Knowledge, experiences, and attitudes toward Mantoux test among medical and health professional students in Italy: a cross-sectional study


Key words: Health care students, tuberculosis surveillance, Mantoux tuberculin skin test, screening

Parole chiave: Studenti universitari, sorveglianza della tubercolosi, test di Mantoux, screening

Abstract

Background. The World Health Organization’s Action Framework for tuberculosis elimination in low-tuberculosis incidence countries includes the screening for active and latent tuberculosis in selected high-risk groups, including health care workers. In this context, medical and health profession students, exposed to nosocomial tuberculosis transmission during training and clinical rotations, are target populations for

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Introduction

Tuberculosis (TB) is the ninth leading cause of death worldwide derived from a single infectious agent (Mycobacterium tuberculosis), ranking above HIV/AIDS. According to the World Health Organization (WHO), 10.4 million people fell ill with TB in 2016: 90% were adults, 65% were male, 10% were HIV-positive people (74% in Africa) and 56% coming from India, Indonesia, China, Pakistan and the Philippines. TB deaths recorded in 2016 were 1.3 million among HIV-negative people and 374,000 among HIV-positive people (1).

TB transmission was often documented in clinical setting where healthcare workers (HCWs) and patients come in contact with people having TB disease (2, 3), particularly in low- and middle-income countries (4, 5). The nosocomial transmission of TB put HCWs and other patients at high risk of infection, leading to a serious threat, particularly when it concerned about drug-resistant and HIV associated TB (6). Due to the TB incidence rate, below 10 cases per 100,000 inhabitants over the last 10 years, Italy is considered a low-burden country, where specific population subgroups are affected (7). The screening for TB can lead to early diagnosis and treatment thereby reducing TB related morbidity and mortality (8). In particular, periodic TB testing of HCWs is recommended as part of a TB Infection Control Plan, also in Italy (9). These testing programs, like Mantoux tuberculin skin test (MTST), should include all the people who have face to face contact or potential exposure to TB, especially anyone working, studying or volunteering in health-care settings (10-12). In the United States, the MTST was the standard method for detecting latent TB infection since the 1930s (13, 14), and is primarily used both to test close contacts of people who have active TB disease, and various groups of people who are at high risk for TB (15).
risk for TB. Screening can also be important in order to identify wards where HCWs are mostly at risk of TB infection (15).

Traditionally, tuberculin skin test (TST) was used for HCWs TB screening; however, its low specificity among BCG (Calmette-Guerin Bacillus)-vaccinated HCWs and the boosting phenomenon of repeated TST may provide false positive results, with a potential negative consequence of unnecessary chest X rays and/or isoniazid prophylaxis (12). The Interferon Gamma Release Assay (IGRA) is a specific and rapid alternative to the TST. IGRA requires only one patient visit and is unaffected by previous BCG vaccination or NTM (nontuberculous mycobacteria) infections. However, keeping in view the cost, and other logistics, TST remains the most preferred method for Latent Tuberculosis Infection (LTBI) diagnosis. IGRA is recommended only in immunosuppressed patients, in vaccines with BCG vaccine, in children <5 years and as confirmation of positive tests.

Appropriate TB knowledge, attitudes and practices are particularly important among health care students (HCSs), because they could be exposed to occupational risks similar to those of HCWs during training activities (16, 17). The HCSs represents the new generation of HCWs: an insufficient knowledge about TB is one of the reasons for which this infectious disease is often not properly diagnosed and treated (16).

In Italy, according to Legislative Decree number 81/08 - Article 2 (9), HCSs are compared to workers because they can be exposed to TB infection during clinic rotations; moreover, they represent potential future physicians or leaders in the fight against TB (16, 18, 19). TB outbreaks among students were reported even in such low-burden countries as Italy (20).

Based on this scientific background, the Italian Study Group on Hospital Hygiene (GISIO) of the Italian Society of Hygiene, Preventive Medicine and Public Health (SItI) promoted a multicentre survey i) to determine the level of knowledge about MTST among HCSs in Italy, ii) to investigate personal experiences; iii) to detect if Italian Universities submit HCSs to MTST like a control measure for identifying latent TB infection.

**Methods**

**Study design**

Members of the GISIO-SItI holding a Professor position at one of the Italian Universities, teaching in medical and health professional courses, were asked to be enrolled in the study. Overall, 17 universities were included in the study, located in the Northern (47%), Central (11.8%), and Southern (41.2%) regions of Italy. The study was carried out between March and April 2018.

All students took part on a voluntary basis, and were not remunerated for their contribution. During the recruitment, a detailed explanation of the objectives of the study was provided to potential participants. After participants’ verbal consent was obtained, they were asked to complete an anonymous questionnaire.

The questionnaire consisted of 7 questions about sociodemographic characteristics (i.e. age, gender), location of the university and degree course, and 9 multiple-choice questions divided into two sections, concerned on: 1) general knowledge of Mantoux test and other TB screening methods (3 items), and 2) personal experiences and practices related to screening for TB (6 items).

To assess the accuracy of the questionnaire, an internal pre-validation procedure was carried out at the University of Bari Aldo Moro, involving 20 fifth-year medical students and 10 second-year nursing students (Cronbach’s alpha = 0.81, indicating good internal consistency). This pilot phase allowed the improvement of the quality of several questions.
Data analysis

The information was entered into a dedicated database, and analysed using Stata SE14. Continuous variables were described as mean ± standard deviation, median, interquartile range (IQR), while categorical variables as proportions. For proportions, the 95% confidence interval (95%CI), where consistent, was indicated. For continuous variables the normality analysis was performed. Continuous variables were compared among groups by Kruskall-Wallis test and Dunn’s multiple comparison test (non-parametric). The categorical variables were compared by Chi-square test.

To evaluate the agreement between what declared by the interviewees about the obligatory nature of the MTST at the University and the actual provisions of the University regulations, the K of agreement test was used.

For each of the following outcomes, i) knowledge of the Mantoux test (YES/NO), ii) knowledge of the first level screening LTBI test (YES/NO), iii) knowledge of the procedure to be implemented in case of positive Mantoux test (YES/NO), the association with age, gender, year of University course, studying at a University where the Mantoux test is mandatory (YES/NO) and groups was analysed through multivariate logistic regression. The adjusted Odds Ratio (aOR) values were calculated, with the 95%CI, and the test z score was performed.

For all tests, significance was set for a value of p<0.05.

The study follows the principles of the World Medical Association Declaration of Helsinki, and does not report any experiment on humans or human samples, nor research on identifiable human material and data.

Results

Study sample

The study involved 5,209 Italian students enrolled in medicine and dentistry (Group 1; n = 1,964; 37.7%), nursing (Group 2; n = 2,337; 44.9%), and other health professions courses (Group 3; n = 908; 17.4%, mostly health assistants, physiotherapists, obstetricians). All questionnaires were correctly fulfilled, and were considered reliable for the analysis. No data were available on the number of non-participants and how this could have affected the results of the survey.

In our sample, the mean age was 22.3 ± 3.6 years (range = 17.0 – 59.0; median = 22.0; IQR range = 20.0 – 23.0). A significant difference was observed when the three groups were compared with respect to the age variable (k = 285.5; p = 0.000) (Table 1). Particularly, the Dunn test showed a statistically significant difference between Group 1 and Group 2 (z = 16.7, p = 0.000), Group 1 and Group 3 (z = 10.0, p = 0.000) and Group 2 and Group 3 (z = 2.8; p = 0.003).

The majority of the recruited individuals were female (64.2%; 95%CI = 62.9-65.5). A significant difference was observed in the female gender prevalence by group (Group 1 = 51.9%; 95% CI = 49.6-54.1; Group 2 = 72.7%; 95%CI = 70.8-74.5; Group 3 = 68.8%; 95%CI = 65.7-71.8; X^2 = 210.8; p = 0.000).

The 58.2% (95% CI = 56.8-59.5) of students attended a university for which the Mantoux test is considered mandatory for matriculation or attending wards. A statistically significant difference was observed in the distribution of proportions of universities mentioned above by group (Group 1 = 52.1%; 95%CI = 49.9-54.4; Group 2 = 64.0%; 95%CI

Table 1 - Mean ± standard deviation, median, IQR range and age variable range, per HCSs group

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mean±SD</th>
<th>Median</th>
<th>Range IQR</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>22.6±2.5</td>
<td>23.0</td>
<td>21.0 – 24.0</td>
<td>17.0 – 59.0</td>
</tr>
<tr>
<td>Group 2</td>
<td>22.1±4.1</td>
<td>21.0</td>
<td>20.0 – 23.0</td>
<td>18.0 – 55.0</td>
</tr>
<tr>
<td>Group 3</td>
<td>22.3±4.0</td>
<td>21.0</td>
<td>20.0 – 23.0</td>
<td>18.0 – 58.0</td>
</tr>
</tbody>
</table>
= 62.0-66.0; Group 3 = 56.3%; 95% CI = 53.0-59.5; \( X^2 = 63.5; p = 0.000 \)).

**General knowledge of Mantoux test and other TB screening methods**

Regarding knowledge of Mantoux test, 84.4% (95% CI = 83.3-85.3) of the students stated that they were aware of the existence of the test. A significant difference was observed in the distribution of responses by group (Group 1 = 84.1%, 95% CI = 82.4-85.7; Group 2 = 88.5%, 95% CI = 87.1-89.8; Group 3 = 74.2%, 95% CI = 71.3-77.0; \( X^2 = 100.9; p = 0.000 \)).

Regarding LTBI’s first-level screening test procedures, 74.4% (95% CI = 73.2-75.6) responded correctly (i.e. Mantoux test), and a significant difference in the distribution of responses by group (\( X^2 = 112.8; p = 0.000 \)) was observed (Figure 1).

About the procedures to be followed when Mantoux test is positive, 22.5% (95% CI = 21.4-23.6) HCSs responded correctly (i.e. IGRA test), with a significant difference in the distribution of responses by group (\( X^2 = 112.8; p = 0.000 \)) (Figure 2).

**Personal experiences and practices related to screening for TB**

The 53.5% (95% CI = 52.2-54.9) of the students declared to have been screened by Mantoux test, and a significant difference in the distribution of tested subjects by group was found (Group 1 = 47.3%, 95% CI = 45.1-49.6; Group 2 = 63.0%, 95% CI = 61.0-64.9; Group 3 = 42.5%, 95% CI = 39.3-45.8; \( X^2 = 28.3; p = 0.000 \)).

Of screened students, 92.8% (95% CI = 91.9-93.9) was tested during degree courses, 2.2% (95% CI = 1.7-2.8) after a contact with TB patients, 1.2% (95% CI = 0.8-1.6) before a trip (mostly to USA and Europe), and 3.8% (95% CI = 3.1-4.6) for other reasons (e.g. competition, employment eligibility, enrollment in the army). A statistically significant difference in the distribution of these proportions by group (\( X^2 = 28.3; p = 0.000 \)) was observed (Figure 3).

The Mantoux test resulted mandatory to attend the clinical stage in the ward (37.7%, 95% CI = 36.4-39.0), for University enrollment (13.4%, 95% CI = 12.5-14.4) and before the degree (2.9%, 95% CI = 2.4-3.3);

![Figure 1 - Procedures (%) to be followed as first screening of LTBI by group](image-url)
it resulted optional in 15.9% (95% CI = 14.9-16.9), while 30.1% (95% CI = 28.9-31.4) of students did not know/answer. A statistically significant difference was found per group ($X^2 = 433.2; p = 0.000$) (Figure 4). According to the agreement test, a discrepancy of 39.6% was observed between the declaration of the students about the obligation of the Mantoux test and the regulations of the respective universities (kappa = 0.4, p = 0.000).

The 34.8% of enrolled students reported to have been convened to perform the
Mantoux test by their University during lessons (51.0%, 95%CI = 48.6-53.4), through an institutional email (39.6%, 95%CI = 37.2-41.9), and student associations (9.4%, 95%CI = 8.1-10.9). A significant difference resulted in the distribution of responses by group ($X^2 = 154.6; p = 0.000$) (Figure 5).

In details, the test was performed at the Occupational Medicine Unit (47.9%, 95%CI = 45.5-50.3), Pneumology (14.8%, 95%CI...
Mantoux test among medical university students in Italy

= 13.1-16.5), Infectious Diseases (11.4%, 95%CI = 9.9-13), Hygiene (11.2%, 95%CI = 9.8-12.8), and other health care structures (14.7%, 95%CI = 13.1-16.5). A statistically significant difference in the distribution of responses by group ($X^2 = 199.6; p = 0.000$) was observed (Figure 6).

In the multivariate analysis, knowledge of the Mantoux test was significantly associated with: to study in a University with the obligation to perform the Mantoux test (aOR = 7.6), with increasing year of the degree course (aOR = 1.6), with increasing age (aOR = 1.1), gender (aOR = 0.6), Group 2 vs. Group 1 (aOR = 1.5) and Group 3 vs Group 1 (aOR = 0.5) (table 2).

Furthermore, a significant association between knowledge of the LTBI first level screening and studying in a University with the obligation to perform the MTST (aOR = 3.1), year of degree course (aOR = 1.6), Group 2 vs. Group 1 (aOR = 1.6), Group 3 vs Group 1 (aOR = 0.6), and gender (aOR = 0.7), while the age resulted slightly associated with the outcome (aOR = 1.03) (table 3).

Table 2 - Analysis of the determinants of knowledge of the Mantoux test (YES / NO) in a multivariate logistic regression model.

<table>
<thead>
<tr>
<th>Variable</th>
<th>aOR</th>
<th>95%CI</th>
<th>z</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.12</td>
<td>1.08 – 1.16</td>
<td>6.1</td>
<td>0.000</td>
</tr>
<tr>
<td>Gender (male vs female)</td>
<td>0.6</td>
<td>0.5 – 0.8</td>
<td>4.9</td>
<td>0.000</td>
</tr>
<tr>
<td>Degree Course year</td>
<td>1.6</td>
<td>1.4 – 1.8</td>
<td>6.7</td>
<td>0.000</td>
</tr>
<tr>
<td>Compulsory Mantoux test</td>
<td>7.6</td>
<td>6.3 – 9.1</td>
<td>20.9</td>
<td>0.000</td>
</tr>
<tr>
<td>Group 2 vs. Group 1</td>
<td>1.5</td>
<td>1.2 – 1.9</td>
<td>4.1</td>
<td>0.000</td>
</tr>
<tr>
<td>Group 3 vs. Group 1</td>
<td>0.5</td>
<td>0.4 – 0.6</td>
<td>6.7</td>
<td>0.000</td>
</tr>
</tbody>
</table>
In the multivariate model, knowledge on how to proceed when MTST is positive was significantly associated with the year of degree course (aOR = 1.6), studying in a University with the obligation to perform the MTST (aOR = 1.5), gender (aOR = 0.8), Group 2 vs. Group 1 (aOR = 0.7), and Group 3 vs group 1 (aOR = 0.5). The age seems to be not associated with the outcome (p>0.05) (table 4).

### Discussion

TB prevention and control has become an important public health issue, attracting substantial attention also towards students on training courses in the health sector (21).

According to Italian Law n.1088/1970, the medical students and nursing students, before enrollment in health professional University courses, had to be subjected to TST, and the cutinegative subjects had to be vaccinated with BCG. After almost 50 years, an important change occurred both in the reference legislation [the students of the medical faculties are considered as workers according to Legislative Decree n. 81/2008 (9)], and the organizational models for the offer of screening and diagnostics tests, also in relation to the autonomy of the Italian Regions in terms of health support strategy.

Regarding anti-TB vaccine, the only one existing since 1921 is a live attenuated vaccine (BCG), which protects for 5-10 years but is not effective in the following period neither for the prevention of the disease nor for the interruption of TB transmission in the population. On November 7, 2001, the Presidential Decree n. 465 stated the conditions under which TB vaccination must be performed: i) infants and children under 5 years of age with negative TST, cohabiting or having close contact with contagious people if the risk of contagion persists; ii)
health personnel, medical students, nursing students and anyone, any qualification, with negative TST, operating in health care environments at high risk of exposure to multi-resistant or high-risk strains and cannot be subjected to preventive therapy, due to clinical contraindications to the use of specific drugs (22).

Actually, in Italy anti-TB vaccination is not compulsory for everyone. In 2013, the Italian Ministry of Health launched the latest TB prevention national guidelines for HCWs, indicating TST as the first-level screening test (23). When TST is positive, results have to be confirmed by enzyme immunoassay tests based on IGRA quantification, proving a superior specificity and sensitivity if compared with TST (24-26). In particular, QuantiFERON-TB test in HCWs has excellent utility and accuracy, especially in BCG-vaccinated populations in low incidence countries (27), but the test is greatly expensive. The Quantiferon-TB Gold Plus is the new generation screening tool with the highest sensitivity for LTBI. In immunocompromised people, Quantiferon-TB negative followed by the TST was demonstrated to be the most cost-effective strategy (28).

Regarding to the University regulations about Mantoux test execution circumstances, our study showed an extreme heterogeneity among the 17 involved Universities, with an adequate level of knowledge (86%) of the existence and rule of Mantoux test but some critical issues about knowledge on diagnostic algorithm to follow in case of positive first step screening resulted. According to our previous survey (17), most of the medical and health professions university students were aware of the existence of the Mantoux test and that Mantoux test is the screening test for LTBI (74%). Students from University in which test is mandatory have higher general knowledge about Mantoux (aOR = 7.6; 95% CI = 6.3-9.1), respectively compared to students from University in which test is not mandatory. Although this result is predictable, it seems that more than a third (39%) of students attending University were unaware of a mandatory TB screening policy. This discordance indicates either the existence of recall bias or the lack of a detailed and clear policy on screening test.

General knowledge of TST was significantly higher in females. This data in literature is contrasting with some studies demonstrating a gender effect on general knowledge about TB (29), and others showing no evidence of association with gender (30). An unexpected result was that nursing students had better knowledge of TST compared to medical, dentistry and professional students. Our previous survey did not detect such pattern (17). In this regard, a recent 2-year study showed that knowledge about TB among undergraduate increased by 50% after 1 month of theoretic and practice education, and by only 25% after 2 years of practice education (31). In Italy, nursing students have more practice training hours compared to medical students who are more dedicated to theoretic classes, especially during the first 2 years of course. Correspondingly, we found that knowledge about TB screening significantly increases over the years of the University and with age of the students.

In terms of personal experiences, 53.5% of students reported to have experienced in the past a screening test for the diagnosis of LTBI, and 92.8% tested during degree courses. Moreover, only 22.5% of students knew that in case of a positive results at the Mantoux test a confirmatory test should be performed. This means that most students are not aware of the importance of IGRA blood tests for TB diagnosis, but they think that Chest-X Ray is an adequate control.

This is worrying because University education is the base of the expertise of future health professionals, especially medical doctors. In Pakistan, a survey was performed to test the level of knowledge of TST among
family physician. Although in a country where TB is endemic (1), the authors found one third of physician consider MTST as a screening tool to detect active TB (32).

Screening was mandatory more in nursing Universities than in other schools, probably because these students have most frequently potential exposure with TB patients and may be at risk of infection. Also, nursing students were convened to perform the screening mostly during the courses, while other students (including medical students) received a mail. In our study, calls by e-mail were not effective to increase screening compliance. In contrast, nursing University strategy was winning because face-to-face contact with students potentially lowered the reluctance to perform the test.

Our study show some limitations. First, we cannot exclude that knowledge found among our students about Mantoux test and other TB screening methods could be due to selection bias. No data is available about students that did not participate to the study; it is plausible that students that did not conduct MTST did not take part to the survey because not interested in this topic. Second, the survey was conducted in only 17 Italian Universities, so our data could be reviewed by a larger survey.

Conclusions

Our study findings underline that it is necessary to improve knowledge about TB among HCSs, upgrading the current health care curricula. An adequate information during lessons is critically important since the students represent potential future physicians or leaders in the fight against TB. It would be necessary to make the Mantoux test mandatory for everyone, to produce a common protocol, valid in all Universities, and to stress the importance to submit all HCSs to periodical screening before clinical rotation, in order to prevent *Mycobacterium tuberculosis* spread, to obtain an early diagnosis, and avoid progression to active disease. Finally, frontal and/or distance learning should also be extended and repeated over time to trainees, volunteers and all workers in the health care setting (9, 22).

Riassunto

*Conoscenza, esperienze e attitudini verso il test di Mantoux tra gli studenti di medicina e delle professioni sanitarie: uno studio trasversale in Italia*

**Introduzione.** Il piano d’azione dell’Organizzazione Mondiale della Sanità per l’eliminazione della tubercolosi nei Paesi con bassa incidenza di tubercolosi prevede lo screening per la tubercolosi attiva e latente in determinati gruppi ad alto rischio, inclusi gli operatori sanitari. In questo contesto, gli studenti di medicina e professioni sanitarie, esposti alla trasmissione nosocomiale di tubercolosi durante l’attività formativa e di tirocinio, rappresentano la popolazione target per lo screening della tubercolosi. Non sono disponibili dati aggiornati sulle pratiche di screening per la tubercolosi e sul grado di conoscenza degli studenti di medicina e professioni sanitarie in Italia.

**Metodi.** Nell’ambito delle attività del Gruppo di Studio Italiano sull’Igiene Ospedaliera della Società Italiana di Igiene, Medicina Preventiva e Salute Pubblica, abbiamo condotto uno studio multicentrico trasversale per valutare conoscenza, attitudini e pratiche su prevenzione e controllo della tubercolosi tra gli studenti di medicina, odontoiatria, scienze infermieristiche e altre professioni sanitarie. Gli studenti hanno aderito allo studio su base volontaria, compilando un questionario a risposta multipla. I dati sono stati analizzati applicando modelli di regressione logistica considerando determinate variabili Università-correlate.

**Risultati.** Hanno partecipato 5.209 studenti provenienti da 17 Università. Il 37,7% erano studenti di medicina e odontoiatria, il 44,9% erano studenti di scienze infermieristiche e il 17,4% erano studenti di altre professioni sanitarie. Età e sesso sono stati distribuiti in modo diversificato nei gruppi, così come il grado di conoscenza e le pratiche sul test cutaneo alla tubercolina.

Il 58,2% delle sedi arruolate prevedeva il test cutaneo alla tubercolina obbligatorio al momento dell’immatricolazione o all’inizio del tirocinio. L’84,4% degli studenti (95% CI = 83,3-85,3) era a conoscenza dell’esistenza del test cutaneo alla tubercolina, il 74,4% (95% CI = 73,2-75,6) sapeva qual è il test di screening di primo livello per la tubercolosi latente, il 22,5% (95% CI = 21,4-23,6) sapeva come procedere dopo un test cutaneo...
alla tubercolina positivo. Complessivamente le conoscenze sulla prevenzione della tubercolosi erano più elevate nei studenti di scienze infermieristiche e più basse negli studenti di altre professioni sanitarie. 

**Discussione.** In Italia, le conoscenze sullo screening della tubercolosi tra gli studenti universitari sono complessivamente buone. Per ridurre alcune criticità rilevate tra i diversi Corsi di studio, sarebbe opportuno uniformare a livello nazionale sia i regolamenti sulle pratiche di screening tubercolare per l’ammissione ai Corsi di studio universitari, sia le attività didattiche sul tema della tubercolosi, da estendere a tutti i lavoratori coinvolti nell’assistenza sanitaria.

**References**