ORIGINAL ARTICLE

Prevalence of Tuberculosis infection among teen-agers in Tuscany

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Key words

TB-infection • Prevalence • Teen-agers

Summary

Introduction. *In Tuscany, Tuberculosis incidence is more than triplicate from 1982 to the beginning of the third millennium. The impact of this trend on open population is not known, as updated studies on Tuberculosis prevalence are not available. Tuberculin skin test provides the currently most widely used tool for assessing Tuberculosis transmission in a community and the prevalence of infection as well.*
The objective of this investigation was the evaluation of tuberculin index by means of the Mantoux test in adolescents eighteen-years old.
Results. *The study was carried out in 21 secondary schools of Siena and its Province; 1,138 students participated to this survey.*
The overall prevalence of subjects with a skin reaction size > 5 mm was 1.6%; if the standard cut-off of 10 mm was used, the overall prevalence of a positive skin reaction was 0.4%. Risk factors for a doubtful or positive reaction were previous immunization with BCG and migration from high-endemicity countries.
Discussion. *In Italy, studies on tuberculin index in young adults are scanty and controversial: our results show a very low Tuberculosis prevalence and an epidemiological pattern typical of countries with low Tuberculosis endemicity.*
Conclusions. *The slightly increase in Tuberculosis incidence has no impact on the prevalence of latent Tuberculosis infection on our geographical area. We conclude that skin-test screening for Tuberculosis should be addressed to high risk population as migrants from Countries reporting high transmission rate, those recently exposed to an infectious case and health-workers.*

Introduction

Tuberculosis (TB) a disease thought to be ready for elimination at least in western countries, has re-emerged at the end of 80's as a major public health threat worldwide.
In Italy the number of cases reached its lowest level in 1980, when 3,322 had been registered; since then an increase has been progressively reported until the beginning of the third millennium; the increase in incidence rate/100,000 was 25%. The incidence pattern differs according to the different geographical areas, being higher in Northern and Central Italy [1].
In Tuscany (Central Italy) the number of incident cases is more than triplicate from 1992 to 2000, when it reached its highest point; since then the incidence have been settled at about 12/100,000 [2].
The increase in the number of new cases, prevalently attributable to immigration from high prevalence areas, the rapid development of disease in HIV infected persons and the problems related to the emergency of drug-resistant strains, brought pressures on Public Health Services and encouraged increased preventive measures and epidemiological surveys.
Tuberculin skin test provides the currently most widely used tool for assessing TB transmission pattern in a community and the prevalence of latent TB infection [3].

The overall objective of this study was to evaluate the prevalence of TB infection among teen-agers attending secondary-level schools in Siena and its Province by means of TB delayed Sensitivity Test using 5 I.U. Purified Protein Derivative (PPD) (Mantoux test).
Specific aims:
– to establish the Tuberculin Index (T.I.) defined as the percentage of Mantoux-positive students eighteen years old;
– to evaluate the annual risk of infection (ARI) defined as the probability that an individual previously uninfected will be infected by *Mycobacterium tubercolosis* during the ensuing period of 1 year: it measures the burden of TB on a geographical area.

According to the results obtained during the first step of our research we decided to miss the second specific objective.

Methods

The Department of Public Health of Siena (USL 7) is divided into four Districts, charged of the activities related to Public Health and Preventive Medicine; health education programmes addressed to students, including training and information about severe and diffuse preventable diseases as HIV/AIDS, drugs, to-

bacco and alcohol abuse take also part of the District staff activities.
This survey was organized and realized by the medical staff of each District in collaboration with the Clinic of Infectious Diseases (Department of Molecular Biology, University of Siena) technical, human and financial supports were provided by both the structures.
The survey was carried out in 2002-2003 during the school-attendance period.
All the secondary level schools of Siena Province were included in the investigation.
The Presidents of school-Direction Board were requested to give their consent to our research; the teachers of each class-room were trained on the objectives of our study in order to achieve an agreement as high as possible; furthermore they were invited to explain to their own students the aim of our investigation and its practical realization.
All the students 18 years old registered and regularly attending the schools were enrolled, without any selection procedure. They were further informed by their teachers and the medical staff on the theoretical and operational aspects of our investigation.
A written informed consent was requested to the students who decided to be submitted to skin test.
The following information were collected and recorded for each participating student: age, sex, health status, school, class-room, date of PPD inoculum and of skin test evaluation, results.
Skin test was always performed and interpreted by three skilled doctors, in order to avoid inconsistency, with a disposable tuberculin syringe and a 26-gauge needle, injecting 0.1 ml (5 I.U) of PPD intradermally on the volar surface of left forearm; after the injection, the equipment wad disposed on safety.
The test was read after 48-72 hours, according to the WHO-IUAT guidelines; it was considered positive if an induration 10 or more mm was measured, doubtful if 5-9 mm. An induration < 5 mm was taken as negative. Tuberculin index was calculated according to the number of positive subjects/100 submitted to the test.
Students with positive or doubtful skin test underwent the following evaluations:

a) clinical history to detect the presence of TB symptoms;
b) physical examination and chest radiograph to rule out an active TB;
c) history of previous household contact with infectious TB case;
d) BCG vaccination status.

Results

The target of our investigation accounted of a group of 1,584 healthy students, 18 years old, attending 21 high school located on the Siena Province.
After being registered, some students stopped the attendance of the school, which in Italy is mandatory until the age of fifteen; some others were missed because absent due to health problems or familial reasons.
A group of students who attended the classrooms when the TB skin test was performed, refused to be submitted to it, though repeatedly entreated about the opportunity of giving their consent to the investigation. Their behaviour was negatively influenced by the so-called "opinion leaders students" who refused to participate to the study. Indeed the rate of agreement was quite different in the same school, from one class-room to another.
The geographical distribution of the schools, the number of the students registered and attending the classrooms, the rate of agreement and the results of the skin test are reported in the Table.
The overall prevalence of subjects with a skin reaction size > 5 mm was 1.6%. If the standard cut-off point of 10 mm was used, the prevalence of a positive Mantoux test was 0.4%.
Among 14 students showing a reaction 5-9 mm 12 reported to have been immunized with BCG in the Country of origin at the time of their infancy; on examination, a scar on the surface of left arm confirmed their information. Two other healthy boys, of Italian origin, were invited to repeat the test some weeks later, in order to better evaluate their TB status; unfortunately, we could not get subsequent information.
Five subjects, whose skin reaction was ≥ 10 mm were requested to undergo further investigations: one was not compliant with our suggestion; the others were negative for TB disease. They were immigrants from Eastern Europe; two of them referred to have previously had household contacts with an infectious TB case.

Tab. I. TB skin test survey in 21 secondary-schools of Siena and its Province.

District	N° of students		N° of partecipants (agreement rate)	N° of positive	
	Registered	Attending		5-9 mm	10 mm
Amiata	41	40	38 (95)	1	
Siena	719	655	572 (87.3)	5	4
Val D'Elsa	415	379	271 (71.5)	3	
Val di Chiana	409	379	302 (79.6)	5	1
Total	1584	1453	1138 (81.4)	14	5

Discussion

To correctly dilute and inject PPD intradermally according to Mantoux technique avoiding any risk for personnel, skill is required; furthermore, this technique is time-consuming, especially when large-scale surveys are performed. Multipuncture tests (MPTs, Tine Test, IMOT, Heaf test) have been proposed for many years as possible alternative methods, as they are easy to carry out and do not involve risks for personnel; nevertheless, they are charged of several problems in terms of sensitivity and specificity, giving controversial results compared with the classical Mantoux technique [4-9].

Advances in scientific knowledge have led to the development of tests that measure the production of interferon γ by T-cells stimulated with *Mycobacterium tuberculosis complex* specific antigens. Encouraging results have been obtained with the T-cell-based assay as it is unaffected by prior BCG vaccination or by *atypical Mycobacteria* exposition [10-13].

Although the new methods have a potential to eventually prevail as an additional help for diagnostic purpose, they are unsuitable for large-scale epidemiological surveys.

Despite the 100 year-old Mantoux test has some drawbacks, up to now it remains the only recommended technique for "on the field" investigation on latent TB infection.

In Italy, epidemiological surveys on TB prevalence by skin test reactivity, targeted to students thirteen old, were mandatory until the end of 90s: at that time, Tine test was used as an easy to handle method for large-scale screening. Most of the studies report a TB prevalence ranging from 2.52 to 4.04 [14]; a T.I. as high as 20% has been reported in a group of 19 years old people living in Milan and surrounding [15].

To our knowledge, in Italy the only published study on tuberculin reactivity using the Mantoux test as "golden standard" report 6.1% TB prevalence and 0.3% A.R.I. in recruits 19-23 years old [16]. Using the same technique, in this research we observed a much lower rate of infection in 1,138 subjects eighteen years old attending high school, who were representative of about 60% of all eighteen agers living in Siena and its Province.

It is worth-noting that T.I. was 0.6% in a previous school-based survey, performed with Tine test during the years 96-97 on 30,000 thirteen years old children by the Personnel of the Department of Public Health of Siena.

Because Mantoux test results may not completely overlap with those obtained by Tine test, the previous and actual investigations carried out on the same geographical area are not strictly comparable. Nevertheless, it is reasonable to suppose that in our area *Mycobacterium tuberculosis complex* circulate at a low degree, as demonstrated by the very slight increasing in T.I. if we consider the overall prevalence of subjects with a skin reaction > 5 mm; it is worth-noting that T.I. is 0.4 if a reaction 10 mm or more is the cut-off.

In our data-set, all but three subjects with a > 5 mm Mantoux positive reaction were of foreign origin, recently migrated from Eastern Europe. It is noticeable that similar results, showing high prevalence of latent TB infection were previously observed in immigrants from four West Africa Countries [17].

The observation that migrants from high endemicity countries are at major risk of TB is confirmed by a study on the incidence of the disease carried out in the last few years: in our area 20% of all the cases were of foreign origin [18].

Our results confirm the trend of Tuberculosis in the recent years in Italy and in other western Europe Countries, which are considered at very low risk of TB infection and disease [19].

We agree with the Pediatric Tuberculosis Collaborative Group report on the use of tuberculin skin testing [20] that Mantoux test should be targeted to some at risk categories. Efforts should be made to address financial and human resources to persons who come from countries where TB is common, those who have been in strict contact with an active TB case and those with occupational risk as healthcare workers.

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