Incidence of latent tuberculosis infection among health science students during clinical training

Mada H. Alsharif, Atheer A. Alsulami, Malikah Alsharef, Amr S. Albanna1, Siraj O. Wali

Abstract:

BACKGROUND: The prevalence of latent tuberculosis infection (LTBI) has been found to be high among students undergoing clinical training. The aim of this study is to determine the incidence of LTBI among undergraduate health science students after their clinical training and to compare the risk between different college specialties.

METHODS: This is a retrospective cohort study of students who completed their clinical training from 2010 to 2017. The risk of LTBI was defined based on the conversion of tuberculin skin test (TST) results from negative at the start of training to positive after the completion of training.

RESULTS: A total of 2000 students were evaluated, of whom 1997 were included in this analysis. Six percent tested positive in the first TST of the initial screening. Ten percent of students with a normal baseline TST converted to positive on the follow-up TST. Clinical training in the college of medicine increased the risk of LTBI by 76% (odds ratio: 1.76; 95% confidence interval: 1.04–2.96; P = 0.03) compared to clinical training in other medical colleges.

CONCLUSIONS: The risk of acquiring LTBI during clinical training in health science colleges is 10%. Students in the college of medicine are at significantly higher risk of LTBI than students of other health science specialties.

Keywords: Latent tuberculosis infection, medical students, tuberculin skin test

Latent tuberculosis infection (LTBI) is defined by the World Health Organization as “a state of persistent immune response to stimulation by Mycobacterium tuberculosis (MTB) antigens without evidence of clinically manifested active tuberculosis (TB).”[1] It is estimated that 23% of the world’s population is infected with MTB and at risk of developing active TB.[2] Despite being an old disease, TB continues to be a major public health concern, especially in low- and middle-income settings such as the middle east and other developing countries. Saudi Arabia reports a high number of incident TB cases annually.[3] Based on the World Health Organization report, the estimated TB incidence rate in Saudi Arabia was 18/100,000 people in 2012, and Saudi Arabia remains a country of moderate TB burden.[1,3,4] The estimated prevalence of LTBI in Saudi Arabia was 9.3%.[4]

Several studies were conducted to determine the populations who are at increased risk of acquiring TB; of those populations, medical students and health-care workers were determined to have a higher prevalence of LTBI.[5-17] A meta-analysis was conducted to estimate the prevalence of TB among high-risk groups and showed an increased prevalence of TB among medical students, interns, and health-care workers.[4,9,18-20]

Undergraduate medical students are exposed to TB patients as health-care...
workers during their clinical training period. This risk might increase if the students lack sufficient knowledge about the disease and its mode of transmission, especially if they do not strictly adhere to the use of personal protective equipment and measures of infection control when dealing with TB or TB suspect patients. The aim of this study is to determine and compare the incidence of LTBI among undergraduate students of different health science colleges after their clinical training.

Methods

The study population consists of all undergraduate students who completed the clinical training in the following colleges from 2010 to 2017: college of medicine, college of dentistry, college of nursing, college of pharmacy, and college of applied medical sciences (including physiotherapy, laboratory science, and nutrition). We included students who were screened for TB with a tuberculin skin test (TST) before and after their clinical training as undergraduates. We excluded students with active TB.

The data were collected using a standardized form that includes age; gender; nationality; college or specialty; date of first, second, and additional TSTs; duration between the TSTs; results of TSTs; follow-up chest X-rays and sputum cultures; comorbid illnesses; and the prescription of isoniazid (INH). The TST was performed by injecting five units of protein-purified derivative intradermally, and the results were reviewed 48–72 h later. A 10 mm or more skin induration was considered a positive result, and for those with a negative result, a second step screening was performed 2 weeks later. An additional TST was performed after the last year of in-hospital training before graduation.

The study was conducted after ethical approval from the Institutional Review Board at King Abdulaziz University Hospital. Permission for access to participants’ data was also obtained from the King Abdulaziz University Hospital. No participant identifiers were used during data collection.

Data analysis

The proportions for dichotomous variables and means for continuous variables were calculated to describe the patients’ characteristics. The risk of TB infection among the students of each college was compared using a Chi-square test and logistic regression analysis. To control for potential confounding factors (age, immigration status, comorbidity, a history of contact with TB patients, and the duration of training between TSTs), multivariate logistic regression analysis was performed. The selection of confounding factors (covariates) that were included in the regression model was based on a priori theoretical assumption using directed acyclic graphs. The result of the regression model was presented as odds ratio (OR) with 95% confidence interval. Statistical significance was determined using the 95% CI and P = 0.05. All analyses were performed using STATA (Version 12, Software StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX, USA: StataCorp LP).

Results

A total of 2000 students were evaluated, of whom 1997 were included in the analysis. The demographic characteristics and the students’ distribution among the different colleges are summarized in Table 1.

Among the 1997 students, 6% tested positive on the first TST of the initial screening; 88% of them underwent chest radiograph, which showed no abnormalities suggestive of pulmonary TB. On the other hand, 10% of students with normal baseline TST tested positive on the follow-up TST after an average duration of 25 months of hospital exposure. INH prophylaxis was prescribed to 48% of the students with positive TST results, as shown in Table 2.

There was a significant difference in the risk of LTBI between students in different colleges during their clinical training [Figure 1]. This difference was not influenced by the duration of the training, as shown in Figure 2. Clinical training in the college of medicine increased the risk of TB infection by 76% compared to clinical training in other medical colleges (adjusted OR: 1.76, 95% CI: 1.04–2.96, P = 0.03; adjusted for age, immigration status, comorbidity, a history of contact with TB patients, and the duration of clinical training).

Discussion

Our study showed that the incidence of LTBI acquired during clinical training is 10%. Across all different health science colleges, medical students were at the highest risk if they do not strictly adhere to the use of personal protective equipment and measures of infection control when dealing with TB or TB suspect patients.

Table 1: General characteristics of included patients

| Characteristics          | n/Total | Estimate | 95% CI    |
|--------------------------|---------|----------|-----------|
| Age (years), mean (SD)   | -       | 23.8 (2.2) | 23.7-23.9 |
| Male sex, (%)            | 693/1996| 34.7     | 32.6-36.9 |
| Saudi nationality, (%)   | 1931/1997| 96.7   | 95.8-97.4 |
| Chronic illness, (%)     | 29/1966 | 1.5      | 1.0-2.1   |
| College, (%)             |         |          |           |
| Nutrition                | 150/1997| 7.5      | 6.4-8.8   |
| Laboratory               | 205/1997| 10.3     | 9.0-11.7  |
| Nursing                  | 394/1997| 19.7     | 18.0-21.5 |
| Pharmacy                 | 98/1997 | 4.9      | 4.0-5.9   |
| Dentistry                | 372/1997| 18.6     | 16.9-20.4 |
| Radiology                | 104/1997| 5.2      | 4.3-6.3   |
| Physiotherapy            | 200/1997| 10.0     | 8.7-11.4  |
| Medicine                 | 474/1997| 23.7     | 21.9-25.6 |

SD=Standard deviation
risk of LTBI. These findings are alarming, considering that Saudi Arabia is a moderate TB-burden country.\cite{25,26}

Our findings are supported by observations from other studies that evaluated the prevalence of LTBI and identified a higher prevalence of LTBI among medical students as well as health-care workers.\cite{5-17}

For instance, a study conducted in Tunisia showed that the prevalence of LTBI was 26.6% among medical interns, which is much higher than what we observed among undergraduate clinical trainees. Based on a recent meta-analysis that included studies of different Iranian populations, the prevalence of LTBI varied across different TB exposure risks, with a prevalence of 25% in the general population and 39% among health-care workers.\cite{5}

Local studies within Saudi Arabia showed that the prevalence of LTBI ranged from 5% to 12% among health science colleges, (namely dental assistance, physiotherapy, midwifery, nursing, and radiology) and was approximately 11% among health-care workers.\cite{6,7}

Comparing different health science specialties in our study population, the risk of LTBI was significantly higher in specialties with closer contact with patients, such as medicine, and lower in specialties with less contact with patients, such as laboratory science and nutrition.

It is notable that INH was prescribed for less than half of our study population, which is considered a high-risk group. Although we cannot explain the reasons for such a low treatment rate, proper management of latent TB infection in this specific population group (health-care personnel) is crucial to achieve public TB control.

The main limitations of this study include the lack of follow-up data regarding the development of active TB disease among LTBI patients and the single-center study design. Despite these limitations, the study had a large sample size that provided enough power to compare different health science colleges. In addition, we measured the incidence of LTBI using initial and follow-up TST results, unlike most published studies that compared the existing LTBI prevalence.

Our findings have important clinical implications for determining the risk of LTBI in a vulnerable group of

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### Table 2: Medical screening among included individuals

| Characteristics                                      | n/total | Estimate | 95% CI   |
|------------------------------------------------------|---------|----------|----------|
| Positive screening (initial) TST (%)                 | 108/1822| 5.9      | 4.9-7.1  |
| Performed CXR* (%)                                   | 96/108  | 88.9     | 81.4-94.1|
| Abnormal CXR* (%)                                    | 0/90    | 0        | 0-4.0    |
| Performed MTB culture* (%)                           | 0/108   | 0        | 0-3.4    |
| Positive follow-up (additional) TST** (%)            | 134/1345| 9.9      | 8.4-11.6 |
| Average follow-up duration (mean, months)            | -       | 24.6 (11.6) | 23.9-25.2|
| INH treatment (%)                                    |         |          |          |
| Among individuals with initial positive TST          | 47/108  | 43.5     | 34.0-53.4|
| Among all individuals with positive TST\#             | 117/242 | 48.3     | 41.9-54.8|

*Among patients with positive TST results, **Among patients with baseline-negative TST results (TST conversion), *Between screening and follow-up TSTs, \#Among patients with positive screening or follow-up TST results. TST=Tuberculin skin tests, CXR=Chest X-ray, MTB=Mycobacterium tuberculosis, INH=Isoniazid, CI=Confidence interval
students who will be practicing medicine and providing care for the general population. These findings underscore the importance of prioritizing TB preventive programs across different health-care specialties, especially for the most vulnerable health science students who are still in training and have little experience with self-care preventive practices. Published studies have shown that less than half of health science students (46.7%) have knowledge about TB and its transmission.[27]

**Conclusions**

In our study population, the risk of LTBI acquired during clinical training among health science students is 10%. Compared to students of other colleges, medical students are at significantly higher risk of LTBI. These observations underscore the importance of applying additional infection control measures to protect undergraduate health science students who are considered a vulnerable population group.

**Acknowledgments**

We would like to thank all the data collectors for their major contribution to this study, namely Khloud B. Fallatah, Mona S. Kojaah, Attheer F. Alsulami, Ibthail Alsahabi, Astabraq Alomran, Ghadah Alnajjar, Fatimah M. Hisan, Maha Alghamdi, Hadeel Albeshi, and Lojain Almadfa.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. World Health Organization. Latent TB Infection: Updated and Consolidated Guidelines for Programmatic Management. Geneva, Switzerland: World Health Organization; 2018.
2. World Health Organization. Global Tuberculosis Report 2018. Geneva, Switzerland: World Health Organization; 2018.
3. Al-Hajjaj S, Varghese B. Tuberculosis in Saudi Arabia: The journey across time. J Infect Dev Ctries 2015;9:222-31.
4. Balkhy HH, El Beltagy K, El-Saed A, Aljasir B, Althaqafi A, Alothman AF, et al. Prevalence of latent Mycobacterium tuberculosis infection (LTBI) in Saudi Arabia; population based survey. Int J Infect Dis 2017;60:11-6.
5. Rezai MS, Tabrizi R, Haghdoost AA, Afshari M, Abedi S, Akbari M, et al. Estimating the prevalence of positive tuberculin skin test reactions in general population and high-risk groups: A meta-analysis. Int J Prev Med 2017;8:97.
6. Abbas MA, AlHamdan NA, Fiala LA, AlEnezy AK, AlQahtani MS. Prevalence of latent TB among health care workers in four major tertiary care hospitals in Riyadh, Saudi Arabia. J Egypt Public Health Assoc 2010;85:61-71.
7. Murad MA, Abdulmageed SS. Tuberculosis screening among health sciences students in Saudi Arabia in 2010. Ann Saudi Med 2012;32:527-9.
8. Xu Y, Schwartzman K. Referrals for positive tuberculin tests in new health care workers and students: A retrospective cohort study. BMC Public Health 2010;10:28.
9. Garber E, San Gabriel P, Lambert L, Saiman L. A survey of latent tuberculosis infection among laboratory healthcare workers in New York city. Infect Control Hosp Epidemiol 2003;24:801-6.
10. Lou JK, Okot-Nwang M, Katamba A. Prevalence of positive tuberculin skin test and associated factors among Makerere medical students, Kampala, Uganda. Afr Health Sci 2015;15:1247-55.
11. Hassan MI, Diab AE. Detection of latent tuberculosis infection among laboratory personnel at a university hospital in Eastern Saudi Arabia using an interferon gamma release assay. J Infect Public Health 2014;7:289-95.
12. Merte JL, Kroll CM, Collins AS, Melnick AL. An epidemiologic investigation of occupational transmission of Mycobacterium tuberculosis infection to dental health care personnel: Infection prevention and control implications. J Am Dent Assoc 2014;145:464-71.
13. Grobler L, Mehtar S, Dheda K, Adams S, Babatunde V, van der Walt M, et al. The epidemiology of tuberculosis in health care workers in South Africa: A systematic review. BMC Health Serv Res 2016;16:416.
14. Van der Westhuizen HM, Dramovski A. When students become patients: TB disease among medical undergraduates in Cape Town, South Africa. S Afr Med J 2017;107:475-9.
15. Bukhary ZA, Amer SM, Emara MM, Abdalla ME, Ali SA. Screening of latent tuberculosis infection among health care workers working in Hajj pilgrimage area in Saudi Arabia, using interferon gamma release assay and tuberculin skin test. Ann Saudi Med 2018;38:90-6.
16. Menzies D, Yosh R, Pai M. Risk of tuberculosis infection and disease associated with work in health care settings. Int J Tuberc Lung Dis 2007;11:593-605.
17. van Rie A, McCarthy K, Scott L, Dow A, Venter WD, Stevens WS, et al. Prevalence, risk factors and risk perception of tuberculosis infection among medical students and healthcare workers in Johannesburg, South Africa. S Afr Med J 2013;103:853-7.
18. Hung WT, Lee SS, Sy CL, Wu KS, Chen JK, Tsai HC, et al. Prevalence of latent tuberculosis infection in BCG-vaccinated healthcare workers by using an interferon-gamma release assay and the tuberculin skin test in an intermediate tuberculosis burden country. J Microbiol Immunol Infect 2015;48:147-52.
19. Toujani S, Cherif J, Mjid M, Hedhli A, Ouahchy Y, Beji M, et al. Evaluation of tuberculin skin test positivity and early tuberculin conversion among laboratory personnel at a university hospital in Eastern Tunisia. Tunisaffos 2017;16:149-56.
20. Moges B, Amare B, Yismaw G, Workineh M, Alemu S, Mekonnen D, et al. Prevalence of tuberculosis and treatment outcome among university students in Northwest Ethiopia: A retrospective study. BMC Public Health 2015;15:15.
21. Setahun H, Matteelli A, Abubakar I, Aziz MA, Baddeley A, Barreira D, et al. Management of latent Mycobacterium tuberculosis infection: WHO guidelines for low tuberculosis burden countries. Eur Respir J 2015;46:1563-76.
22. Targeted tuberculin testing and treatment of latent tuberculosis infection. This official statement of the American Thoracic Society was adopted by the ATS board of directors, July 1999. This is a joint statement of the American Thoracic Society (ATS) and the Centers for Disease Control and Prevention (CDC). This statement was endorsed by the council of the Infectious Diseases Society of America (IDSA). September 1999, and the sections of this statement. Am J Respir Crit Care Med 2000;161:S221-47.
23. Al Jahdali HH, Baharoon S, Abba AA, Memish ZA, Alrajhi AA, AlBarak A, et al. Saudi guidelines for testing and treatment of latent tuberculosis infection. Ann Saudi Med 2010;30:38-49.
24. El-Helely M, Khan W, El-Saed A, Balkhy HH. Pre-employment screening of latent tuberculosis infection among healthcare professionals. Mediterr J Hematol Inf Dis 2017;9. Article 3.
workers using tuberculin skin test and quantiFERON-TB gold test at a tertiary care hospital in Saudi Arabia. J Infect Public Health 2014;7:481-8.

25. American College Health Association. Tuberculosis screening and targeted testing of college and university students. J Am Coll Health 2011;59:670-7.

26. Lönnroth K, Migliori GB, Abubakar I, D’Ambrosio L, de Vries G, Diel R, et al. Towards tuberculosis elimination: An action framework for low-incidence countries. Eur Respir J 2015;45:928-52.

27. AlSalem S, AlEisa A, Raslan I, BinJawhar A, Khouqeer A, Gad A. Tuberculosis: Awareness among students in a Saudi University. Health 2015;7:175-82.