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Detection of latent tuberculosis infection among laboratory personnel at a University Hospital in Eastern Saudi Arabia using an interferon gamma release assay

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Summary
Background/aims: A few recent reports have demonstrated an elevated prevalence of latent tuberculosis infection (LTBI) among laboratory personnel. We sought to evaluate the prevalence of LTBI among laboratory personnel using the QuantiFERON-TB Gold In-Tube (QFT-GIT) assay and to assess the risk factors associated with positive test results.
Methods: The study population included laboratory personnel who were working in the routine diagnostic laboratories of different departments of a university hospital. Subjects were interviewed using a standardized questionnaire that assessed information related to risk factors for LTBI and underwent the QFT-GIT assay.
Results: Positive QFT-GIT tests results were detected in 19.4% (26/134) of the laboratory personnel. The following factors were significantly associated with positive QFT-GIT results: age $\geq$ 30 years [odds ratio (OR): 4.741, 95% CI: 1.41—17.50, $P = 0.004$]; duration of employment in the healthcare profession >10 years ($P < 0.0001$); and non-Saudi nationality (OR: 21.67, 95% CI: 6.69—73.94, $P < 0.0001$).

Abbreviations: LTBI, latent tuberculosis infection; TST, tuberculin skin test; MTB, *Mycobacterium tuberculosis*; BCG, Bacillus Calmette-Guérin; NTM, non-tuberculous mycobacteria; RD1, region of difference; IFN-γ, interferon gamma; IGRAs, interferon gamma release assays; ESAT-6, early secreted antigenic target 6; CFP-10, culture filtrate protein 10; CDC, Centers for Disease Control and Prevention; HCWs, health care workers; QFT-GIT, QuantiFERON-TB Gold In-Tube; OR, odds ratio; CI, confidence interval.

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Conclusion: These data highlight the need for effective institutional TB infection control plans. Additionally, our data reinforce the necessities of pre-employment and regular LTBI screening of laboratory personnel and the importance of offering preventive therapies to positive subjects to prevent the progression to active disease.

Introduction

Tuberculosis in Saudi Arabia is still not fully controlled, despite the enormous efforts exerted by the Ministry of Health. Saudi Arabia is still a country in the intermediate prevalence category [1]. Several factors may play vital roles in the ongoing transmission of TB in Saudi Arabia, including a high number of expatriates, the Hajj pilgrimage, Omra, and the social habits of Saudi citizens.

The current treatment strategy for active TB is inadequate for disease elimination, partially due to latent TB infections (LTBIs). It has been estimated that one-third of the world population has an LTBI [2], with an annual risk of 0.1% of developing active TB [3]. Therefore, identifying and treating latently infected subjects who are at an increased risk of progressing to active disease are key elements of TB control programs [4]. Such preventive treatment diminishes the risk of subsequently developing active TB by approximately 90% [5].

Over the last century, the tuberculin skin test (TST) has been the traditional testing method for the diagnosis of LTBI in different populations throughout the world [6]. However, the TST has many limitations. The test uses a relatively crude mix of antigens from *Mycobacterium tuberculosis* (MTB); as a result, false-positive reactions can occur because of previous Bacillus Calmette-Guérin (BCG) vaccination or sensitization to non-tuberculous mycobacteria (NTM) [7].

To overcome the relatively low specificity associated with the TST, antigens encoded in the region of difference (RD1) of the MTB genome were used to develop T lymphocyte-based interferon (IFN)-γ release assays (IGRAs), which became commercially available in 2005. IGRAs measure the cellular immune responses to a few MTB-specific antigens, including early secreted antigenic target 6 (ESAT-6) and culture filtrate protein 10 (CFP-10) of the RD1 in comparison with the mixed non-specific antigens used in the TST [8].

IGRAs are standardized, quality-controlled laboratory tests that provide results within 24 h. They have excellent specificity and are unaffected by BCG and NTM [7,9]. Unlike the TST, they require a single patient visit, the result is read by an instrument and, thus, is objective, and they do not have a 'booster' effect. IGRAs appear to be at least as sensitive as the TST [7].

IGRAs may seem too expensive at first glance. However, taking into account the expense of follow-up examinations due to false-positive TST results, the overall cost associated with IGRA screening is fairly acceptable. The use of IGRAs is steadily increasing in low or intermediate incidence countries. In 2005 and in 2010, the US Centers for Disease Control and Prevention (CDC) recommended that IGRAs be used in all situations in which the TST is currently used [10].

Health care workers (HCWs) have been known to be at a high risk for TB infections due to occupational exposures to patients with TB infections or specimens with MTB [11]. Additionally, HCWs are at a particular risk for the progression to TB disease [12]. Regarding the prevalence of LTBI among HCWs, few studies have been conducted in high or intermediate incidence settings. Furthermore, many of these studies used the TST and were thus hampered by its low specificity and its cross reactivity with BCG and NTM infections [13].

According to Saudi national policy, as well as countries of East Asia, from which most of the expatriates are always recruited, all infants are required to be vaccinated with BCG. The usefulness of the TST in detecting LTBI is therefore limited due to the possibility of false positives as a result of BCG vaccination [7].

A few recent reports showed a higher prevalence of LTBI in laboratory personnel than in other HCWs, but they included only a limited number of laboratory personnel [8,11,14]. There has been no large-scale study that specifically focused on the issue of LTBI in laboratory personnel who have a high level of exposure to specimens from patients with TB. This study was undertaken to evaluate the prevalence of LTBI among laboratory personnel at a university hospital using IGRAs and to assess the risk factors related to positive test results.