







Analysis of the incidence of latent *Mycobacterium tuberculosis* infection among primary health care professionals in two Brazilian capitals

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TO THE EDITOR:

One quarter of the world's population is estimated to have latent *Mycobacterium tuberculosis* infection (LTBI), which generates potential new cases of active tuberculosis.⁽¹⁾ Most cases progressing to active disease occur within the first 2-5 years after exposure to a tuberculosis index case.⁽²⁾ Health care professionals in whom there has been conversion of an LTBI test—tuberculin skin test (TST) or interferon-gamma release assay (IGRA)—are at risk of developing active disease. Therefore, the Brazilian National Ministry of Health⁽³⁾ recommends annual LTBI screening of this group and the prescription of prophylaxis for those cases in which any of the tests used in order to diagnose this infection have converted.

In the present study, QuantiFERON-TB Gold In-Tube test (QFT; Qiagen, Hilden, Germany), an IGRA, was used to determine the incidence of LTBI among primary health care professionals in two Brazilian capitals: Vitória (incidence rate = 40/100,000 population); and Manaus (incidence rate = 71/100,000 population).

This was a prospective cohort study, conducted between 2011 and 2013, involving primary health care professionals (physicians, nurses, nursing assistants or technicians, and community health agents) who received QFT at two different time points, between 18 and 24 months of follow-up.

All participating professionals gave written informed consent. Blood sample collection for the QFT and rapid HIV testing was carried out as described by Souza et al.,⁽⁴⁾ as were other methodological details.

In 2013, the cohort was evaluated again. In addition to the previous inclusion criteria, having a negative result on the first QFT was considered an inclusion criterion for the second phase of the study. To minimize variability, similar protocols were used for the baseline and follow-up tests.

Since, at that time, QFT results were not standardized for diagnosing LTBI in Brazil,⁽⁵⁾ participants with positive results in the first phase of the study were evaluated by an infectious disease specialist, who considered QFT and TST results. At that time, those with TST conversion were referred to the local tuberculosis control program.

The present study was approved by the Research Ethics Committee of the Federal University of Espírito Santo,

located in the city of Vitória, Brazil (Protocol no. 007/10, March of 2010). All information was coded and stored anonymously in a database created with Microsoft Excel for Windows. For the descriptive analysis, we used STATA software, version 13.1 (StataCorp LP, College Station, TX, USA), and we included the estimate of the risk of QFT conversion, calculated using the actuarial method Cumulative Incidence Based on the Life-Table Interval Approach (Actuarial Life Table).^(6,7) In this method, the cumulative probability of an event over a given time interval ($t_0 - t$) is the proportion of new events over that period, the denominator being the initial population (N_0) corrected for losses (W) that are assumed to be evenly distributed over the time interval of interest; therefore, on average, it is as if all losses occur in the middle of the observation period ($W/2$), according to the following equation^(6,7):

$$R_{(t_0-t)} = \frac{1}{\left(N_0 - \left(\frac{W}{2}\right)\right)}$$

where $t_0 - t$ is the time interval of interest (between 18 and 24 months); I is the number of new cases at $t_0 - t$ (QFT conversion occurred in 12 primary health care professionals); N_0 is the number of individuals at risk at the beginning of the follow-up period (339 primary health care professionals); and W is the number of losses at $t_0 - t$ (276 primary health care professionals).

In the first phase of the study, 339 primary health care professionals were evaluated, 303 (89.4%) of whom were women, and the median age (interquartile range) was 41 (26-63) years.

The prevalence of LTBI, as determined by QFT, was 23.3% in the first phase of the study. Therefore, 260 primary health care professionals were eligible for follow-up, given that their first QFT result was negative. Because of the high turnover of these professionals in the public health care system, plus their absence from the health care facilities on the scheduled day, 63 primary health care professionals (24.2%) were available for the second evaluation.

The median age in the second phase of the study was 46 (39-53) years, 10 individuals (16.4%) reported morbidity, and only 7 (11.1%) reported having had close

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contact with someone with tuberculosis in the last 2 years. With regard to occupational and biosafety characteristics, 44 individuals (69.8%) reported having cared for tuberculosis patients in the last 2 years, and 40 (64.4%) reported that N95 masks were not always available for use.

Considering random losses and the ratio of the proposed calculation, the probability of QFT conversion between 18 and 24 months of follow-up was 7.4%.

Studies have shown that the rate of IGRA conversion among health care professionals in low- and middle-income countries ranges from 10-30%.⁽⁸⁾ In studies conducted in primary and secondary care settings in countries with high tuberculosis incidence rates, the reported rate of IGRA conversion ranges from 14-22%.⁽⁹⁾ In a study conducted in a tertiary care setting in India, the rate of IGRA conversion was 11.6%.⁽¹⁰⁾ However, in none of those studies were losses to follow-up considered in the calculation of the incidence of IGRA conversion.

To our knowledge, this was the first study to provide estimates of the incidence of LTBI among primary health care professionals in Brazil and to use an IGRA as a diagnostic test to evaluate this measure of frequency.

However, the present study has some limitations: loss to follow-up was high (approximately 75%); and, because there was no reference test for the diagnosis of LTBI, the estimated incidence of LTBI may have been influenced by the performance of the QFT.

Among the tuberculosis control strategies proposed by the World Health Organization and the End TB strategy, the diagnosis and treatment of LTBI is of note as one of the actions that can produce the necessary changes. Finally, proper assessment, screening, and treatment of people at risk for LTBI, such as health care professionals, are some of the actions that can contribute to ending the tuberculosis epidemic by 2035.

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