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#### EPIDEMIOLOGY

# Tuberculin skin test conversion among health sciences students: A retrospective cohort study

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#### SUMMARY

Previous studies have reported that health sciences students are at greater risk for tuberculosis infection, especially in developing countries. The objective of this study was to estimate the prevalence, incidence, and factors associated with latent tuberculosis infection among Health Sciences students in Peru. Students enrolled at private university (in Lima – Peru) are tested annually for tuberculosis infection by tuberculin skin test. Data on tuberculin skin test results between 2002 and 2009 was used in this retrospective cohort study, a total of 4842 students were included. Tuberculin skin test conversion was defined as the change of tuberculin skin test from negative (<10 mm) to positive ( $\geq 10$  mm) after 48 –72 h of inoculation. Baseline tuberculin skin test positivity was 1.0% (95%CI: 0.6%–1.3%), whereas tuberculin skin test conversion incidence was 12.4 per 100 person-years (95%CI: 11.8–13.0). This study showed that students from clinical careers in close contact with patients had an increased risk of tuberculosis infection in the internship, especially Medicine, Dentistry, Medical Technology and Nursing. Administrative, environmental and personal protection measures should be implemented and evaluated periodically in order to reduce the risk of exposure.

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#### 1. Introduction

Tuberculosis (TB) is a public health problem worldwide, with an estimated number of 8.8 million new cases and 1.1 million deaths in 2010.<sup>1</sup> Greater incidence rates have been observed in developing countries due to high levels of poverty, low income, inadequate distribution of resources and malnutrition, all of which limit the impact of disease control strategies.<sup>2</sup> Among Latin American countries, Peru had one of the highest TB incidence rates (106 per 100,000 person-years) in 2010.<sup>1</sup>

Health workers experience greater vulnerability to TB because of close contact and frequent exposure to TB patients, inappropriate environmental conditions in hospitals, and limited or lack of biosafety measures.<sup>3,4</sup> For example, in 1999 at one Peruvian national hospital, the incidence of active TB among health workers was found to be 1.2% per year,<sup>5</sup> nine times the national TB incidence rate. Additionally, this report found that 16.6% of patients diagnosed between 1994 and 2007 in the Peruvian TB control program were health workers.<sup>5</sup>

Prevalence of tuberculosis skin test (TST) positivity in health care workers ranges between 33% and 79%, whereas rates of TST conversion varies between 0.5% and 20%,<sup>6–9</sup> although only 5% of newly infected cases develop active disease after two years of infection.<sup>10,11</sup>

Students of the health sciences often have patient contact during their training and are exposed to TB.<sup>12</sup> For this population, annual TST conversion rate fluctuates between 3.4% and 18.1%,<sup>13,14</sup> with greater risk during clinical rotations<sup>13,15</sup> and the final years of their training.<sup>13,16,17</sup> Inappropriate implementation of biosafety measures in hospitals that host clinical rotations<sup>18</sup> and limited knowledge about TB transmission mechanisms<sup>17</sup> may be responsible for these findings.

The main objective of this study was to estimate the incidence and factors associated with TST conversion among health sciences students at a private university in Lima, Peru. In addition, the baseline prevalence of TST positivity in this group was estimated.



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#### 2. Methods

#### 2.1. Study design, setting, and participants

This is a retrospective cohort study using data from baseline and follow-up clinical evaluations performed annually on undergraduate health science students at the Universidad Peruana Cayetano Heredia (UPCH) in Lima, Peru.

UPCH is a private, non-profit university located in Lima, Peru, with eight schools and more than 6000 students per year. UPCH is the leading university in Peru in medicine and health sciences, and provides undergraduate and post-graduate education. The main careers at UPCH are Medicine, Medical Technology, Dentistry, Health Administration, Nursing, Education, Sciences, Veterinary Medicine and Psychology. Each career takes 5 years to complete with the exception of Medicine which is a 7-year career.

We analyzed data from 2002 to 2009. Since this is a secondary analysis, only students with complete information were considered.

#### 2.2. Definition of variables

TST positivity at baseline was defined as a student having a positive TST result ( $\geq$ 10 mm) in the first year (baseline)<sup>19,20</sup>; whereas TST conversion was defined as the TST change from negative (<10 mm) to positive ( $\geq$ 10 mm) after 48–72 h of inoculation using the Mantoux method during follow-up.<sup>21</sup> Students with a positive TST at baseline were excluded from the analysis of TST conversion. Follow-up time was defined as the number of years up to TST conversion among students starting with a negative TST result.

The variable career was categorized into three groups: veterinary, non-clinical and clinical. Clinical careers included Dentistry, Nursing, Medical Technology and Medicine. Careers with infrequent contact with TB patients (Education, Sciences, and Health Administration) were grouped as "non-clinical careers" and used as a reference category. Even among the clinical careers, students do not have contact with patients or hospital environments during their first year. In subsequent years, the curriculum requires training in hospital settings, increasing their contact with patients. The final year for each career is an internship, a full-time practicum at a hospital. Medical students also have an externship during their second to last year, which also implies long-term, close contact with patients in a hospital. Veterinary students have some exposure to animals in their second year; this exposure increases during their 4th and 5th years of study. During their last year, the Veterinary students are also exposed to human patients at a hospital while studying zoonotic diseases.

Other variables considered in the analysis were: age, categorized according to quartiles; body mass index (BMI) categorized as  $\leq$ 18.5 (underweight), 18.5 to <25 (normal), and  $\geq$ 25 (overweight/obesity)<sup>22</sup>; self-reported prior TB contact, asked during their baseline medical exam and defined as having had close contact with a relative with TB in the last year; year of career, defined as the year ended for the student at the moment of the clinical exam; and internship (yes vs. no), defined as being in the last year of the career.

#### 2.3. Procedures

All students are required to go through an annual medical examination which includes a physical examination, as well as questions regarding medical and psychological history. All clinical assessments are performed using routine procedures at a private clinic selected by UPCH. During the evaluations students are tested for TB infection by TST using a standardized protocol.<sup>19</sup> Data from these visits was collected through an electronic health record system.

#### 2.4. Data analysis

First, a description of the population was performed comparing students with complete information versus those without complete information using Chi squared tests. All of the remaining analyses only included students with complete information. Second, prevalence and 95% confidence intervals (95%CI) were calculated at baseline and for the last available evaluation for each student. Third, incidence density (per 100 person-years) and 95% CIs were calculated using information on TST conversion including only students with a negative TST at baseline and at least one follow-up evaluation. Those students with a TST conversion during follow-up were not considered in further incidence analysis. Incidence density was also calculated by career, year of career and by calendar year.

Finally, using a forward stepwise technique, incidence rate ratio (IRR) and 95%CI for variables associated with TST conversion were obtained using generalized linear models with binomial family, log link and data analysis for correlated data. In addition, only using information from the last two years of career, a secular trend for TST conversion incidence was calculated using Chi square for trend. All data analysis was performed using STATA 11 (STATA Corporation, College Station, Texas, US).

#### 2.5. Ethical issues

Approval for this project was granted by the Institutional Review Board (IRB) at UPCH. As only de-identified data was used, the requirement for informed consent was waived.

#### 3. Results

#### 3.1. Description of the participants

From the total of 9875 students in the university, between 2002 and 2009, only 5580 students were recorded in the clinic's database. A total of 18,537 clinical evaluations were obtained from the 5580 students. From those students, 4842 (86.8%) met our inclusion criteria of providing complete data and were included in the analysis. The students' median age at baseline was 18 years (interquartile range: 17–20) and 31.3% were males. Most students belonged to Medicine (23.5%) and Medical Technology (20.9%). Details of other characteristics at baseline of those participating in the study are seen in Table 1.

Baseline TST positivity prevalence was 1.0% (95% CI: 0.6-1.3%), whereas prevalence of TST positivity using the last available evaluation of the students was 38.1% (95% CI: 36.8-39.5%).

#### 3.2. Incidence of TST conversion

The overall incidence density of TST conversion was 12.4 per 100 person-years (95% CI: 11.8–13.0). The annual incidence of TST conversion for students from non-clinical careers was 9.0 per 100 person-years (95% CI: 7.7–10.4), whereas for students from clinical careers was 13.2 (95% CI: 12.5–14.0). Medical Technology and Nursing students had the greatest incidence (see Table 2).

Analysis stratified by career, showed higher incidences in the last two years of Medicine (33.9 per 100 person-years; 95% CI: 21.9–52.5), Medical Technology (22.8; 95% CI: 18.1–28.6) and Nursing (20.8; 95% CI: 16.6–25.9, see Figure 1).

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