RESEARCH ARTICLE

Risk of latent tuberculosis infection among healthcare workers in Italy: a retrospective study with Quantiferon Test

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Keywords

Summary

Objective. *The latent tuberculosis infection (LTBI) is a state of persistent immune response to stimulation by Mycobacterium Tuberculosis antigens without clinical manifestation: the healthcare workers (HCWs) have a higher exposure risk so prevention is an important challenge for occupational medicine. The aim of our study is to evaluate the prevalence of LTBI among HCWs of the Foundation Policlinic "Tor Vergata".*

Methods. *This is a retrospective study conducted by analyzing*

the clinical records of 825 HCWs of the PTV, from January 1st to December 31th 2016. To evaluate the TB infection we used the Quantiferon TB Gold interferon-gamma release assay.

Results. *Our study underlines the low prevalence of LTBI in the Italian healthcare workers.*

Conclusion. *Although the LTBI status is not contagious, the diagnosis and the safety strategies require specific clinical and preventive considerations.*

Introduction

Tuberculosis (TB) is one of the top 10 causes of death worldwide: according to the last World Health Organization (WHO) Global report, 10.0 million (range: 8.9-11.0 million) people fell ill with TB in 2019, and 1,6 million died for this infective disease. Despite some progress in the pipeline for the new diagnostic methodic, TB research and development did not improve new drugs and vaccine efficacy [1]. Studies in literature underline that in about 70% of incident cases of TB there is a reactivation of a past infection.

The latent tuberculosis infection (LTBI) is a state of persistent immune response to stimulation by Mycobacterium Tuberculosis antigens without evidence of clinically manifested active TB so the fast identification and prophylactic treatment of individuals with LTBI is crucial for the elimination of the disease [2, 3].

Approximately two billion people in the world are affected by LTBI: in Italy, the National Health Institute reports that the incidence of TB in 2019 is 6.5 case/100.000 inhabitants [4, 5].

The WHO classified Italy as a low incidence country, even if there are groups of population with increased probability to contract TB infection [6]. The healthcare workers (HCWs) have a higher exposure risk to tuberculosis, because of their activities in the hospital setting: the prevention of this new-old infective disease is an important challenge for the occupational medicine [2].

The HCWs may contract the Mycobacterium Tuberculosis

in nosocomial environment by the infected patient or get infected in the community setting and being itself a source of infection for colleagues and patients.

According to Italian Legislation is mandatory for Occupational Doctor to evaluate all work risks, including the exposure to biological agents, like viral hepatitis or tuberculosis, and to improve the safety strategies in order to prevent the spread to operators or to limit the severity of its consequences [7]. For the evaluation of TB work risks, in 2013 the Italian Ministry of Health has classified healthcare settings into 5 increasing levels of risk related to a growing risk of infection [8]. Health surveillance flow chart is established according to the level of risk of the structure to which the HCWs are employed [9, 10].

Although the importance of the early identification and treatment of the LTBI among hospital workers is known, only few studies have evaluated the correlation between the infection exposure risk classification and the increased incidence of active disease [11-13].

The aim of our study is to evaluate the prevalence of LTBI in the HCWs of the Foundation PTV Policlinic "Tor Vergata" (PTV) of Rome related to the main demographical and occupational risk factor.

Methods

This is a retrospective study conducted by analyzing all the clinical records of HCWs of the PTV, who

underwent the annual occupational medical visit from January 1st to December 31th 2016. The analyzed sample included medical doctors, nurses, laboratory and radiology technicians. To evaluate the TB infection we extracted from the clinical records the results of the Quantiferon - TB Gold (QFT-G, Qiagen) interferon-gamma (IFN-γ) release assay, highly specific and sensitive. The limit of this test is that it cannot distinguish between active tuberculosis disease and latent tuberculosis infection [14].

Analytical data were extracted from ModuLab, software that was adopted by Chemical Analytical Laboratory of PTV during the investigation period. For each study subject Quantiferon plus results were collected as well as the following data: age, gender, job category, seniority of work.

According with the manufacturer published criteria, the test was classified as positive when the antigen specific IFN gamma serum values was equal or higher than the cut-off level of 0,35 IU/ml, compared to a negative control [15]. All HCWs having positive Quantiferon test were studied by specific clinical examination and traditional radiology and retested during the following year.

Analyses were performed using IBM Stata 11 statistical package software. Results were considered statistically significant a P value threshold of < 0.05.

Results

We collected the clinical records of 825 HCWs: 284 men and 541 women. Positive Quantiferon result was found in the 4.2% of the sample (35 from 825 subjects). All those subjects were classified as LTBI after the radiological and clinical evaluation; among those HCWs, 17 were male and 18 female.

Regarding job task, 22 of LTBI operators were employed as nurses, 11 were doctors, 2 technicians.

Main demographic and occupational charateristics of the study population are shown in Table I.

Among operators who resulted positive at Quantiferon test, 7/35 (%) had a negative determination during the previous 12 months, being classified as new TB conversion, whereas 28/35 LTBI cases had a previous positive Quantiferon result.

No case of active TB has been documented between those subjects in the year following the study. We evaluated the association between LTBI and main demographic and occupational factors (gender, age class, seniority, risk level of employment setting, and job task).

After tested in a multivariate regression model the only variable statistically associated with a higher frequency of LTBI was gender, whereas all the other risk factors tested negative at the regression analysis (Tab. II).

Finally we calculated the conversion rate for TB (negative to positive result during the 1 year period) both in high and low risk setting; we found no statistical difference in the conversion rate between the different risk levels (P = 0.56 at χ^2 test).

Tab. I. Main characteristics of the study population.

Variables	N	%
Subjects	825	100
Sex		
Male	284	34.4
Female	541	65.6
Mean (SD) age, year	42.9	
Age		
≤ 40 years old	283	34.3
> 40 years old	542	65.7
Seniority		
≤ 10 years	348	34.3
> 10 years	477	65.7
Job		
Nurse	546	66.2
Medical doctor	181	21.9
Laboratory staff	8	1.0
Technical staff	74	9.0
Others	16	1.9
Working area[§]		
Low-average risk (groups A, B, C)	687	83.3
High risk (groups D, E)	138	16.7
IGRA test outcomes		
Negative	790	95.8
Positive	35	4.2

[§] Tuberculosis prevention in healthcare workers and similar. Italian Ministry of Public Health 2013.

Tab. II. IGRA test outcomes by the main characteristic of the study population.

Variables	Positive IGRA	%	P value univariate	P value multivariate
Sex				
Male	19/284	6.7	0.017	0.015
Female	16/541	3.0		
Age				
≤ 40 years old	5/283	1.8	0.006	0.068
> 40 years old	30/542	5.5		
Seniority				
≤ 10 years	9/348	2.6	0.031	0.142
> 10 years	26/447	5.5		
Job				
Nurse	21/546	3.8	0.46	
Medical doctor	12/181	6.6		
Laboratory technician	0/8	0.0		
Technical staff	2/74	2.7		
Others	0/16	0.0		
Working area[§]				
Low-average risk (groups A, B, C)	5/138	3.6	0.82	
High risk (groups D, E)	30/687	4.4		

[§] Tuberculosis prevention in healthcare workers and similar. Italian Ministry of Public Health. 2013.

Discussion

The healthcare workers have an increased exposure risk to tuberculosis, because of their activities in the hospital setting: in Italy for tuberculosis, the healthcare setting

is classified in 5 levels according to growing exposure risk, from A to E [8]. LTBI condition has been defined by the positivity to Quantiferon test and the negativity to the clinical-radiological assessment, conducted for the purpose of excluding an active infection [16, 17]. Our study confirms the low prevalence of LTBI among healthcare operators in Italian hospital: we found 35 subjects with LTBI off a sample of 825. This data compared with other similar studies conducted among different sanitary population of various countries, shows a lower prevalence of LTBI condition, 4.2% *vs* mean LTBI percentages of 9.2% of other groups [11, 12, 18, 19]. According to this data in our study the prevalence of LTBI assessed by Quantiferon test is statistically related with gender. Furthermore, the low LTBI prevalence in our sample can be associated to the effectiveness of the safety strategies planned by the Amministration and the Occupational Medicine of PTV since 2005, that allows early detecting and reporting of suspected or confirmed case of TB. In previous studies conducted in our hospital during the period 2007/2013, the mean prevalence of positive tests was 5.5% [20]. Lamberti et al retrospective study in 2016 in Naples, based on a sample of students of dentistry showed a prevalence of 2.84% for LTBI [13]. Male Sex, in our study, seems to be statistically associated with LTBI: this data confirms that male gender is a greater tuberculosis risk, as already reported in literature [18]. The work seniority and the higher age class (> 40 years old) showed also an increased risk of latent tuberculosis even if this association was found to be not statistically significant. Moreover, in order to evaluate Italian Health Ministry TB classification for hospital setting to predict the risk of contagion for HCWs, we evaluated the correlation between the areas of employment and the rate of conversion TB test: surprisingly in our study working in high risk setting was not related to a greater prevalence of LTBI and we found no conversion rate differences among high and low work risk groups. In a previous evaluation relative to the year 2014 we found a 16% reversion rate [20], while in the present study no positive QFT test reverted, probably due to the improved standardization of the specific collection, storage and transport procedures. It is also reported that reversion may be indicative of recent exposure to a patient with active and infective Tuberculosis [21, 22]. According to the progression and reactivation rate reported in literature [1, 3], for our sample we may estimate that about 2 to 4 HCWs affected by LTBI could develop the active tuberculosis throughout working life, so as reported by the main scientific statements [1, 2, 7], prophylactic therapy should be offered to those who don't have contraindications.

Conclusions

The control of work exposure to TB infection in the hospital setting represents a major health issue for the Occupational medicine specialists. Results of our study underline the low prevalence of LTBI in the Italian healthcare workers; although LTBI status is not contagious, given the risk of reactivation of active tuberculosis following immunosuppressive treatment or other medical conditions, a specific TB control program should be improved in order to prevent the nosocomial spread of the infection. Based on the results of our study, serial screening for latent TB infection should include all HCWs, regardless to risk classification of the employment setting.

Ethical statement

Ethics approval and consent to participate: all procedures performed in this study were approved by the ethical committee of Policlinic Tor Vergata.

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Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

LC: conception and design of the study; acquisition of data, final approval of the version to be submitted.
CF: revising the article critically for important intellectual content
MF: acquisition of data.
SB: acquisition of data.
SG: drafting the article or revising it critically for important intellectual content.
LMD: analysis and interpretation of data.
Mattone Pier Francesco: analysis and interpretation of data.
MTD: drafting the article or revising it critically for important intellectual content.
OB: acquisition of data.
AM: drafting the article or revising it critically for important intellectual content.
AP: conception and design of the study.
PL: conception and design of the study, drafting the article or revising it critically for important intellectual content, final approval of the version to be submitted.

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