






## Latent Tuberculosis Infection in Healthcare Workers: A Cross-Sectional Study from a Tertiary Hospital in Central Anatolia

 Zeynep Ture,<sup>1</sup>  Berna Demir,<sup>2</sup>  Fatih Elönü,<sup>3</sup>  Gamze Kalın Ünüvar,<sup>1</sup>  Ahmet Öztürk<sup>4</sup>

<sup>1</sup>Department of Infectious Diseases, Erciyes University Faculty of Medicine, Kayseri, Türkiye

<sup>2</sup>Department of Intensive Care Unit, Erciyes University Faculty of Medicine, Kayseri, Türkiye

<sup>3</sup>Department of Infection Control Committee, Erciyes University, Kayseri, Türkiye

<sup>4</sup>Department of Biostatistics, Erciyes University Faculty of Medicine, Kayseri, Türkiye

### ABSTRACT

**Objective:** This study assessed the incidence and risk factors of latent tuberculosis infection (LTBI) among healthcare workers (HCWs) in a tertiary healthcare institution in Central Anatolia.

**Materials and Methods:** A prospective study was conducted. From January 1 to June 30, 2024, HCWs who visited the personnel follow-up outpatient clinic were diagnosed with LTBI based on tuberculin skin test results. Demographic data, occupation, workplace and duration of employment, and risk factors for tuberculosis exposure inside and outside the workplace were compared between HCWs with and without LTBI.

**Results:** A total of 101 HCWs participated in the study. LTBI was detected in 19 HCWs (19%). The median age of healthcare workers was 36 years, with the majority being nurses (40%) and university graduates (60%). There were no differences between LTBI and non-LTBI groups in terms of demographic data, occupational, and non-occupational tuberculosis contact risks. Examination of chest X-ray findings revealed that HCWs with LTBI had more abnormal findings, with a statistically significant difference in the rate of calcification ( $p=0.003$ ). Among HCWs with LTBI, the use rate of filtering facepiece (FFP-3) masks when in contact with suspected or confirmed tuberculosis patients was lower (31% and 45%).

**Conclusion:** This study identified latent tuberculosis in one out of every five healthcare workers. Routine examination and periodic chest X-rays for HCWs are crucial for predicting latent tuberculosis. Healthcare workers should be educated on the correct use of personal protective equipment.

**Keywords:** Healthcare worker, latent tuberculosis, personal protective equipment, tuberculosis.



#### Cite this article as:

Ture Z, Demir B, Elönü F, Kalın Ünüvar G, Öztürk A. Latent Tuberculosis Infection in Healthcare Workers: A Cross-Sectional Study from a Tertiary Hospital in Central Anatolia. J Clin Pract Res 2024;46(5):484–490.

#### Address for correspondence:

Zeynep Ture.  
Department of Infectious Diseases, Erciyes University Faculty of Medicine, Kayseri, Türkiye  
**Phone:** +90 352 437 52 85  
**E-mail:** dr.zeynepture@gmail.com

**Submitted:** 16.07.2024  
**Revised:** 16.09.2024  
**Accepted:** 02.10.2024  
**Available Online:** 25.10.2024

Erciyes University Faculty of Medicine Publications - Available online at [www.jcprres.com](http://www.jcprres.com)



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### INTRODUCTION

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis complex* bacilli, which can be transmitted from an individual with active tuberculosis to a healthy person through airborne droplets.<sup>1</sup> In 2022, an estimated 10.6 million people globally were diagnosed with tuberculosis, including 1.3

million children. Between 2020 and 2022, the incidence rate of tuberculosis increased by 3.9%, reversing a two-decade trend of decreases averaging approximately 2% per year. Globally in 2022, TB caused an estimated 1.3 million deaths.<sup>2</sup>

Adults exposed to *Mycobacterium tuberculosis* have a 5% risk of developing active tuberculosis disease. In 95% of individuals, the infection remains inactive; in the remaining 5%, the infection reactivates over the years.<sup>1</sup> Groups at the highest risk of contracting new tuberculosis infections include those who have had close contact with individuals with pulmonary tuberculosis, casual contacts, homeless populations, drug users, residents and staff of nursing homes, and healthcare professionals working in pulmonology and emergency rooms in highly endemic countries.<sup>3</sup>

Latent tuberculosis infection (LTBI) refers to an immune response to *Mycobacterium tuberculosis* antigens in a person without active tuberculosis infection.<sup>4</sup>

Approximately 25–30% of the world's population has LTBI, and about 10% of these cases, particularly within the first two years, may progress to active tuberculosis.<sup>5</sup> Populations at high risk for reactivation of latent tuberculosis infection include patients with acquired immune deficiencies, organ transplant recipients, chemotherapy patients, individuals with silicosis or renal failure, and patients taking anti-tumor necrosis factor (anti-TNF) medications. Additionally, common conditions such as diseases and the use of systemic glucocorticoid medications are associated with a moderate risk for reactivation.<sup>3</sup> Healthcare workers are at risk of both primary infection and reactivation.<sup>6</sup>

The frequency of LTBI among healthcare workers (HCWs) in developing countries is estimated at 54% (ranging from 33–79%).<sup>7</sup> Studies indicate that health science students who visit primary care facilities and specialized pulmonary hospitals also have a high rate of LTBI.<sup>8,9</sup> The risk of LTBI in HCWs depends on the local prevalence of tuberculosis, the characteristics of the healthcare facility and healthcare workers' activities, and the effectiveness of prevention and control measures.<sup>5</sup>

The risk of tuberculosis in healthcare workers varies depending on the healthcare institution and unit in which they work, and is 0.6–2 times higher than in the general population.<sup>10</sup> This study aimed to determine the incidence of latent tuberculosis and identify risk factors in healthcare workers who attended our hospital's personnel follow-up clinic. Additionally, it sought to identify significant risk potentials in HCWs with LTBI and to implement necessary control measures.

## KEY MESSAGES

- The latent tuberculosis rate among healthcare workers at our hospital is 19%.
- The rate of abnormal findings on chest X-rays was higher in healthcare workers with latent tuberculosis infection.
- Rates of personal protective equipment use when in contact with suspected or confirmed tuberculosis patients were low among all healthcare workers.

## MATERIALS AND METHODS

### Study Design

This study was designed as a prospective observational study. The research was conducted in a tertiary healthcare institution with a 1,300-bed capacity. The institution employs a total of 4,250 healthcare workers, including 1,100 physicians, 950 nurses, 500 administrative staff, and 1,700 other medical staff members. A tuberculin skin test (TST) was administered to healthcare workers who attended the healthcare personnel follow-up clinic between January 1 and June 30, 2024. The study included all HCWs who consented to participate and visited the personnel follow-up clinic within the designated time frame.

In addition to the TST, a survey was administered to healthcare professionals to assess other risk factors for LTBI. This survey included questions on the occupation of the healthcare worker, duration of service, work area, presence of comorbidities, and any personal or family history of tuberculosis.

Chest radiography was performed on healthcare professionals deemed appropriate based on their history and physical examination findings. The tuberculin skin test was administered after obtaining informed consent from participants. After 72 hours, the TST results were evaluated by the same nurse who performed the test. Both the TST results and chest radiography findings were recorded.

**Number of Cases:** The sample size was calculated as 100 (50/50) using the Pass power analysis, where the expected effect size was 60%, the alpha margin of error was 0.05, and the power (1-beta) was 95%.

### Definitions

**Latent Tuberculosis:** Induration greater than 15 mm in Bacille Calmette-Guérin-positive (BCG-positive) cases and greater than 10 mm in BCG-negative cases was deemed positive. A tuberculin skin test was repeated 10 days later to rule out the booster phenomenon in personnel where induration was not initially detected.

**Healthcare Worker (HCW):** The following categories of healthcare workers were considered: physicians, nurses, other HCWs (including secretaries, administrative staff, statisticians), and cleaning staff (including personnel involved in cleaning, laundry, and disinfection).

**Working Area:** The division, space, or service where employees are assigned.

**Service Time:** The duration of employment at the medical facility in years.

**Comorbidity:** Any long-term illness that increases the risk of complications or impairs functioning.

**History of Tuberculosis:** A history of tuberculosis at least once was noted for each participant.

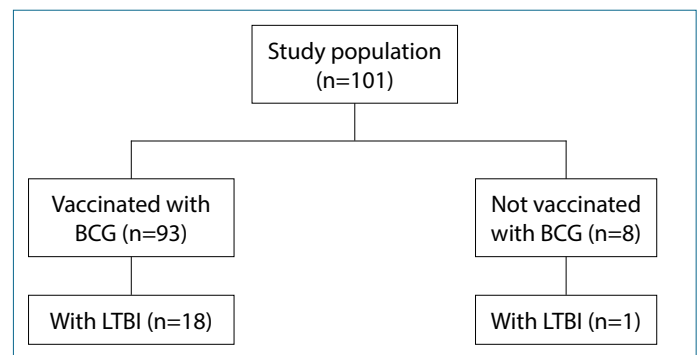
### Statistical Analysis

Data were analyzed using the SPSS 22.0 statistical package program. Demographic data, comorbidities, and risk factors were compared between healthcare workers considered to have latent tuberculosis infection and those who were not. Chi-square or Fisher's exact test was used for qualitative variables, and the Shapiro-Wilk normality test was applied to continuous variable data. For variables that did not show a normal distribution, the Mann-Whitney U test was applied. Significant variables were further evaluated through multivariate backward stepwise binary logistic regression analysis with a 95% confidence interval (CI 95%). A p-value of less than 0.05 was considered statistically significant.

This study was approved by the Ethical Committee of the University of Erciyes (approval no. 2024-94, dated 14.02.2014).

## RESULTS

A total of 101 healthcare workers who presented to the personnel follow-up clinic during the designated period were included in this study. The median age was 36, and 40% of the participants were male. Most healthcare professionals had a university or doctorate-level education (79%). Of the HCWs, 41 were employed in intensive care units and had contact with an average of one active tuberculosis patient per month. The median number of years in the profession was 10, with 50% having over 10 years of experience. The median duration of employment in the current unit was four years, and 70% of the units had an isolation room. Sixty HCWs lived in their city of birth and had resided in Kayseri for an average of 27 years. Additionally, 34% of healthcare workers reported smoking, with an average consumption of 5 pack-years. Thirty-four percent of healthcare professionals had a chronic disease, with chronic lung diseases being the most commonly reported. Forty-six percent of healthcare workers always



**Figure 1.** Distribution of latent tuberculosis cases in Bacille Calmette-Guérin (BCG)-vaccinated and unvaccinated healthcare workers.

used N-95 masks when in contact with patients suspected or confirmed to have tuberculosis. Ninety-three healthcare workers were immunized against tuberculosis in childhood and had a median of two BCG scars. TST results showed an induration greater than 15 mm in 18 healthcare workers with a vaccination history, and in one healthcare worker with no vaccination history, an induration over 10 mm was recorded (Fig. 1). Latent tuberculosis infection was identified in a total of 19 healthcare workers (Table 1).

In Table 2, demographic data and risk factors of healthcare workers with and without LTBI were compared. No significant differences were observed between the groups regarding demographics, profession, unit of employment, region of birth and residence, or comorbidities. When radiological imaging findings from the past year were compared, the rate of normal chest X-ray findings was higher in HCWs without LTBI ( $p=0.010$ ). Additionally, higher rates of fibrotic bands, hilar expansion, and calcification on chest radiography were noted in HCWs with LTBI. The elevated calcification rate was statistically significant ( $p=0.003$ ). Active tuberculosis was not detected in any HCWs with latent tuberculosis following physical, laboratory, and radiological examinations.

## DISCUSSION

In this study, 93% of HCWs who visited the personnel follow-up outpatient clinic during the specified period had BCG scars, indicating a history of tuberculosis vaccination. Since the establishment of tuberculosis control associations in our country in 1918, efforts to increase immunization rates and ensure the continuous and regular use of antituberculosis drugs have been ongoing.<sup>1</sup> The BCG vaccine has been included in childhood immunization since 1949 and has been found to be 60-80% effective in preventing disseminated tuberculosis and tuberculous meningitis in children. However, the vaccine

has no effect on the recurrence of primary tuberculosis or on latent tuberculosis.<sup>11</sup> A study in Northern Ireland that examined the relationship between BCG vaccination and tuberculosis incidence in adults reported a lower incidence of tuberculosis in regions with neonatal vaccination policies.<sup>12</sup> Similarly, a retrospective study that examined clinical and laboratory data of 51 pediatric patients diagnosed with tuberculosis reported a vaccination rate of 55%.<sup>13</sup> In a globalized world, an increase in the incidence of tuberculosis is anticipated in our country due to the rise in wars and migration. Thus, adherence to national vaccination policies is important.<sup>14</sup> This study reported a high rate of tuberculosis vaccination among healthcare workers, a group at high risk of contact with active tuberculosis patients.

This study found a latent tuberculosis infection rate of 19% among healthcare workers. These rates may vary depending on the incidence of tuberculosis in different countries. For example, a 2023 study in a hospital in Northern Peru reported a latent tuberculosis infection rate of 17.86% among 308 HCWs.<sup>15</sup> In Myanmar, where tuberculosis incidence rates are higher, a screening of 500 healthcare workers reported an incidence rate of 31.2%.<sup>16</sup> A latent tuberculosis screening was conducted on 4,354 HCWs in Korea between 2013 and 2018, detecting latent tuberculosis infection in 927 (21.3%) individuals.<sup>17</sup> In a meta-analysis, the overall prevalence of latent tuberculosis infection among healthcare workers ranged from 27.9% to 88.8%, while in control groups, it ranged from 8.2% to 72.3%. Compared to control groups, HCWs had a higher likelihood of LTBI, with an odds ratio (OR) of 1.78.<sup>18</sup> In a study from Türkiye comparing 127 healthcare workers with 127 controls, the LTBI incidence was 21.8% among HCWs and 8.2% in the control group.<sup>10</sup> In latent tuberculosis infection screenings conducted specifically among pulmonology personnel, incidence rates were recorded at 13.2% and 5.8% across different years.<sup>6</sup> The active tuberculosis incidence rate in a country is the most important factor determining LTBI incidence in the general population; it should be noted that this rate is likely even higher among healthcare workers.

No significant differences were found between the groups in terms of risk factors such as age, occupation, unit of employment, or average monthly contact with active TB patients when comparing HCWs with and without LTBI in this study. However, literature reports identify risk factors such as working in high-risk units,<sup>19</sup> having a long employment duration,<sup>20</sup> being 35 years of age or older,<sup>21</sup> male gender,<sup>22</sup> and working as a physician.<sup>23</sup> Notably, the rate of N-95 mask use among HCWs in contact with known active tuberculosis patients was very low for those both with and without LTBI. The World Health Organization recommends the use of personal protective equipment, specifically FFP-2 or N95 masks, for respiratory protection when in contact with active or suspected

**Table 1.** Clinical-epidemiological characteristics of healthcare workers

Total (n=101)	n (%)
Age (min–max), years	36 (23–54)
Male sex (%)	40 (40)
Education level (%)	
Primary-secondary	1 (0.99)
High school	21 (20.7)
University	67 (66.3)
PhD	12 (11.8)
Profession (%)	
Physician	21 (20.7)
Nurse	42 (41.5)
Cleaning staff	18 (17.8)
Others	20 (19.7)
Working area (%)	
Emergency	19 (18.8)
Intensive care units	41 (40.5)
Infection-chest clinic	10 (9.9)
Other outpatient clinics	11 (10.8)
Other clinics	20 (19.8)
Working in a high-risk area (%)	60 (59.4)
Number of tuberculosis patient exposures (min–max)	1 (0–8)
Service time (years) (min–max)	10 (1–30)
Working period in profession (%)	
0–5 Years	30 (29.7)
5–10 Years	21 (20.7)
>10 Years	50 (49.5)
Working time in current unit (years) (min–max)	4 (1–30)
Isolation room in unit (%)	71 (70.2)
Born in kayseri (%)	60 (59.4)
Smoking history (%)	34 (33.6)
Any comorbidity (%)	34 (33.6)
Diabetes mellitus (%)	7 (6.9)
Hypertension (%)	3 (2.9)
Chronic kidney disease (%)	1 (0.99)
Chronic obstructive pulmonary disease (%)	8 (7.9)
History of anti-tnf use (%)	5 (4.95)
History of corticosteroid treatment (%)	3 (2.97)
Family history of tuberculosis (%)	2 (1.98)
Use of N95 mask with patients diagnosed /suspected with tb (%)	
Always	43 (42.5)
Sometimes	20 (19.8)
Rarely	35 (34.6)
History of tuberculosis vaccination (%)	93 (92)
Number of BCG scars (%)	2 (1–3)
Latent tuberculosis infection (%)	19 (19)

**Table 2.** Comparison of epidemiological and clinical data of healthcare workers with and without latent tuberculosis infection

	With LTBI (n=19)	Without LTBI (n=82)	p
Age (min–max), years	0 (23–49)	36 (23–54)	0.593
Male sex (%)	9 (47)	31 (37)	0.442
Education level (%)			0.788
Primary-secondary	0 (0)	1 (1.2)	
High school	3 (15.7)	18 (21.9)	
University	13 (68.4)	54 (65.8)	
PhD	3 (15.7)	9 (10.9)	
Profession (%)			0.457
Physician	4 (21.05)	17 (20.7)	
Nurse	6 (31.5)	36 (43.9)	
Cleaning staff	5 (26.3)	13 (15.8)	
Others	4 (21.3)	16 (19.4)	
Working area (%)			0.328
Emergency	3 (15.7)	16 (19.5)	
Intensive care unit	7 (36.8)	34 (41.4)	
Infection-chest clinic	4 (21.05)	6 (7.3)	
Other outpatient clinics	3 (15.7)	8 (9.7)	
Other clinics	2 (10.5)	18 (21.9)	
Number of tuberculosis patient exposures (min–max)	1 (0–8)	1 (0–6)	0.372
Service time (years)	12 (2–25)	10 (1–30)	0.821
Working period in profession (%)			0.613
0–5 years	4 (21.05)	26 (31.7)	
5–10 years	5 (26.3)	16 (19.5)	
>10 years	10 (52.6)	40 (48.7)	
Working time in current unit (years) (min–max)	5 (1–25)	4 (1–30)	0.334
Isolation room in unit (%)	13 (68.4)	58 (70.7)	0.843
Born in Kayseri (%)	12 (63.1)	48 (58.5)	0.912
Smoking history (%)	6 (31.5)	28 (34.1)	1.000
Pack-years smoking (n=34) (min–max)	9 (4–28)	5 (1–60)	0.211
Any comorbidity (%)	7 (36.8)	27 (32.9)	0.955
Diabetes mellitus (%)	1 (5.2)	6 (7.3)	1.000
Hypertension (%)	2 (10.5)	1 (1.2)	0.161
Chronic obstructive pulmonary disease (%)	2 (10.5)	6 (7.3)	1.000
History of corticosteroid treatment (%)	1 (5.2)	2 (2.4)	1.000
Family history of tuberculosis (%)	1 (5.2)	2 (2.4)	1.000
Use of N95 mask with patients diagnosed/suspected with TB (%)			0.494
Always	6 (31.5)	37 (45.1)	
Sometimes	2 (10.5)	18 (21.9)	
Rarely	8 (42)	27 (32.9)	
History of tuberculosis vaccination (%)	17 (89)	76 (92)	1.000
Number of BCG scars (min–max)	2 (1–3)	2 (1–3)	0.228
Chest chest radiography findings in last year (n=34) (%)			
Normal	5 (26)	19 (23)	<b>0.010</b>
Fibrotic band	4 (21)	1 (1)	0.101
Hilar expansion	3 (15)	1 (1)	0.265
Calcification	7 (37)	1 (1)	<b>0.003</b>

LTBI: Latent tuberculosis infection; TB: Tuberculosis; BCG: Bacille Calmette-Guérin.



tuberculosis cases.<sup>24</sup> A study assessing the effectiveness and duration of various personal protective equipment types found that only N95 masks, among surgical masks, effectively protected against tuberculosis particles, with protection lasting three days.<sup>25</sup> It has been reported that the use of FFP-2 masks among healthcare workers in high-risk units during the Coronavirus Disease 2019 (COVID-19) pandemic was associated with a statistically significant decrease in the incidence of both active and latent tuberculosis.<sup>26</sup> The importance of personal protective equipment should be especially emphasized in countries with a high incidence of tuberculosis, particularly for professionals with a high risk of exposure, such as HCWs.

When chest X-ray findings of healthcare workers from the past year were examined, findings such as hilar enlargement, fibrotic bands, and calcification were found to be more common in the group with LTBI. A meta-analysis of 26 clinical studies analyzing radiological findings in patients with latent tuberculosis infection reported that calcified nodules were more common in these patients.<sup>27</sup> Another study examining chest X-ray findings in 236 patients with latent tuberculosis infection found that fibrotic scars with a diameter of  $\geq 2$  cm<sup>2</sup> and/or calcified nodules  $\geq 1.5$  mm were particularly significant.<sup>28</sup> These findings suggest that regular annual examinations and periodic chest X-ray imaging for HCWs is useful in predicting latent tuberculosis infection.

## CONCLUSION

In this cross-sectional study assessing the incidence of latent tuberculosis infection in HCWs at a tertiary healthcare institution, the incidence of LTBI was found to be 19%. Demographic data, occupation, and other risk factors did not differ between HCWs with and without LTBI, though atypical findings were more common in those with LTBI on radiologic examination. The study results and questionnaire responses revealed that HCWs with LTBI had low rates of personal protective equipment use when working with high-risk patients. Emphasizing the importance of personal protective equipment among HCWs in developing countries like our country, where tuberculosis incidence is high, is essential, and further studies should be conducted to improve compliance rates. This study is limited by its small sample size and short duration. Multi-center studies with larger participant groups are needed to identify risk factors for LTBI in HCWs.

**Ethics Committee Approval:** The Erciyes University Clinical Research Ethics Committee granted approval for this study (date: 14.02.2014, number: 2024-94).

**Author Contributions:** Concept – ZT; Design – ZT; Supervision – ZT, AÖ; Materials – ZT, BD, FE, GKÜ; Analysis and/or Interpretation – ZT, AÖ; Literature Search – ZT, BD; Writing – ZT; Critical Reviews – ZT.

**Conflict of Interest:** The authors have no conflict of interest to declare.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Use of AI for Writing Assistance:** Not declared.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Peer-review:** Externally peer-reviewed.

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