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RESEARCH ARTICLE

Prevalence and Risk Factors for Latent Tuberculosis Infection among Healthcare Workers in a Low Incidence Country

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Abstract:

Background:

Tuberculosis prevention is a major goal in the hospital setting. Because of the possible progression or reactivation of latent disease, the screening of healthcare workers is an important issue in the TB control program. The aim of the study was to assess the prevalence of LTBI (latent tuberculosis infection) and to evaluate the main risk factors related to this condition in a teaching hospital in Italy.

Methods:

We reviewed the data of a tuberculosis screening conducted on 3622 healthcare professionals in a teaching hospital in Rome. All subjects were evaluated by QuantiFERON test which if positive, was followed by appropriate clinical and diagnostic procedures.

Results:

Latent Tuberculosis Infection LTBI condition was detected in 2.1% of the cases, most commonly in men. Male gender, higher age class, country of birth and nurse job were statistically related with the positivity to QuantiFERON test.

Conclusion:

LTBI was relatively uncommon in our population, however, given the potential risk of reactivation and progression to overt disease, the screening of healthcare workers and students is recommended in the hospital of low-incidence countries.

Keywords: Latent tuberculosis, Contact screening, QuantiFERON, Occupational health, Bacillus, Mycobacterium.

Article History

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1. INTRODUCTION

Tuberculosis (TB) is a major public health problem that bears many occupational consequences [1].

130 years after the discovery of the tubercle Bacillus, the prevalence of infection remains high. It has been estimated that approximately one-third of the world's population carries tubercular Mycobacterium in a latency State, which accounts for over 2 billion people [2]. There are 8.6 million new cases per year and nearly 2 million deaths/year, 30% of which are preventable with the appropriate treatment.

With TB incidence rate being considerably below 10 cases per 100,000 inhabitants over the last 10 years, Italy [3] is characterized by a low incidence in the general population,

with a concentration of most cases in some risk groups and in some age groups. In the decade between 2004 and 2014, an average of 4300 cases of tuberculosis were notified annually, 52% of which were in foreigners.

Despite being preventable and treatable, tuberculosis is still one of the most dramatic health emergencies, and it was declared as a global emergency in 1993 by the WHO due to the health, economic and social burden that it bears.

Known risk factors for tuberculosis infection include living in overcrowded communities, immigration from endemic areas and individual conditions such as malnutrition, alcoholism, diabetes, drug addiction, HIV infection, age [1].

Healthcare workers (HCWs) are at higher risk of being exposed to tuberculosis compared to the general population [1], even in countries with low TB incidence, such as Italy. In these workers, the assessment of latent (LTBI) and active (TBA)

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tuberculosis is part of the annual health surveillance program aimed to prevent occupational diseases [2].

Because of the severity of their symptoms, individuals with an active contagious form of tuberculosis have a higher chance of being hospitalized and can remain for hours or days at the health care facility with a pending diagnosis. For these reasons, the prevention of nosocomial transmission of tuberculosis represents prominent public health and occupational requirement [4, 5]. However, it is also important to note that healthcare providers may contract an infectious disease outside of the workplace, thus representing a source of infection to colleagues and patients that are more likely to be affected.

A case of untreated active infectious pulmonary tuberculosis can infect 10-15 people within a year [6]. Of these individuals, a percentage between 3 and 10% will be infected, half of whom will become ill within one to two years while the others might develop the illness at any point of their residual life [4]. On average, 10% of people with LTBI develop TB disease in their lifetime, half of which become ill within 2 years after exposure [1]. About 70% of incident cases of TB are a result of the reactivation of a past infection [1, 4, 6]. For these reasons, the identification and prophylactic treatment of individuals with LTBI are crucial for the elimination of the disease.

According to Italian law [7, 8], it is mandatory for employers to evaluate all risks in the workplace, including the risk of exposure to biological agents, and to implement measures to prevent the spread to operators or to limit the severity of its consequences. For this purpose, great importance is given to health surveillance of tuberculosis infection. In fact, the surveillance of LTBI in HCWs is considered fundamental for tuberculosis prevention.

The aim of our study was to estimate LTBI prevalence and evaluate associated risk-factors among Italian HCWs

2. METHODS

LTBI is defined as a state of a persistent immune response to stimulation by Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB. The prevalence of the LTBI was retrospectively evaluated by analyzing the results of the QuantiFERON-TB Gold (QFT) tests performed in the HCWs of a teaching hospital in Rome. The health workers in the study were evaluated during the annual health surveillance program performed in 2015.

The tests results were classified according to the interpretative guidelines provided by the manufacturer. Tests were classified as “positive” or “negative”, respectively, if higher or lower response than the cut-off value of 0.35 IU / ml of INF- γ was detected in at least one test tube (TB1 or TB2). All the workers with a “positive” result had to perform diagnostic tests to exclude active tuberculosis such as chest X-ray, and blood chemistry. The final medical evaluation was done by a specialist in infectious diseases. A subject was diagnosed as affected by LTBI in the case of positivity to the QFT-Plustest in the absence of clinical-radiological and serological signs of active infection.

The analyzed sample included medical doctors, nurses, lab and radiology technicians and medical students. Positive LTBI

workers were assessed again within a year since the first positive serological result. We also analyzed the phenomenon of reversion which was defined as the possible reversal of QFT-Plus test positivity in the year after the revealing of positivity (2016).

Data were analyzed using the statistical software IBM SPSS. A p-value of 0.05 was taken as the level of statistical significance. The inference of the analyzed factors was expressed as OR and respective 95% Confidence Intervals (95% C.I.) and p-value.

3. RESULTS

3622 clinical records were examined (1295 men and 2327 women); the average age of the population was 32.2 ± 10.5 years in males and 33.5 ± 11.1 years in women, respectively. LTBI was diagnosed in 77 subjects (2.1% of the sample). The mean age of the subjects with LTBI was 42.9 ± 12.8 years vs 31.8 ± 10.5 for the subjects that tested negative; (p 0.001 at T-test). The prevalence of LTBI in relation to mail demographic and occupational factors of the studied population is shown in Table 1. Male gender, age 40 years, foreign country of birth and nurse job was related to the risk of LTBI after testing those factors in a multivariate analysis (Table 2).

Table 1. Prevalence of LTBI in the working population per gender, age group, country of birth and occupation.

Variables	Number of subject with LTBI	LTBI Prevalence %	P value
Subjects	77/3622	2.1	-
Age	-	-	-
40 years old	27/2627	0.4	0.01
≥ 40 years old	24/993	5.2	
Sex	-	-	-
Male	38/1295	2.9	0.05
Female	39/2327	1.7	
Country of birth	-	-	-
Italy	69/3471	1.9	0.01
Foreign country	8/151	5.3	
Job category	-	-	-
Nurse	36/652	5.5	0.01
Other professions	41/2970	1.5	

Table 2. Risk factors for LTBI in the study population (multivariate analysis).

-	Odds Ratio	95% C.I.	P value
Male gender	1.69	1.07-2.66	0.05
Age ≥ 40 years	4.43	2.32-6.14	0.01
Foreign country of birth	6.00	2.68-13.43	0.01
Nurse job	3.77	2.32-6.14	0.01

The reversion phenomenon (defined by the negativization of a positive test) was documented in 2 subjects (2.6% of the positive cases). LTBI subjects in relation to the date of first positive feedback and reversal of the test were classified as shown in Table 3.

Table 3. The number of subjects with LTBI per gender and time of onset.

-	Males	Females	Total
First Diagnosis	23	22	45
Confirmed Positive	10	13	23
Conversions	5	4	9
Total LTBI	38	39	77

Conversion rate among our population was 0.5% (9 confirmed positive test among 1455 subjects who had previous negative determination in the year 2014).

Among the subjects classified as having LTBI, most consisted of nurses (36/77; 46,8 percent), while medical students (17/79; 22,0%), physicians (14/77; 18,2%), and technicians (10/77; 13,0%) were less represented. For 59 subjects, chemoprophylaxis was prescribed by infectious disease specialist. Eighteen subjects refused therapy while 9 did not return to visit after the prescription. No case of active TB has been documented between subjects LTBI positive in the year following the study.

4. DISCUSSION

The QuantiFERON test is confirmed to be a useful diagnostic tool, that is easy to perform on groups of exposed workers. It has been sufficiently validated in clinical use and comes with a good positive predictive value. The results of our study confirm the low prevalence of the LTBI condition among the Italian population. When compared with data from studies carried out among hospital population, our work shows a lower prevalence of LTBI condition (2.6% *versus* mean LTBI percentages of 9.2% found in other studies) [9 - 12]. This difference is reasonably related to the low average age of the sample, which equates to a shorter period of exposure.

Moreover, the lower prevalence of LTBI found in our population can be related to the effectiveness of the administrative and environmental control plan carried out in our hospital since 2005, that provides for early reporting of suspected or confirmed case of TB. In previous studies conducted in our hospital [15] during the period 2007/2013, the mean prevalence of positive tests was 5.5%.

A small retrospective study conducted by Lamberti *et al.* in 2016 [11] on a population of dentistry students showed a prevalence of 2.84% for LTBI, which is in line with what was found in our study. The same authors in previous studies of larger populations showed a prevalence of 1.29%.

After testing in a multivariate analysis, LTBI condition was statistically related to the male gender, age 40years, and birth in a foreign state (out of Italy); moreover, nurses work, in our study, seems to be associated with a higher prevalence of LTBI as reported in the literature [12]. The phenomenon of reversion, defined as the reversal of QFT-Plus test positivity in the year after the revealing of positivity and widely described in the literature [13 - 15], manifested in 2.5% of positive results. This phenomenon appeared to be common in subjects with lower values of IFN production at QuantiFERON test.

In a previous evaluation relative to the year 2014 we found a 16% reversion rate, much higher than the actual. Actions taken in our hospital to implement standardization of proce-

dures for specimen collection, storage and transport of samples during the study year, may justify the lower incidence of the phenomenon than in previous statistics. It is also known that reversion may be indicative of transient infections that can occur when someone is exposed to infectious cases of active tuberculosis [16, 17]; a more timely identification and management of cases may have had, therefore, an impact in lowering this phenomenon.

A large number of positive cases (17/79; 22,0%) were reported among medical students who nevertheless constituted the largest population in our sample. Although these subjects need to be included in programs for the prevention of infection and diagnosis of latent tuberculosis infection, they are not usually considered a possible source of risk for operators and patients. Despite the frequency of LTBI in these subjects is reported to be very low [18, 19], the results of our study confirm the need to extend the evaluation of LTBI to this population.

Given the rate of progression and reactivation reported in the literature [1, 3], we can estimate that among the individuals of our study affected by LTBI, 2 to 4 workers will develop active tuberculosis throughout working life.

Regarding the suitability for the job, according to the main scientific statements [1, 4, 6], preventative therapy should be offered to those who don't have contraindications. Workers who refuse to submit to this therapy will not be automatically excluded from their occupation. However, an occupational medicine specialist will evaluate whether transferring them in a ward with a lower risk for operator-patient contagion. In the first 2 years following the diagnosis, health surveillance must be performed every six months at most. Subjects with a reversion of a positive test or conversion-reversion phenomenon need to be re-evaluated by occupational medicine specialist according to the risk evaluation.

CONCLUSION

The results of our study confirm the low prevalence of LTBI in the Italian healthcare workers. Despite this, the condition of LTBI is not contagious and the different circumstances of diagnosis require specific clinical and preventive considerations.

AUTHORS' CONTRIBUTIONS

LC contributed to study design and interpretation of results and was the major contributor in writing the paper; AN and AJ interpreted data results and was a contributor in writing the paper; FP collected references and participated in statistical analysis; AP interpreted data results; AM contributed to study design and interpreted data results.

LIST OF ABBREVIATIONS

LTBI	=	Latent Tuberculosis Infection
TB	=	Tuberculosis
HCWs	=	Healthcare Workers
TBA	=	To Be Announced
QFT	=	QuantiFERON-TB
CI	=	Confidence Intervals

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All procedures performed in this study were approved by the ethical committee of Policlinic Tor Vergata.

HUMAN AND ANIMAL RIGHTS

No animals/humans were used for studies that are the basis of this research.

CONSENT FOR PUBLICATION

Written consent was obtained from all participants.

AVAILABILITY OF DATA AND MATERIALS

The data sets used and/or analyzed during the current study are available from the corresponding author.

FUNDING

None.

CONFLICT OF INTEREST

The authors declares no conflict of interest, financial or otherwise.

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Declared none.

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