

# A Comparison of Two-Step Tuberculin Skin Test between Health-Care Workers and Nonhospital Employees

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## Abstract

**Background:** The tuberculin test is widely used to identify tuberculosis infection. Some individuals infected with *Mycobacterium tuberculosis* may have an initial negative skin test reaction to tuberculin. The two step purified protein derivative skin test can decrease misinterpretation of tuberculin test. This study was aimed at comparing the two- step tuberculin skin test and booster phenomenon in health care workers and non hospital employees.

**Methods:** One hundred and eighty five health service employees from Razi University Hospital and 181 non hospital employees were subjected to an initial tuberculin skin test. Those who were negative on the first test underwent a second one 2 weeks later. The reactions to the tests were measured 72 hours later. Tests with an induration of  $\geq 10$  mm was considered positive. Moreover, second tests with an induration of at least 6 mm increase relative to the relevant first tests were considered positive.

**Results:** Compared to non hospital employees (n=79, 43.6%), a significantly higher number of health care workers (n=113, 61.1%) were positive on the first tuberculin test. 18.5 % of health care workers and 31.5% of non hospital employees demonstrated a boosted reaction after the second tuberculin test. The occurrence of boosted reaction was significantly associated with age both groups. There was no association between the presence of BCG scars and the occurrence of boosted reaction.

**Conclusion:** the present study shows that the prevalence of TB was higher among health care worker than non hospital employees. Moreover, it demonstrated that non hospital employees had a higher age-associated booster reaction to the second tuberculin skin test than health care workers. Therefore, to avoid missing false negative cases, it would be necessary to do a second tuberculin test for subjects with a negative reaction to the initial test, especially in subjects older than 40 years.

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**Keywords** • Tuberculosis infection • tuberculin test • health care worker

## Introduction

*Mycobacterium tuberculosis* is a major global public health problem.<sup>1</sup> The detection and monitoring of *M. tuberculosis*

infections are essential to controlling its spread.<sup>2</sup> Historically, health care workers have carried a higher burden of tuberculosis infection than that of the general public. The potential for transmission of *M. tuberculosis* in healthcare facilities is recognized risk for both patients and healthcare workers.<sup>3</sup>

The tuberculin skin test (TST) is the method of choice for the detection of latent *M. tuberculosis* infections.<sup>4</sup> Some subjects, who are non reactive to an initial tuberculin skin test, may have a positive reaction to a subsequent tuberculin test. This phenomenon, known as the "booster effect," is said to result from the boosting of the anamnestic response.<sup>5,6</sup> Two-step testing, namely the administration of a second tuberculin test after 1 to 3 weeks when there is not a significant reaction to a first test, is the procedure recommended in the initial examination of hospital employees. The procedure helps a boosted response to be elicited in those with remote tuberculosis (TB) infection. The reaction to the boosted (second) test is considered to indicate the infection status of the person tested.<sup>7</sup> Numerous studies have been conducted on Two-step tuberculin skin testing and booster effect in health care worker.<sup>5,6,8</sup> However, relatively few studies have compared this reaction and phenomenon between health care workers and non hospital employees (NHE). The objectives of the present study were to: 1) define the frequency of TB infection among hospital workers and NHEs, 2) define the frequency of the booster effect in hospital workers and NHE, and 3) identify specific factors associated with the booster effect.

## Subjects and Methods

The study was approved by ethics review Board, Guilan University of Medical Sciences. The aim and protocol of the study was explained to all participants, and informed written consents were obtained from all of them. Three hundred sixty six healthy volunteers including 185 health care workers of Razi Hospital and 181 non hospital employees (school teachers) participated in the study. Health care worker used to work in high risk wards such as infectious diseases, thorax surgery, hemodialysis and radiology. All participants were asked to complete a standard questionnaire regarding demographic characteristics including age, gender and previous BCG vaccination.

An initial tuberculin skin test (TST-1) was administered to all subjects using the mantoux

method.<sup>9</sup> A dose of five tuberculin units of purified protein derivative (PPD, from Razi Institute, Tehran, Iran) was injected intracutaneously into the volar surface of the forearm, and 48-72 hours later the skin tests were read. Tests with an induration of 10 mm or larger were considered as positive, and tests with an induration of under 10 mm as negative.<sup>9</sup> Subjects with negative tuberculin skin tests received a second tuberculin skin test (TST-2) two weeks later, at a site approximately 10 cm away from the previous intracutaneous injection. Booster reaction was defined as positive if the resultant induration of the TST-2 was  $\geq 10$  mm or was at least 6 mm more than the induration resulting from TST-1.<sup>10</sup> Trained personnel administered and read the tuberculin skin tests.

The analysis of the findings was performed using two-tailed Chi Square test and Statistical Package for Social Sciences (SPSS, version 11.5). A P value of  $\leq 0.05$  was considered statistically significant.

## Results

There was no significant difference between the age, in years, of health care workers ( $36.5 \pm 8.7$ ) and that of non hospital employees ( $36.94 \pm 8.2$ ).

The number of health care workers ( $n=113$ , 61.1%) that demonstrated positive reactions to the initial tuberculin skin test was significantly ( $P=0.001$ ) higher than that of non hospital employees ( $n=79$ , 43.6%).

The percentage of health care workers who had a positive TST-1 reaction was higher among those working in the TB wards (71.8%) than among those working in other ward (53/2%).

Seven health care workers and 10 non hospital employees with a negative reaction to TST-1 refused to participate in the TST-2, and were excluded. There was no significant difference between the percentage of non hospital workers with negative reaction to TST-1 who demonstrated a positive reaction to TST-2 (29/92, 31.5%) and health care workers with negative reaction to TST-1 and positive reaction to the TST-2 (12/65, 18.5%).

There was an association between the age of participants and the occurrence of booster reaction in health care workers ( $P=0.034$ ) as well as non hospital employees ( $P=0.006$ ). Subjects older than 40 years in both groups were more likely to have a booster reaction than younger individuals (table 1). There was no significant ( $P=0.086$ ) association between the presence of previous BCG scars and the occurrence of positive booster reactions (table 2).

**Table 1:** The rate of occurrence of booster reaction among health care workers (HCWs) and nonhospital employees (NHE) stratified based on the age of the participants.

Age	HCWs	P value	NHE	P value
20-29	2/32 (6.2%)	0.034	3/21 (14.2%)	0.006
30-39	5/19 (26.3%)		9/38 (23.7%)	
40-49	5/14 (35.7%)		17/33 (51.5%)	

**Table 2:** The rate of occurrence of booster reaction among health care workers (HCWs) and nonhospital employees (NHEs) stratified based on the absence and presence of BCG scars.

BCG Scar	HCWs	NHEs	P value
Absent	3/16(18.7%)	8/30 (26.6%)	0.086
Present	9/49(18.3%)	21/62(33.8%)	

## Discussion

Health care workers are at high risk of TB, and their screening for the disease is an important component of infection control programs. Tuberculosis is endemic in Iran.<sup>11</sup>

However, little is known about the TST and booster reaction in the population of Iranian adults. Therefore, an evaluation of the frequency of boosted reaction and the associated factors would be important for the assessment of TST reactivity in Iran, which has a high frequency of tuberculosis and a routine BCG vaccination policy.

The findings of the present study indicated a high frequency (61%) of tuberculosis infection in health care workers. Such a finding receives support from a fairly recent systematic review,<sup>12</sup> which reported that the prevalence of latent tuberculosis infection among HCWs was 54% (range 33% to 79%).

The boosted reaction to the second TST developed in 18.5% and 31.5% of health care workers and non hospital employee, respectively. There is no agreement on the definition of a boosted reaction in previous studies, which have reported a range of 0 to 59% for it.<sup>13-19</sup>

The findings of the present study are similar to that of a previous study, which was characterized as an intermediate incidence of TB and a routine BCG vaccination program.<sup>13</sup> The present study showed that booster reaction in non hospital employees was more than that in health care workers. Such an increased booster reaction might be due to previous exposure to TB in HCW than in non-hospital employees.

The findings of the present study indicate that there was no association between the presence of a BCG scar and the rate of boosted reaction. This finding is consistent with some previous reports.<sup>19,20</sup> In a number of previous studies BCG vaccination was reported to be one of influential factors on booster phenomenon. The lack of a BCG effect in the present study could be due to

BCG vaccinations during infancy. Such an speculation receives support from a study by Menzies and colleagues, who reported that BCG vaccination received in infancy had little effect on the boosted reaction.<sup>10,21,22</sup> Moreover, the present study showed that boosted reaction was associated with increasing age. This finding is consistent with other studies, which documented a positive relationship between the boosted reaction and the increase of age.<sup>13,17,19</sup>

## Conclusion

The present study shows that the prevalence of TB was higher among health care worker than non hospital employees. Moreover, it demonstrated that non hospital employees had a higher age-associated booster reaction to the second tuberculin skin test than health care workers. Therefore, to avoid missing false negative cases, it would be necessary to do a second tuberculin test for subjects with a negative reaction to the initial test, especially in subjects older than 40 years.

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**Conflict of Interest:** None declared

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