB's incubation period being under a month, biases are plausible. More rigorously designed studies are needed.

Conclusions

Our study indicates that both TST and IGRA tests can be employed for LTBI detection. The IGRA positivity rate was higher among HCWs with over a decade of service. Screening for latent tuberculosis infection is crucial to prevent transmission that could escalate into severe and potentially fatal outcomes for patients and HCWs. Yet, while screening, the cost-effectiveness must be weighed, and primary transmission triggers should be addressed.

Conflict of Interest

We declare no conflict of interest concerning this study.

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