Active tuberculosis among health care workers in Portugal*, **

Tuberculose ativa entre profissionais de saúde em Portugal

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Abstract

Objective: To determine the incidence of active tuberculosis (TB) in a cohort of health care workers (HCWs). **Methods:** Descriptive study of active TB cases identified in an occupational health screening of 6,112 HCWs between 2005 and 2010. Cases of active TB were defined as those in which *Mycobacterium tuberculosis* was identified by direct microscopy or culture; those in which there were symptoms or clinical signs of TB and necrotizing granuloma, as detected by histology; and those in which the radiological findings were consistent with active TB. **Results:** Among the 6,112 HCWs evaluated, we identified 62 cases of active TB: pulmonary TB (n = 43); pleural TB (n = 15); lymph node TB (n = 2); pericardial TB (n = 1); and cutaneous TB (n = 1). Seven HCWs were asymptomatic at the time of diagnosis. Of the 62 cases of active TB, 48 developed within the first 10 years of occupational exposure in the workplace, 36 of those occurring within the first 5 years. Physicians and nurses accounted for the highest numbers of cases (22 and 21, respectively). **Conclusions:** In HCWs employed in Portugal, the TB burden is high. Physicians and nurses are the HCWs who are at the highest risk of developing active TB. We found the risk of developing this disease to be highest in the first years of exposure, as has been reported in previous studies. In high-incidence countries, TB screening of HCWs is important for controlling the transmission of this disease.

Keywords: Tuberculosis/diagnosis; Occupational health; Health personnel.

Resumo

Objetivo: Determinar a incidência de tuberculose (TB) ativa em uma coorte de profissionais de saúde (PS). **Métodos:** Estudo descritivo dos casos de TB ativa identificados entre 2005 e 2010 no rastreio de medicina do trabalho efetuado em 6.112 PS. Casos de TB ativa foram definidos como aqueles com identificação de *Mycobacterium tuberculosis* por microscopia direta ou cultura; aqueles com sintomas ou sinais clínicos de TB e granuloma necrotizante, detectado por histologia; e aqueles com achados radiológicos consistentes com TB ativa. **Resultados:** Dos 6.112 PS avaliados, houve 62 casos de TB ativa (TB pulmonar, em 43; TB pleural, em 15; TB ganglionar, em 2; TB do pericárdio, em 1; TB cutânea, em 1). Sete PS estavam assintomáticos no momento do diagnóstico. Dos 62 casos de TB ativa, a doença ocorreu nos primeiros 10 anos de exposição ocupacional em 48 e nos primeiros 5 anos em 36. A maioria dos casos verificou-se em médicos e enfermeiros (22 e 21, respectivamente). **Conclusões:** O impacto da TB em PS em Portugal é elevado. Os médicos e enfermeiros são os PS com o maior risco de desenvolver TB ativa. Tal como relatado em estudos prévios, parece haver um risco mais elevado de desenvolver essa doença nos primeiros anos de exposição. Em países de elevada incidência, o rastreio de TB nos PS é importante no controle da transmissão dessa doença.

Descritores: Tuberculose/diagnóstico; Saúde do trabalhador; Pessoal de saúde.

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Introduction

According to the World Health Organization (WHO), the year 2008 brought 9.4 million new cases of tuberculosis (TB) and 1.8 million TB-related deaths, approximately 500,000 of which were in patients infected with HIV. It is estimated that multidrug-resistant TB cases accounted for another 500,000 cases. The number of affected individuals has led the WHO to categorize the disease as a global emergency.[1] In Portugal, the incidence of TB was 24 new cases/100,000 population in 2009.[2] Despite a reduction observed in recent years, Portugal still has one of the highest TB incidence rates among European Union countries.[2]

Health care workers (HCWs) are at an increased risk of infection with *Mycobacterium tuberculosis* because they are exposed to patients with active disease in settings that favor transmission, especially when working in inadequately ventilated spaces and when performing procedures involving contaminated aerosols.[3-5] Given this increased risk of contracting the disease in the workplace, TB is considered an occupational disease in Portugal.[6] In any given geographic area, the incidence of TB in HCWs is related to the incidence in the general population of that area,[7] added to the profession-specific risk.[8-10]

In Portugal, despite the mandatory reporting of active TB cases, there are no official records of the numbers of affected HCWs. The goal of this study was to determine the incidence of active TB cases among HCWs at a general hospital in Portugal.

Methods

In this descriptive study, the occupational risk of *M. tuberculosis* infection was assessed in 6,112 HCWs (Table 1), all of whom were working or training at the São João Hospital, located in the city of Porto, Portugal, between 2005 and 2010. On the basis of the 2005 Centers for Disease Control and Prevention (CDC) guidelines and taking into consideration the number of beds, together with the mean annual number of patients diagnosed with TB (258 patients, with an HCW to TB patient ratio of 17.2 to 1), the TB risk at the facility has been classified as "moderate".[10] The HCWs were examined at hiring and thereafter on a regular annual basis. Occasional examinations were performed in symptomatic HCWs and in cases of ongoing TB contact. Using a questionnaire, we collected data related to age, gender, work sector, length of employment as an HCW, BCG vaccination status, symptoms, and history of TB. For each HCW, the risk of TB transmission was classified on the basis of the CDC classification,[10] as follows: low—for HCWs who will never be exposed to persons with known or suspected TB or to clinical specimens that might contain *M. tuberculosis*; moderate—for HCWs who might be exposed to persons with TB or to clinical specimens that might contain *M. tuberculosis*; or high/ongoing—for HCWs working in a sector in which there is a risk of person-to-person transmission of *M. tuberculosis* or evidence of such transmission (among patients or HCWs) within the last year.

The data analyzed in this study were collected as part of a screening program aimed at identifying HCWs with latent TB infection (LTBI) or active TB. The screening consisted of the following: evaluation of respiratory symptoms (cough, sputum, hemoptysis, and chest pain) and constitutional symptoms (fatigue, anorexia, fever, and hyperhidrosis); chest X-ray at hiring, in the presence of symptoms, and in HCWs meeting the criteria for LTBI; and tuberculin skin test (TST) with 2 tuberculin units of PPD in 0.1 mL (RT23; Statens Serum Institut, Copenhagen, Denmark), unless contraindicated (previous TST induration ≥ 10 mm, previous diagnosis of TB with appropriate treatment, severe viral infection/immunization with a live-virus vaccine within the past month, extensive burns, or eczema). Since 2007, in vitro ELISA, based on IFN-gamma (IFN-γ) release assay (IGRA, QuantiFERON-TB Gold In-tube; Cellestis, Carnegie, Australia), has been performed simultaneously with TSTs.

Individuals with a TST induration ≥ 10 mm and an IFN-γ response ≥ 0.35 IU/mL were considered positive for infection. Those in whom *M. tuberculosis* was identified by direct microscopy or by culture (on Löwenstein-Jensen medium) were classified as having active TB, as were those with symptoms or clinical signs of TB and presenting with necrotizing granuloma detected by histology. A diagnosis of active TB was also made in cases of radiological abnormalities consistent with the disease in the pleura or lung

Table 1 - Characteristics of health care workers screened for tuberculosis, São João Hospital, Porto, Portugal, 2005-2010.

Characteristic	n = 6,112
Gender, n (%)	
Male	1,669 (27.3)
Female	4,443 (72.7)
Job description, n (%)	
Aide	905 (14.8)
Administrative Assistant	373 (6.1)
Nurse	2,045 (33.5)
Physicians	1,714 (28.0)
Technician	513 (8.4)
Other	562 (9.2)
Length of employment, n (%)	
0-5 years	2,364 (38.7)
6-10 years	1,003 (16.4)
11-15 years	776 (12.7)
≥ 16 years	1,969 (32.2)
Ratio of HCWs to TB inpatients[a]	17.2:1
BCG vaccination, n (%)	
Yes	3,721 (60.9)
No	2,391 (39.1)
> 3 times	436 (7.1)
Symptomatic, n (%)	207 (3.4)
Alterations on chest X-rays, n (%)	108 (3.3%)[b]

HCW: health care worker. [a]Mean annual number of TB inpatients, 258. [b]Chest X-rays performed in only 3,276 of the 6,112 HCWs.

parenchyma (apical fibrosis). We defined LTBI as infection with *M. tuberculosis*, without any clinical manifestation, and presenting with a TST induration ≥ 10 mm or an IFN-γ response ≥ 0.35 IU/mL, assuming that active TB had been ruled out. All HCWs diagnosed with active TB were also screened for HIV-1 and -2 antibodies by ELISA. Cases of LTBI and suspected cases of active TB were referred to the pulmonology department of our hospital.

The screening program was conducted in accordance with the objectives of the São João Hospital Commission for the Prevention and Control of Tuberculosis. The anonymity of the participating HCWs was guaranteed.

Results

Infection with *M. tuberculosis* was evaluated in 6,112 HCWs (4,443 females and 1,669 males) who were working or training at São João Hospital between 2005 and 2010. Using the CDC criteria,[10] we determined that, in the most recent evaluation, the risk of exposure to TB was low in 687 (11.2%) of the HCWs evaluated, whereas it was moderate in 4,008 (65.6%) and high/ongoing in 1,417 (23.2%). The mean age was 38 ± 11 years, and the mean length of employment was 12 ± 11 years. Of the 6,112 HCWs evaluated, 3,721 (60.9%) had been vaccinated with BCG, as confirmed by their vaccination record or by the presence of a vaccination scar (Table 1). On the symptoms portion of the questionnaire, 207 (3.4%) of the HCWs reported respiratory or general symptoms. Of the 3,276 chest X-rays taken, 108 (3.3%) revealed abnormalities (Table 1).

Over the course of the study period, there were a total of 62 cases of active TB (Table 2), the incidence peaking in the years 2005 to 2007 (Figure 1). Among those 62 cases, there were 43 cases of pulmonary TB (multidrug-resistant in 2), 15 cases of pleural TB, 2 cases of TB in the cervical lymph nodes, 1 case of pericardial TB, and 1 case of cutaneous TB. Among those with pulmonary involvement, M. tuberculosis was identified by direct microscopy or culture in 34. Seven HCWs were asymptomatic at the time of diagnosis (made on the basis of a positive culture in 4 and on the basis of highly suggestive radiological images in 3). In all 62 HCWs diagnosed with active TB, the serology was negative for HIV-1 and -2. Of the 62 cases of active TB evaluated in the present study, 48 (77%) developed within the first 10 years of occupational exposure in the workplace, 36 (58%) occurring within the first 5 years (Figure 2).

The distribution of the 62 HCWs with active TB by work sector, stratified by the level of risk, was as follows: 4 (6.5%) worked in low-risk sectors; 40 (64.5%) worked in moderate-risk sectors; and 18 (29.0%) worked in high-risk sectors. Similarly, the distribution by professional group was as follows: 22 (35.5%) were physicians; 21 (33.9%) were nurses; 9 (14.5%) were aides; 5 (8.1%) were technicians; and 5 (8.1%) held other positions.

Among the cases of active TB, the results of the TST and IGRA performed at the time of diagnosis were available in 53 and 28 cases, respectively, and were positive in 50 and 26. These data are reported in greater detail in Table 3. Of the 2 cases in which the IGRA results were negative at the time of diagnosis, one

Table 2 - Description of active tuberculosis cases among health care workers, São João Hospital, Porto, Portugal, 2005-2010.

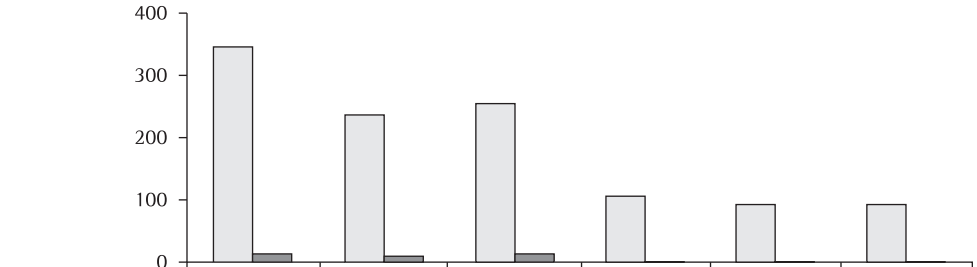
Case	Sex	Age	Position	Risk in sector	Year of diagnosis	Years as an HCW	Presentation	Symptoms at diagnosis	Chest X-ray	*Mycobacterium tuberculosis*[a]	TST (mm)	IFN-γ (IU/mL)
1	F	23	Nurse	Moderate	2005	1	Pulmonary	Yes	Abnormal	Positive	20 (p)	nd
2	F	32	Physician	Moderate	2005	4	Pleural	Yes	Abnormal	Negative	13 (p)	nd
3	F	22	Nurse	High	2005	< 1	Pulmonary	Yes	Abnormal	Negative	nd	nd
4	F	48	Nurse	High	2005	10	Pulmonary	Yes	Abnormal	Positive	0 (n)	nd
5	M	26	Physician	Moderate	2005	1	Pleural	Yes	Abnormal	Negative	nd	nd
6	F	53	Nurse	Moderate	2005	32	Pleural	Yes	Abnormal	Negative	20 (p)	nd
7	F	61	Aide	Moderate	2005	18	Pulmonary	Yes	Abnormal	Positive	nd	nd
8	F	29	Physician	Moderate	2005	2	Pulmonary	Yes	Abnormal	Positive	16 (p)	nd
9	F	36	Technician	Moderate	2005	10	Pulmonary	Yes	Abnormal	Positive	20 (p)	nd
10	M	43	Aide	Moderate	2005	17	Pulmonary	Yes	Abnormal	Positive	19 (p)	nd
11	F	26	Nurse	Moderate	2005	3	Pleural	Yes	Abnormal	Negative	12 (p)	nd
12	F	51	Aide	High	2005	7	Lymph node	Yes	nd[b]	Negative	nd	nd
13	F	28	Nurse	High	2005	3	Pleural	Yes	Abnormal	Negative	16 (p)	nd
14	F	31	Nurse	Moderate	2005	8	Pulmonary	Yes	Abnormal	Positive	15 (p)	nd
15	M	50	Other	Low	2005	22	PP	Yes	Abnormal	Positive	nd	nd
16	F	27	Nurse	Moderate	2005	5	Pleural	Yes	Abnormal	Negative	12 (p)	nd
17	F	28	Nurse	Moderate	2005	5	PM	Yes	Abnormal	Positive	18 (p)	nd
18	F	40	Nurse	Moderate	2005	16	Pulmonary	No	Abnormal	Positive	18 (p)	nd
19	F	29	Physician	High	2005	4	Pleural	Yes	Abnormal	Negative	nd	nd
20	M	26	Physician	Moderate	2006	2	Pleural	Yes	Abnormal	Negative	nd	nd
21	F	23	Nurse	Moderate	2006	1	MDR-P	No	Abnormal	Positive	18 (p)	nd
22	F	35	Other	Moderate	2006	4	Pleural	Yes	Abnormal	Positive	17 (p)	nd
23	F	32	Physician	High	2006	2	PP	Yes	Abnormal	Negative	20 (p)	nd
24	F	37	Physician	High	2006	3	MDR-P	Yes	Abnormal	Positive	nd	nd
25	F	56	Nurse	High	2006	32	Pulmonary	Yes	Abnormal	Positive	16 (p)	nd
26	F	38	Aide	High	2006	14	Pulmonary	Yes	Abnormal	Negative	14 (p)	nd
27	F	33	Nurse	Moderate	2006	11	Pulmonary	Yes	Abnormal	Negative	15 (p)	nd
28	F	36	Physician	High	2006	2	Pulmonary	Yes	Normal	Positive	18 (p)	nd
29	F	38	Aide	High	2006	8	Pulmonary	Yes	Abnormal	Positive	18 (p)	nd
30	F	26	Nurse	High	2006	4	Pulmonary	Yes	Abnormal	Positive	19 (p)	nd
31	F	31	Technician	Moderate	2006	5	Pulmonary	No	Abnormal	Negative	16 (p)	nd

HCW: health care worker; TST: tuberculin skin test; nd: no data; (p): positive; (n): negative; PP: Pleuro-pulmonary; PM: Pulmonary-mediastinal; MDR-P: Multidrug-resistant pulmonary; and Ad. Assist.: Administrative Assistant. [a]Identified by direct microscopy or culture. [b]No data at this writing; presumably normal at diagnosis (in 2005). [c]No data at the time of diagnosis; 0.14 IU/mL one month after beginning TB treatment.

Table 2 - Continued...

Case	Sex	Age	Position	Risk in sector	Year of diagnosis	Years as an HCW	Presentation	Symptoms at diagnosis	Chest X-ray	*Mycobacterium tuberculosis*[a]	TST (mm)	IFN-γ (IU/mL)
32	M	29	Physician	High	2006	4	Pulmonary	Yes	Abnormal	Positive	nd	nd
33	M	25	Nurse	Moderate	2007	3	Pleural	No	Abnormal	Negative	20 (p)	0.42 (p)
34	F	28	Nurse	Moderate	2007	6	Pulmonary	Yes	Abnormal	Positive	17 (p)	2.11 (p)
35	F	27	Physician	High	2007	1	Pleural	Yes	Abnormal	Negative	17 (p)	nd
36	M	32	Physician	Moderate	2007	1	Pulmonary	Yes	Abnormal	Positive	nd	0.65 (p)
37	F	49	Technician	Moderate	2007	19	Pulmonary	Yes	Abnormal	Negative	25 (p)	19.76 (p)
38	F	26	Ad. Assist.	Low	2007	5	Pleural	Yes	Abnormal	Negative	13 (p)	4.25 (p)
39	M	30	Physician	Moderate	2007	3	Pleural	Yes	Abnormal	Negative	14 (p)	8.87 (p)
40	F	30	Aide	Moderate	2007	10	Pulmonary	Yes	Abnormal	Positive	18 (p)	nd[c]
41	F	29	Physician	Moderate	2007	4	Pleural	Yes	Abnormal	Negative	13 (p)	0.65 (p)
42	M	30	Physician	Moderate	2007	4	Pulmonary	Yes	Abnormal	Positive	18 (p)	3.17 (p)
43	F	30	Technician	High	2007	8	Pulmonary	Yes	Abnormal	Positive	22 (p)	0.92 (p)
44	M	33	Physician	High	2007	2	Pericardium	Yes	Abnormal	Negative	12 (p)	0.40 (p)
45	F	30	Physician	High	2007	6	Pulmonary	Yes	Abnormal	Negative	16 (p)	2.13 (p)
46	M	45	Physician	Moderate	2007	19	Pulmonary	Yes	Abnormal	Positive	Na	2.11 (p)
47	F	39	Physician	High	2008	3	Pulmonary	No	Abnormal	Positive	18 (p)	3.97 (p)
48	F	25	Nurse	High	2008	3	Pulmonary	Yes	Abnormal	Positive	16 (p)	6.32 (p)
49	F	26	Physician	Moderate	2008	1	Pulmonary	Yes	Abnormal	Positive	15 (p)	0.17 (n)
50	F	34	Nurse	High	2008	12	Pulmonary	Yes	Abnormal	Positive	12 (p)	3.50 (p)
51	F	50	Other	Moderate	2008	11	Cutaneous	Yes	Normal	Positive	21 (p)	49.09 (p)
52	F	25	Physician	Moderate	2008	< 1	Pulmonary	Yes	Abnormal	Positive	13 (p)	1.30 (p)
53	F	27	Nurse	High	2009	3	Pulmonary	Yes	Abnormal	Positive	17 (p)	1.96 (p)
54	M	25	Other	Low	2009	4	Pulmonary	Yes	Abnormal	Positive	8 (n)	1.83 (p)
55	F	29	Nurse	High	2009	3	Pleural	Yes	Abnormal	Negative	13 (p)	2.10 (p)
56	F	61	Aide	Low	2009	33	Lymph node	Yes	Normal	Negative	19 (p)	0.28 (p)
57	F	26	Physician	Moderate	2009	< 1	Pulmonary	No	Abnormal	Positive	14 (p)	3.57 (p)
58	F	38	Aide	Moderate	2010	7	Pulmonary	Yes	Abnormal	Positive	19 (p)	1.40 (p)
59	F	31	Technician	Moderate	2010	6	Pulmonary	Yes	Abnormal	Positive	10 (p)	4.59 (p)
60	M	55	Aide	High	2010	36	Pulmonary	Yes	Abnormal	Positive	6 (n)	13.75 (p)
61	F	30	Nurse	Moderate	2010	9	Pulmonary	Yes	Abnormal	Negative	23 (p)	18.61 (p)
62	F	25	Physician	High	2010	1	Pulmonary	No	Abnormal	Negative	20 (p)	8.53 (p)

HCW: health care worker; TST: tuberculin skin test; nd: no data; (p): positive; (n): negative; PP: Pleuro-pulmonary; PM: Pulmonary-mediastinal; MDR-P: Multidrug-resistant pulmonary; and Ad. Assist.: Administrative Assistant. [a]Identified by direct microscopy or culture. [b]No data at this writing; presumably normal at diagnosis (in 2005). [c]No data at the time of diagnosis; 0.14 IU/mL one month after beginning TB treatment.



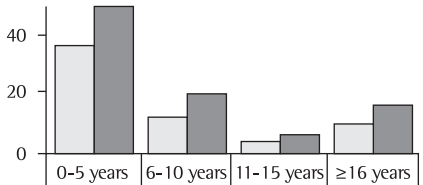
	2005	2006	2007	2008	2009	2010
TB (prevalence)	350.9	240	258	110.8	92.4	92.4
TB (number)	19	13	14	6	5	5

Figure 1 - Annual incidence of active tuberculosis (TB, per 100,000 population) among health care workers, São João Hospital, Porto, Portugal, 2005-2010.

was a case of pulmonary TB, *M. tuberculosis* being identified in a sputum sample, and one was a case of TB of the cervical lymph nodes, granulomas being found in a biopsy sample. In both of those cases, IGRA was repeated after 6 months, and the results remained negative.

Discussion

At the hospital under study, the prevalence of LTBI was 55.2% when the diagnostic criterion was a TST ≥ 10 mm, compared with 25.9% when an IFN-γ response ≥ 0.35 IU/mL was used as the criterion, and these results have been published elsewhere.[11] Prophylactic treatment with isoniazid was prescribed for HCWs in whom the infection had occurred within the last two years or who were considered to be at high risk for developing active TB. None of those who completed the treatment developed active TB, which underscores the importance of screening for and treating LTBI as a means of preventing active TB.



	0-5 years	6-10 years	11-15 years	≥16 years
TB (n)	36	12	4	10
% HCWs	58	19.5	6.5	16

Figure 2 - Analysis of the 62 cases of active tuberculosis (TB) identified between 2005 and 2010 among health care workers (HCW) at São João Hospital, Porto, Portugal, stratified by the number of years employed as an HCW (years of potential exposure to TB) prior to diagnosis.

Studies based on DNA analysis have shown that TB transmission occurs in the working environment.[12,13] Despite this evidence, other authors do not recognize an increased risk of TB in HCWs. This is because some studies conducted in developed countries with higher incomes have found the incidence of TB to be lower in HCWs than in the general population.[9] Some authors suggest that, in countries with a higher mean income, where TB is more common in HCWs who are first-generation immigrants, TB is acquired in the community and is unrelated to occupational risk.[14] Therefore, there could be differences between low- and high-income countries in terms of the recognition of TB as an occupational disease. De Vries et al.[12] evaluated 67 HCWs with TB and found that 42% of the infections had been acquired in the hospital, compared with 28% that had been acquired in the community and 30% that had been acquired abroad.

For persons employed as HCWs in Portugal, TB is considered an occupational disease,[6] which entitles affected individuals to significant compensation, up to several tens of thousands of Euros. In the absence of a clear distinction between TB cases that are truly work-related and those that are acquired in the community, the expenditures related to such compensation are considerable. Therefore, epidemiological tools (e.g., DNA fingerprinting) should be used as a means of documenting TB as an occupational disease. The fact that we did not employ such tools represents a major limitation of the present study.

Although there is a clear relationship between the number of hospitalized TB patients and TB incidence in HCWs, the risk

Table 3 - Cases of active tuberculosis, by year, among health care workers, São João Hospital, Porto, Portugal, 2005-2010.

Year	n	TST	n	TST conversion	n	IGRA	n
2005	19	≥ 15 mm	9	Conversion	3	No data	
		≥ 10 and < 15 mm	3	No conversion	9		
		< 10 mm	1	No data	7		
		No data	6				
2006	13	≥ 15 mm	9	Conversion	7	No data	
		≥ 10 and < 15 mm	1	No conversion	3		
		< 10 mm	0	No data	3		
		No data	3				
2007	14	≥ 15 mm	8	Conversion	6	Conversion	12
		≥ 10 and < 15 mm	4	No conversion	4		
		< 10 mm	0	No data	4	No data	2
		No data	2				
2008	6	≥ 15 mm	4	Conversion	1	Conversion	5
		≥ 10 and < 15 mm	2	No conversion	3		
		< 10 mm	0	No data	2	No conversion	1
2009	5	≥ 15 mm	2	Conversion	2	Conversion	4
		≥ 10 and < 15 mm	2	No conversion	2		
		< 10 mm	1	No data	1	No conversion	1
2010	5	≥ 15 mm	3	Conversion	1	Conversion	5
		≥ 10 and < 15 mm	1	No conversion	3		
		< 10 mm	1	No data	1	No conversion	0
Total	62	≥ 15 mm	35	Conversion	20	Conversion	26
		≥ 10 and < 15 mm	13	No conversion	24		
		< 10 mm	3	No data	18	No conversion	2
		No data	11				

TST: tuberculin skin test; and IGRA: IFN-gamma release assay.

is more closely related to the infrastructure and maintenance of the facility than to the number of TB admissions per HCW.[15] Factors related to the increased risk for HCWs include delayed diagnosis,[16] misdiagnosis in the initial evaluation, advanced age, absence of suspicious clinical signs (e.g., coughing), lack or inadequacy of personal protective equipment and preventive measures, and inadequate ventilation, especially in polyvalent hospital wards.[16,17] The control of TB as a nosocomial disease requires, above all, the adoption of collective measures, such as the rapid identification of suspected or confirmed cases of active TB, the rapid implementation of airborne precautions, and the use of surgical masks or N95 respirators by the HCWs.[18]

Although BCG vaccination has proven effective in reducing the most severe forms of TB, its efficacy in preventing pulmonary TB is variable.[19,20] Given the limited effectiveness of BCG vaccination,[19,20] strategies for preventing TB should be based on the identification and treatment of LTBI as a means of reducing the number of infected individuals and the risk of progression to active TB.[21] It is generally accepted that treating LTBI reduces the risk of developing active TB by more than 50%.[18,21-24]

In the present study, we observed an apparent relationship between duration of exposure and risk of TB, the risk of developing active TB being higher in the first years of exposure. This temporal relationship, as previously reported,[25] is similar to that found for recent TST conversions, the time to which is directly proportional to risk, i.e., when the conversion is more recent, the risk of progression to active TB is greater.[26] The small number of active TB cases in our sample precluded appropriate statistical confirmation of the influence of age and years of exposure as risk factors for active TB development. If future results support our data, additional efforts should be made to provide HCWs with adequate education about infectious

diseases and preventive strategies, from the hire date onward.

In our study, the distribution of active TB cases was not uniform across years, the number of cases peaking at 19 (equivalent to 351/100,000 population) in 2005, whereas the incidence in the general population of the city of Porto was only 45.4/100,000 population in 2006.[27] After the implementation of the screening program at the hospital under study, there was a significant reduction in the number of new cases of active TB among HCWs. In 2009, as well as in 2010, there were only 5 such cases (equivalent to 93/100,000 population), less than a third of the incidence in 2005, although still three times higher than that reported for the general population of the area (33.7/100,000 population) in 2009.[2] The reduction in the number of cases of active TB in HCWs between 2005 and 2010 probably reflects the efforts made to identify at-risk populations and to treat recently infected HCWs with LTBI who were considered to be at high risk of developing active TB, as well as the implementation of effective personal protection and educational programs for HCWs.

Seven of the active TB cases evaluated were diagnosed in asymptomatic HCWs who were screened because of ongoing exposure and the risk of person-to-person transmission of *M. tuberculosis* or evidence of such transmission (among patients or HCWs). Four of those cases were AFB-positive, and chest X-ray findings were abnormal in all 7. Such cases underscore the need for a planned screening program, especially when there is exposure to individuals (patients or co-workers) with contagious forms of TB and the appropriate preventive measures are not in place.

Most of the cases of active TB diagnosed during the study period were cases of pulmonary TB, which was multidrug-resistant in 2 of those cases. Among the cases of extrapulmonary TB, a case of cutaneous TB, attributed to an occupational accident in a microbiology laboratory, is noteworthy for its rarity.

Most of the active TB cases occurred in HCWs assigned to moderate- or high-risk sectors (less than 7% of such cases occurred in sectors classified as low risk), which lends credence to the idea that there is a relationship between occupational exposure and active TB. The cases that occurred in low-risk sectors might represent a community-acquired form of the disease, or a nosocomial form acquired in "common" areas. As previously mentioned, this distinction could have been made through the use of DNA fingerprinting. In addition, we found the incidence of active TB to be similar among physicians and nurses (1.28% and 1.03%, respectively), who routinely have closer contact with patients and constitute the largest occupational groups among HCWs.

The sensitivity of IGRA in patients with TB has been reported to be between 81% and 89%.[28,29] In a recent study conducted by Diel et al., IGRA had a 100% negative predictive value for progression to active TB in close contacts with a high pre-test likelihood of disease.[30] In our study, IGRA came into use in 2007 and was performed at the time of diagnosis in 28 of the cases of active TB reported since that time. In 26 of those 28 cases, the IGRA results were positive (sensitivity of 93%). Among the 51 active TB cases for which TST results are available, the results were positive in 48 (sensitivity of 94%), although there was a high number of false positives. Of the 2 cases in which the IGRA results were negative, 1 was a case of AFB-positive pulmonary TB and the other was a case of TB in the cervical lymph nodes. The TST results were positive in both of those cases.

In conclusion, in HCWs employed in Portugal, the TB burden is high. There seems to be a relationship between the duration of exposure and the risk of developing TB, that risk being higher in the first years of exposure. The incidence of TB in physicians is similar to that observed for nurses. The sensitivity of IGRA at the time of diagnosis is greater than 90% in patients with active TB. In high-incidence countries, TB screening is particularly important because it can identify asymptomatic HCWs with LTBI or active TB.

References

1. World Health Organization [homepage on the Internet]. Geneva: World Health Organization. [cited 2011 Mar 29]. Global Tuberculosis Control 2010. WHO Report 2010. [Adobe Acrobat document, 218p.] Available from: http://whqlibdoc.who.int/publications/2010/9789241564069_eng.pdf
2. Direcção-Geral da Saúde [homepage on the Internet]. Lisboa: Direcção-Geral da Saúde. [cited 2011 Mar 29]. Programa Nacional de Luta Contra a Tuberculose (PNT), Março de 2010 - Dia mundial da tuberculose. [Adobe

Acrobat document, 20p.] Available from: http://www.dgs.pt/upload/membro.id/ficheiros/i012626.pdf
3. Maciel EL, Prado TN, Fávero JL, Moreira TR, Dietze R. Tuberculosis in health professionals: a new perspective on an old problem. J Bras Pneumol. 2009;35(1):83-90.
4. Saleiro S, Santos AR, Vidal O, Carvalho T, Costa JT, Marques JA. Tuberculose em profissionais de saúde de um serviço hospitalar. Rev Port Pneumol. 2007;13(6):789-99.
5. Rodrigues PM, Moreira TR, Moraes AK, Vieira Rda C, Dietze R, Lima Rde C, et al. Mycobacterium tuberculosis infection among community health workers involved in TB control. J Bras Pneumol. 2009;35(4):351-8.
6. Portugal. Decreto Regulamentar n.º 76/2007, de 17 de Julho de 2007. Diário da República Portuguesa, Lisboa, 1a Série, n 136, 17 de Julho de 2007.
7. Institute of Medicine [homepage on the Internet]. Washington, DC: Institute of Medicine. [cited 2011 Mar 29]. Tuberculosis in the workplace. http://books.nap.edu/openbook.php?record_id=10045
8. Menzies D, Joshi R, Pai M. Risk of tuberculosis infection and disease associated with work in health care settings. Int J Tuberc Lung Dis. 2007;11(6):593-605.
9. Raitio M, Tala E. Tuberculosis among health care workers during three recent decades. Eur Respir J. 2000;15(2):304-7.
10. Centers for Disease Control and Prevention [homepage on the Internet]. Atlanta: Centers for Disease Control and Prevention. [cited 2011 Mar 29]. Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005. [Adobe Acrobat document, 147p.] Available from: http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf
11. Torres Costa J, Silva R, Sá R, Cardoso MJ, Nienhaus A. Results of five-year systematic screening for latent tuberculosis infection in healthcare workers in Portugal. J Occup Med Toxicol. 201026;5:22.
12. de Vries G, Sebek MM, Lambregts-van Weezenbeek CS. Healthcare workers with tuberculosis infected during work. Eur Respir J. 2006;28(6):1216-21.
13. Diel R, Seidler A, Nienhaus A, Rüsch-Gerdes S, Niemann S. Occupational risk of tuberculosis transmission in a low incidence area. Respir Res. 2005;14;6:35.
14. Hill A, Burge A, Skinner C. Tuberculosis in National Health Service hospital staff in the west Midlands region of England, 1992-5. Thorax. 1997;52(11):994-7.
15. Manangan LP, Bennett CL, Tablan N, Simonds DN, Pugliese G, Collazo E, et al. Nosocomial tuberculosis prevention measures among two groups of US hospitals, 1992 to 1996. Chest. 2000;117(2):380-4.
16. Menzies D, Fanning A, Yuan L, FitzGerald JM. Hospital ventilation and risk for tuberculous infection in Canadian health care workers. Canadian Collaborative Group in Nosocomial Transmission of TB. Ann Intern Med. 2000;133(10):779-89.
17. Greenaway C, Menzies D, Fanning A, Grewal R, Yuan L, FitzGerald JM, et al. Delay in diagnosis among hospitalized patients with active tuberculosis--predictors and outcomes. Am J Respir Crit Care Med. 2002;165(7):927-33.
18. Whalen CC. Diagnosis of latent tuberculosis infection: measure for measure. JAMA. 2005;293(22):2785-7.
19. Colditz GA, Brewer TF, Berkey CS, Wilson ME, Burdick E, Fineberg HV, et al. Efficacy of BCG vaccine in the prevention of tuberculosis. Meta-analysis of the published literature. JAMA. 1994;271(9):698-702.
20. Rodrigues LC, Diwan VK, Wheeler JG. Protective effect of BCG against tuberculous meningitis and miliary tuberculosis: a meta-analysis. Int J Epidemiol. 1993;22(6):1154-8.
21. Centers for Disease Control and Prevention [homepage on the Internet]. Atlanta: Centers for Disease Control and Prevention. [cited 2011 Mar 29]. Targeted tuberculin testing and treatment of latent tuberculosis infection. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm
22. Torres Costa J, Sá R, Cardoso MJ, Silva R, Ferreira J, Ribeiro C, et al. Tuberculosis screening in Portuguese healthcare workers using the tuberculin skin test and the interferon-gamma release assay. Eur Respir J. 2009;34(6):1423-8.
23. Mack U, Migliori GB, Sester M, Rieder HL, Ehlers S, Goletti D, et al. LTBI: latent tuberculosis infection or lasting immune responses to M. tuberculosis? A TBNET consensus statement. Eur Respir J. 2009;33(5):956-73.
24. Wilkinson KA, Kon OM, Newton SM, Meintjes G, Davidson RN, Pasvol G, et al. Effect of treatment of latent tuberculosis infection on the T cell response to Mycobacterium tuberculosis antigens. J Infect Dis. 2006;193(3):354-9.
25. Heimbeck J. Immunity to Tuberculosis. Arch Internal Med 1928;41:336-42.
26. Horsburgh CR Jr. Priorities for the treatment of latent tuberculosis infection in the United States. N Engl J Med. 2004;350(20):2060-7.
27. Direcção-Geral da Saúde [homepage on the Internet]. Lisboa: Direcção-Geral da Saúde. [cited 2011 Mar 29]. Tuberculose: Ponto da Situação em Portugal em 2006, dados preliminares em Março de 2007. [Adobe Acrobat document, 4p.] Available from: http://www.dgs.pt/upload/membro.id/ficheiros/i009162.pdf
28. Mori T, Sakatani M, Yamagishi F, Takashima T, Kawabe Y, Nagao K, et al. Specific detection of tuberculosis infection: an interferon-gamma-based assay using new antigens. Am J Respir Crit Care Med. 2004;170(1):59-64.
29. Diel R, Loddenkemper R, Nienhaus A. Evidence-based comparison of commercial interferon-gamma release assays for detecting active TB: a metaanalysis. Chest. 2010;137(4):952-68.
30. Diel R, Loddenkemper R, Niemann S, Meywald-Walter K, Nienhaus A. Negative and Positive Predictive Value of a Whole-Blood Interferon-{gamma} Release Assay for Developing Active Tuberculosis: An Update. Am J Respir Crit Care Med. 2011;183(1):88-95.

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