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Latent tuberculosis infection in medical students in the Northeast of Mexico

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ABSTRACT

Background: Medical students are considered to be personnel with a high level of risk for developing latent tuberculosis infection (LTBI). One possible reason is lack of knowledge about the transmission, prevention, and biosafety standards for tuberculosis disease.
Objective: This research aimed to determine the rate of LTBI among medical students studying in a private School of Medicine in Monterrey, Mexico.
Methods: In this cross-sectional study, we obtained blood samples from 174 medical students. LTBI was diagnosed using the QuantiFERON®-TB Gold Plus test. The prevalence of LTBI was compared with the socio-demographic data of the students and their level of knowledge and use of personal protective equipment (PPE).
Results: The proportion of LTBI in the students was 20.6%. Medical students in their first few years of medical school had a lower prevalence of LTBI than students in their final years of medical school. Additionally, students with a low level of knowledge on LTBI and low use of proper PPE had a higher prevalence of LTBI.
Conclusions: In a School of Medicine in Monterrey, Mexico, the proportion of medical students with LTBI was low but the proportion increased in advanced students. Students who demonstrated adequate knowledge and use of respiratory protective masks had lower prevalence rates for LTBI.

1. Introduction

Tuberculosis is the leading cause of death in infectious diseases worldwide. According to the World Health Organization (WHO), a quarter of the world's population is infected with tuberculosis and more than 10 million new cases occur each year [1]. In countries with a high or medium prevalence of tuberculosis, infection can be seen within the first few years of life [2]. Most patients infected with tuberculosis retain *Mycobacterium tuberculosis* within their bodies in a state of persistent immune response without symptoms, a condition known as latent tuberculosis infection (LTBI) [3]. People with LTBI represent an important reservoir for the development of new cases of tuberculosis [4], as it is recognised that 10% of people with LTBI develop active tuberculosis sometime in their lifetime, commonly within the first 2–5 years after infection [5]. Those with diminished immunity have an increased risk of developing active tuberculosis [6,7]. Each person with active tuberculosis can infect 10–15 people each year [8]. Health personnel and medical students are considered to be personnel at high risk for developing LTBI or active tuberculosis [9–12]. This may be related to a lack of knowledge about transmission, prevention, biosafety standards and diagnosis of tuberculosis among professionals and students within the health sector [13,14]. This means that the risk of tuberculosis infection is significantly higher in a hospital setting than in the community. It is therefore important to increase infection control measures as well as to ensure access to LTBI treatment so that health workers will avoid nosocomial transmission of tuberculosis [15].

This study aimed to determine the rate of LTBI in medical students enrolled in a School of Medicine in Monterrey, Mexico.

2. Methods

2.1. Study design

A cross-sectional study was conducted at a School of Medicine in

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Monterrey, Mexico. The frequency of LTBI in medical students in their first 3 years (pre-clinical years) was compared with the proportion of LTBI found in students in their final 3 years (clinical years).

The protocol was submitted to the University of Monterrey Research Committee, and the corresponding permits were obtained from the directors of the school. Students were invited to participate in this research by visits to each classroom during which the nature of the study was explained. The students who agreed to participate signed an informed consent form and answered a questionnaire designed to collect their socio-demographic data, current health conditions and medical history and their knowledge and use of personal protective equipment (PPE). Finally, LTBI was determined using the QuantiFERON®-TB Gold Plus test (QFT®-Plus).

2.2. Population

The University of Monterrey is a private university located in northern Mexico where education courses for several professional careers are offered. A full medical degree education requires 6 years of study. For the first 3 years, the students are in classrooms and do not tend to patients (pre-clinical years). During the last 3 years, they commonly go to hospitals and take care of patients (clinical years). Each year, approximately 1,200 students are enrolled to study for a degree in medicine.

We recruited all healthy medical students from August to December 2019 of any age and sex who agreed to participate in this study. The exclusion criteria were individuals diagnosed with active tuberculosis or with clinical characteristics of active tuberculosis, positive smears or positive cultures. Additionally, those whose veins were difficult to access or resulted in insufficient samples were excluded. Finally, those students who did not complete the questionnaire were removed from the study.

Diagnosis of LTBI in Mexico is limited to people in close contact with patients with active disease and receive treatment only LTBI patients younger than 6 years. As LTBI is not detected in Mexico regularly, there is no official data on the prevalence of this infection. Health workers or medical students are not screened regularly to detect LTBI and normally students do not receive training on tuberculosis prevention. Students receive information about the transmission mechanism of *M. tuberculosis* only in pre-clinical years. Students in clinical years must purchase their own facial masks, and they normally work in government hospitals that do not support them with any kind of protection.

2.3. Sample size

The sample size was calculated to find differences between groups greater than 10%, with a 95% confidence interval and a test power of 80%. We divided 166 individuals into two groups: the first group included students who were enrolled in their first 3 years of medical school and the second group included students who were enrolled in their last 3 years.

The sampling was done by quotas, selecting the same number of students in each level. Fifty-five students were chosen from each year to achieve enrolment of 166 students for every 3 years, regardless of age or sex.

2.4. Procedures

All participants (n = 174) completed a socio-demographic questionnaire and answered questions regarding their knowledge of the use of PPE. Clinical and socio-demographic data from students were obtained with interviews by trained public health personnel using a standardised questionnaire. The main questions in this questionnaire were about age, sex, Bacillus Calmette–Guérin (BCG) vaccination, as well as knowledge and use of PPE. Basically, the students were asked about the type of personal protection they should use to avoid getting infected while treating with patients with tuberculosis. If they answered that a respirator was needed and that they used it, it was considered that they knew and used PPE. Otherwise, it was considered that they were unaware about PPE or did not use PPE.

A total of 4 mL of peripheral blood was taken from each participant to perform a QFT®-Plus test. The blood was obtained by direct puncture of the peripheral veins of the participants. The pre-requisites for obtaining these samples included fasting for at least 6 h and providing informed consent to take the samples. The procedure for the QFT®-Plus test was as follows: the test was performed by qualified laboratory personnel who were blinded to the clinical details of the patient. After peripheral blood samples were taken, blood samples were placed in four collection tubes of the QFT®-Plus kit, that is, 1 mL was placed in each tube. The first tube, designated as the negative control, did not contain antigens. The next two tubes contained TB1 and TB2 (antigenic peptides associated with the *M. tuberculosis* complex), respectively. The fourth tube contained a mitogen or positive control. The tubes were incubated for 16–24 h at 37 °C. Interferon-gamma (IFN-γ) values (UI/mL) were then determined using an enzyme-linked immunosorbent assay plate from a kit and an enzyme-linked immunosorbent assay plate reader. The QFT®-Plus test was considered positive for an IFN-γ response to either tuberculosis antigens if it was significantly above the IFN-γ (IU/mL) value found in the negative control tube. The diagnosis of latent tuberculosis was made according to the results of the QFT®-Plus test. The results were considered positive, negative or undetermined according to the criteria established by the manufacturer's software.

2.5. Statistical analysis

All questionnaire data were placed in a Microsoft Office Excel database. Statistical analyses were conducted using SPSS version 25.0. The prevalence of people with LTBI was calculated on the basis of the total positive tests in the sample population. The differences in frequency were derived using a chi-squared test. Statistical significance was defined as $p \leq 0.05$.

3. Results

A total of 174 medical students from different grade levels were reviewed. The average age, the proportion of those with knowledge and use of PPE and the percentage of those who received a BCG vaccination are shown in Table 1.

The medical students had an overall LTBI frequency of 20.6%. The frequency of LTBI in the medical students in their pre-clinical years was compared with the proportion of LTBI found in students in their clinical years. Those who were in their first 3 years of medical school had a LTBI prevalence of 7.6%, whereas those in the last 3 years of medical school had a LTBI prevalence of 35.4%. The difference was statistically significant (p = 0.001) (Table 2). In this student population, 89.7% had been vaccinated with BCG and only 21.8% of the students were aware

Table 1
Descriptive variables of medical student population.

Variables		*Mean*	*SD*
Age		21.42	2.25
		n	%
Sex	Female	101	58.0
	Male	73	42.0
Year	First (1–3, Pre-clinical)	92	52.8
	Last (4–6, Clinical)	82	47.2
BCG	Yes	156	89.7
	No	18	10.3
Knowledge (PPE)	Yes	38	21.8
	No/Do not know	136	78.2

BCG: Bacillus Calmette–Guérin; PPE: personal protective equipment; SD: Standard deviation.

Table 2
Cross analysis of variables according to the presence of latent tuberculosis Infection (LTBI).

Variables		*LTBI (+)*	*%*	*LTBI (−)*	*%*	*P value*
Sex	Female	20	19.8	81	80.2	0.88
	Male	16	21.9	57	78.1	
Year	First	7	7.6	85	92.4	0.001
	Last	29	35.4	53	64.6	
BCG	Yes	31	19.9	125	80.1	0.63
	No	5	27.8	13	72.2	
Knowledge (PPE)	Yes	3	7.9	35	92.1	0.04
	No/Do not know	33	24.3	103	75.7	

BCG: Bacillus Calmette–Guérin; PPE: personal protective equipment.

about PPE or appropriately used PPE. Additionally, students who were unaware about or did not use PPE had a significantly increased prevalence of LTBI than those with better knowledge about PPE and used it appropriately. Only 21.8% of the students were aware about PPE and appropriately used PPE when treating patients diagnosed with tuberculosis. Furthermore, only 7.9% of students who were aware about PPE and appropriately used PPE had LTBI, whereas 24.3% of the students who were unaware about or did not use PPE were infected, which showed a statistically significant difference (Table 2).

4. Discussion

The proportion of LTBI in students in a private medical school in Monterrey, Mexico was 20.6%, which was lower than the global burden of LTBI declared by the WHO in 2018 (25%) [3]. Moreover, only 7.6% of students in the pre-clinical years of medical school had LTBI. In Monterrey, Mexico, there are at least three universities with medical schools; two are private and one is public. Private universities normally enrol students of high socioeconomic status. At this socioeconomic level in the Northeast of Mexico, the rates of tuberculosis and LTBI are low [16]. The official Mexican standard for the application of vaccines is a recommendation but not an obligation, and only 89% of the students received the BCG vaccine. In Mexico, there is a general thought that tuberculosis affects only the poor [17], leading to lower compliance with BCG vaccinations in higher socioeconomic classes. A total of 35.4% of the LTBI cases were found in students who were enrolled in their last 3 years of medical school. This may be because they were in contact with patients with pulmonary diseases, including active tuberculosis, without the use of respirators or protective masks.

In a prospective study in India, it was found that medical residents had a higher risk of developing LTBI [18] because they spent more time in hospitals and had prolonged contact with patients. In that study, the proportion of residents with LTBI after 12 months of observation was 26.8%. It was noted that they rarely used PPE, which was similar to the results of our own study. Another prospective study on medical students conducted in Italy found that those with a higher risk of LTBI were foreign students coming from countries with a high prevalence of tuberculosis [19].

A cross-sectional survey done in Namibia showed that there was a time-related risk between the student's age and year of study with that of a positive tuberculin skin test [20]. The study showed a strong association between knowledge of and exposure to tuberculosis, with 26.7% of the students in the sixth year of medicine having a positive tuberculin skin test. Older students and those further along in their academic studies had more knowledge of tuberculosis.

Our results showed that people who were unaware about or did not use respirators or protective masks had a higher risk of developing LTBI. Note that students in the pre-clinical years had less knowledge of tuberculosis and PPE use, but they also had less exposure. Clinical year students tended to have more knowledge, but also more exposure. The relationship between the level of knowledge and prevalence of LTBI is independent of the relationship between the level of exposure and the prevalence of LTBI.

Although some studies on medical students and other non-medical student populations [21] have shown a general lack of knowledge about tuberculosis and recommend that there is indeed a need for improvement, our results showed an association between the lack of knowledge and use of preventive measures, such as the use of respirators or protective masks, and a higher presence of LTBI.

With the coronavirus disease 2019 pandemic, the use of PPE has become an issue [22]. However, health personnel still do not recognise tuberculosis as a disease in which a similarly high level of PPE use is necessary [23]. We should introduce a similar level of urgency for the use of PPE to prevent tuberculosis.

The proportion of LTBI in students enrolled in a private medical school in Monterrey, Mexico, was 20.6%. The proportion of infected students increased from 7.6% in students in the pre-clinical levels to 35.4% in the clinical levels. This represents a nearly five-fold growth in the prevalence of LTBI in the clinical years compared with the pre-clinical years. The association between the lack of knowledge and use of PPE increased LTBI rates almost three-fold.

Ethical considerations

This work respects the established health research laws and in the Helsinki code for human research and has been approved by the Research Ethics Committees of the University of Monterrey with the number 10-04a-2016-CIE. All participants provided their written informed consent before being included in the study.

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CRediT authorship contribution statement

Sofía T. Lozano-Díaz: Investigation, Software. **Erick R. Santaella-Sosa:** Conceptualization, Formal analysis. **Jesus N. Garza-González:** Methodology, Formal analysis. **Philippe Stoesslé:** Methodology, Supervision, Validation. **Javier Vargas-Villarreal:** Supervision, Validation. **Francisco González-Salazar:** Conceptualization, Project administration, Writing – original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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