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Original article

Infecção latente pelo *Mycobacterium tuberculosis* em trabalhadores da saúde na Bahia

Latent Infection by Mycobacterium tuberculosis in health Workers in Bahia, Brazil

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RESUMO

Objetivo: Estimar a prevalência de positividade do Teste Tuberculínico (TT) no rastreamento da infecção latente pelo *Mycobacterium tuberculosis* (ILTB) e identificar fatores associados entre trabalhadores da Atenção Primária à Saúde (APS) e média complexidade no segundo maior município do Estado da Bahia. **Métodos:** Inquérito epidemiológico, com 370 participantes, que avaliou dados sociodemográficos, ocupacionais, consumo de tabaco, álcool e variáveis relacionadas à tuberculose (TB), no período de abril/2021 a março/2022. Aplicou-se o TT por via intradérmica, com leitura após 72h. **Resultados:** A prevalência de positividade do TT foi de 41,3% e 17,6% para TT ≥ 5mm e TT ≥ 10mm, respectivamente. Para TT ≥ 5mm, as variáveis associadas foram: possuir cicatriz da vacina Bacilo Calmette-Guérin (BCG) e contato prévio com pessoas com TB. **Conclusão**: A prevalência de positividade do TT foi elevada entre os participantes do estudo. Fazem-se necessárias medidas de proteção ambiental, coletiva e individual para redução do risco de ILTB.

PALAVRAS-CHAVE: Trabalhadores da Saúde. Tuberculose latente. Teste Tuberculínico. Tuberculose.

ABSTRACT

Objective: To estimate the prevalence of tuberculin test (TT) positivity in screening for Latent Mycobacterium tuberculosis Infection (LTBI) and to identify associated factors in Primary Health Care (PHC) and medium complexity workers in the second largest municipality in the State of Bahia, Brazil. **Methods:** Epidemiological survey with 370 workers on sociodemographic and occupational data, tobacco and alcohol use and variables related to Tuberculosis (TB), during April 2021 and March 2022. TT was applied intradermally, with reading after 72 hours. **Results:** The prevalence of positive TT was 41.3% and 17.6% for TT ≥ 5mm and TT ≥ 10mm, respectively. For TT ≥ 5mm, the associated variables were: presence of Bacillus Calmette-Guérin (BCG) vaccine scar and previous contact with TB patients. **Conclusion:** The prevalence of TST positivity was high among study participants. Environmental, collective and individual protection measures are necessary to reduce the risk of LTBI.

KEYWORDS: Health Personnel. Latent Tuberculosis. Tuberculin Test. Tuberculosis.

INTRODUÇÃO

Tuberculosis (TB) is a preventable and curable airborne infectious disease caused by Mycobacterium tuberculosis, which still has high incidence and mortality rates in Brazil and worldwide [1]. In 2022, the World Health Organization (WHO) estimated that 10.6 million people developed active TB and there were 1.3 million deaths from the disease worldwide [2].

Brazil is among the 30 countries that concentrate more than 80% of the global incidence of the disease. It is also on the list of priority countries for TB control and TB/HIV co-infection [3]. In 2022, Brazil registered an incidence of 38.0 TB cases/100,000 inhabitants and 2.72 TB deaths/100,000 inhabitants [4] and together with other BRICS countries (Brazil, Russia, India, China and South Africa) account for around 50% of the world's TB cases [5].

In 2015, WHO launched the End TB Strategy, which aims to reduce TB cases by 90%, deaths by 95% and eliminate the economic catastrophic costs for families affected by the disease up to 2035, compared to 2015 [6]. TB transmission is influenced by demographic factors such as increasing urbanization, social factors (precarious and overcrowded housing, food insecurity) and economic factors (inequality in income distribution), and is one of the most prevalent diseases among people living in poverty in the world. The most vulnerable population groups to TB include people deprived of liberty, the indigenous population, people with HIV/AIDS and Healthcare Workers (HCWs) [7].

When a healthy person is exposed to Mycobacterium tuberculosis, they have an approximate 30% chance of becoming infected, as there are related factors such as degree of exposure, infectivity and individual immunological factors that corroborate the onset and establishment of the infection. The Latent Infection by Mycobacterium tuberculosis (LTBI) occurs when the infected individual does not manifest active disease and can remain healthy for many years, without transmitting the bacillus and with partial immunity [7,8]. The risk of developing active TB is greatest in the first two years after primary infection, but it can occur at any time during life. WHO estimates that around a quarter of the world's population has LTBI [2].

HCWs are individuals who work in health care and surveillance services, such as hospitals, clinics, outpatient clinics and health departments, including those who provide direct health care services such as doctors, nurses, nursing technicians, nutritionists, physiotherapists, pharmacists, psychologists, teachers and health students in health services, Community Healthcare Workers (CHWs), Endemic Disease Control Agents (EDCs), administrative employees, including receptionists and security guards, and supportive service workers including the cleaning staff, doorman, stretcher-bearers and cooks [1].

Due to continuous exposure to different occupational risks, HCWs may be at greater risk

and/or vulnerability to ILTB, the occurrence of which may be related to length of exposure at work, delay in diagnosing the infection, type of work activity, professional category, absence or scarcity of Personal Protective Equipment (PPE), besides environmental and administrative control measures [9-13]. HCWs illness is worrying because, as well as the possibility of developing and transmitting TB, it also involves a reduction in the number of human resources in health services, compromising the quality of care, especially in the Unified Health System (SUS) [1,13,14].

This study aimed to estimate the prevalence of positive tuberculin skin test (TST) results for LTBI screening and to verify the association between TST positivity, sociodemographic and occupational characteristics, tobacco and alcohol consumption and variables related to TB in HCWs in Primary Health Care (PHC) and medium-complexity health care services in the second largest municipality in the state of Bahia, Brazil.

METHODS

Study design

This is a survey with a sample of workers of the public healthcare network in the municipality of Feira de Santana, Bahia, Brazil, with an area of 1,304 km^2 and a population of 616,279 inhabitants [15.] Participants were recruited and interviewed at their workplace from April 2021 to March 2022. HCWs working in urban and rural areas were included.

Sampling

In calculating the sample size, the study adopted the following criteria: the total population of 2,257 HCWs, outcome proportion equal to 50% (to maximize the sample size, since it estimates the highest possible N), error of 3% and confidence level of 95%. The estimated sample was 942 HCW. Due to low adherence of the participants to the TT, a final sample of 370 HCWs was obtained.

HCWs were stratified by level of service complexity and occupational groups. The participation in the sample composition (number of people studied in each stratum) corresponded to the percentage participation of the groups in the target population. This strategy sought to ensure that groups with a smaller number were represented in the sample in a similar proportion to the total population. The stratified random sample was selected according to the following procedures: 1. Obtaining and organizing the list (provided by the Municipal Health Department)

of all HCWs according to the services and occupational group (strata of study interest); 2. Definition of the sample size and calculation of the percentage participation according to the established strata; 3. Selection, by a list of random numbers, of the HCW to be studied; 4. Contact with selected HCWs, interview and testing for LTBI in the workplace.

Data collection

The questionnaire was structured based on sociodemographic variables (gender, age, skin color/ethnicity and schooling); tobacco and alcohol consumption; work related variables (professional category, working time in current occupation, working hours, PPE availability in the workplace, contact with biological material at work, work in a high-risk biological environment, participation in training at work and variables about TB (previous vaccination with BCG - Bacillus Calmette-Guérin, BCG vaccine scar, previous contact in the last two years with people with active TB).

PPD-RT23® (Purified Protein Derivative, State Serum Institute, Copenhagen, Denmark) was used, with two tuberculin units (2UT) at a dose of 0.1ml administered intradermally in the middle third of the anterior surface of the left forearm. The TST reading was taken 72 hours after application, measuring the largest transverse diameter of the area of palpable induration with a transparent millimeter ruler, with a reading greater than or equal to 5mm being considered positive [7].

Individuals who tested positive for HIV, those who had received previous treatment for LTBI or had been diagnosed with active TB and pregnant women were excluded from the study. The TST was administered and read according to WHO and the Brazilian Ministry of Health guidelines, by trained professionals at a municipal TB treatment reference unit, following standardized procedures in the Brazilian Manual of Recommendations for Tuberculosis Control and the Brazilian Protocol for LTBI Surveillance [7,8].

To reduce loss of participants, up to three visits were made to the workplace on different days, shifts and at different times. In cases where a worker was not present at the time of the visit or refused to take part, another worker with similar characteristics (same health service, occupational group and gender as the one drawn) was invited to take part instead.

Data analysis

The study variables were described using proportions (%). The prevalence of TST positivity was estimated considering positive results for two different TST cut-off points (≥ 5mm and ≥ 10mm), with 95% confidence intervals (95%CI). The chi-square test was used to analyze

bivariate associations, with a significance level of 5% ($p<0.05$). All analyses were carried out using the SPSS® 22.0 statistical package.

LTBI testing is recommended during HCWs work admission and annual examinations. In this group, a positive result is considered when the diameter of the induration is greater than or equal to 10mm, except in the presence of comorbidities such as HIV infection, diabetes mellitus or use of immunosuppressive drugs. In these situations, results greater than or equal to 5 mm are considered positive [7]. In this study, the analyses were carried out for both cut-off points.

Ethics

This study is part of the research project "Surveillance and monitoring of infectious diseases among workers in the health sector" approved by the Research Ethics Committee of the State University of Feira de Santana, Bahia, Brazil (Opinion n.º 4.088.070; CAAE n.º 90204318.2.0000.0053CAAE: 2.897062). All participants signed an informed consent form.

RESULTS

The prevalence of TST positivity among the 370 HCWs included in the study, considering the TST ≥ 5mm and TST ≥ 10mm cut-off points, was 41.3% (95%CI: 36.4-46.5) and 17.6% (95%CI: 14.0-21.8), respectively. The majority of participants was female (84.6%), with a mean age of 44 years, brown skin color (59.7%) and no higher education (53.6%). As for lifestyle habits, the majority did not report smoking (78.1%); however, there was a predominance of positive results for both TST cut-off points among smokers compared to non-smokers. In addition, 63.1% (227/360) did not drink alcohol. Associations between sociodemographic variables and TST positivity were not statistically significant (Table 1).

Table 1 – Sociodemographic and lifestyle habits characteristics by healthcare workers (HCWs) in the municipality of Feira de Santana, State of Bahia, Brazil, 2021-2022

Variables	Frequency	TST ≥ 10mm		TST ≥ 5mm	
		TST+	p-value	TST+	p-value
	n (%)	n (%)		n (%)	
Sex (n=370)					
Female	313(84.6)	57(18.2)	0.446	131(41.8)	0.646
Male	57(15.4)	8(14.0)		22(38.6)	
Age group in years (n=370)					
18-29	25(6.8)	2(8.0)	0.201	7(28.0)	0.349
30-39	86(23.2)	11(12.8)		32 (37.2)	
40-49	148(40.0)	32 (21.6)		64 (43.2)	
50 or more	111(30.0)	20 (18.0)		50 (45.0)	
Use of tobacco (n=345)					
No	289(78.1)	53(18.3)		122(42.2)	
Yes	18(4.9)	5(27.8)	0.416	8(44.4)	0.438
Former smoker	10(3.7)	5(13.2)		12(31.6)	
Use of alcohol (n=360)					
No	227(63.1)	41(18.1)	0.714	57(42.7)	0.606
Yes	133(36.9)	22(16.5)		91(40.1)	
Ethnicity/Skin color *(n=370)					
Mixed/Brown	221(59.7)	39(17.6)	0.150	90(40.7)	
Black	116(31.3)	24(20.7)		52(44.8)	0.475
Other**	33(9.0)	2(6.1)		11(33.3)	
Level of education (n=364)					
Did not complete high school	195(53.6)	33(16.9)	0.835	76(39.0)	0.482
Completed high school	169(46.4)	30(17.7)		72(42.6)	
Use of tobacco (n=345)					
No	289(78.1)	53(18.3)		122(42.2)	
Yes	18(4.9)	5(27.8)	0.416	8(44.4)	0.438
Former smoker	10(3.7)	5(13.2)		12(31.6)	
Use of alcohol (n=360)					
No	227(63.1)	41(18.1)	0.714	57(42.7)	0.606
Yes	133(36.9)	22(16.5)		91(40.1)	

Note: in the variables analyzed, the numbers vary due to loss of information; TST: Tuberculin skin test; *Self-reported skin color. **Other: White/ yellow / indigenous

Source: prepared by the authors

CHWs (30.7%; 113/368) and technical professionals (21.5%; 79/368) were the most common occupations among the study participants. However, support service workers (50.0%)

and ACEs (22.5%) had a higher frequency of TT positivity at the TT ≥5mm and TT ≥10mm cut-off points, respectively. Regarding time in the job, the majority of study participants (62.4%) reported more than 10 years in the job and this group had a higher frequency of TT positivity at both cut-off points, TT ≥5mm (42.4%) and TT ≥10mm (19.1%). The majority worked 40 hours or more per week (79.0%) (Table 2).

Table 2 - Occupational variables associated with TST positivity in healthcare workers (HCWs) in the municipality of Feira de Santana, State of Bahia, Brazil, 2021-2022

Variables	Frequency	TST ≥ 10mm		TST ≥ 5mm	
		TST+	p-value	TST+	p-value
	n (%)	n (%)		n (%)	
Occupation (n=368)					
CHW	113(30.7)	20(17.7)	0.744	47(41.6)	0.776
Health technicians	79(21.5)	13(16.5)		33(41.8)	
Healthcare providers	66(17.9)	12(18.2)		29(43.9)	
EDC agents	49(13.3)	11(22.5)		19(38.8)	
Administrative employees	41(11.2)	4(9.8)		13(31.7)	
Support services workers*	20(5.4)	4(20.0)		10(50.0)	
Working time in current occupation (n=370)					
≤ 10 years	139(37.6)	21(15.1)	0.335	55(39.6)	0.589
> 10 years	231(62.4)	44(19.1)		98(42.4)	
Weekly working hours (n=361)					
20-36 hours	76(21.0)	11(14.5)	0.403	36(47.4)	0.204
40 hours or more	285(79.0)	53(18.6)		112(39.3)	
Contact with biological material (n=355)					
Yes	204(57.5)	33(16.2)	0.457	85(41.7)	0.909
No	151(42.5)	29(19.2)		62(41.1)	
Working in a high-risk environment (n=312)					
Yes	246(78.8)	47(19.1)	0.865	100(40.7)	0.630
No	66(21.2)	12(18.1)		29(43.9)	
Availability of PPE at workplace (n=304)					
Yes	175(57.6)	32(18.3)	0.781	68(38.9)	0.142
No	129(42.4)	22(17.0)		61(47.3)	
Received on-the-job training (n=304)					
Yes	212(58.1)	42(19.8)	0.239	97(45.7)	0.061
No	153(41.9)	23(15.0)		55(36.0)	

Note: in the variables analyzed, the numbers vary due to loss of information; Definition of abbreviations: ACS: Community Health Agent. PPE: Personal Protective Equipment *Support service: receptionists. security guards. cleaning staff. porters. stretcher-bearers and cooks.

Source: prepared by the authors

We found that 94.2% of the HCWs reported having been vaccinated with BCG, and 91.1% had a vaccination scar. In addition, 76.7% reported no previous contact with people with TB in the last 2 years and 94.7% had never previously undergone TST. The bivariate analysis showed that, at the TST ≥ 10mm cut-off point, no variable analyzed was associated with TST positivity. For the TST ≥ 5mm cut-off point, the presence of a BCG vaccine scar (p=0.009) and previous contact with people with TB in the last two years (p=0.027) were statistically associated with a higher frequency of TST positivity (Table 3).

Table 3 – TB-related variables associated with TST positivity in healthcare workers (HCWs) in the municipality of Feira de Santana, State of Bahia, Brazil, 2021-2022

Variables	Frequency	TST ≥ 10mm		TST ≥ 5mm	
		TST+	p-value	TST+	p-value
	n (%)	n (%)		n (%)	
BCG vaccination (n=326)					
Yes	307(94.2)	57(18.6)	0.762	129(42.0)	0.647
No	19(5.8)	3(15.8)		9(47.4)	
BCG scar (n=302)					
Yes	275(91.1)	55(20.0)	0.111	122(44.4)	0.009
No	27(8.9)	2(7.4)		5(18.5)	
Contact with TB patient in the last two years (n=317)					
No	243(76.7)	41(16.9)	0.091	93(38.3)	0.027
Yes	74(23.3)	19(25.7)		39(52.7)	
Previous TST (n=321)					
No	304(94.7)	55(18.1)	0.079	121(39.8)	0.120
Yes	17(5.3)	6(35.3)		10(58.8)	

Note: in the variables analyzed, the numbers vary due to loss of information; Definition of abbreviations: BCG: Bacillus Calmette-Guérin; TT: tuberculin test; TB: tuberculosis.

Source: prepared by the authors

DISCUSSION

In our study, the prevalence of TST positivity among HCWs varied according to the different cut-off points, being highest at the TST ≥ 5mm. In similar studies, TST positivity at this cut-off point ranged from 40.6 to 60.8% [9,11,17,18]. At the TST ≥10mm cut-off point, the results of

the studies ranged from 32 to 60% of TST positivity [5,9,11,16,24]. A study of 394 HCWs conducted in a referral hospital in the state of Pernambuco, Brazil, found similar prevalence rates to our study, with 40.5% for TST ≥ 5mm and 32% for TST ≥ 10mm [9].

The prevalence of TT positivity estimated in our study was lower than that found in other countries which also have a high TB burden. In Bangladesh, a study of 449 HCWs found a prevalence of TST positivity of 54% [22]. A meta-analysis of 20 studies found an overall prevalence of LTBI of 51.5%, ranging from 33.3 to 88.8%[25].

There was also a predominance of females among the positive cases at both TST cut-off points. In general, women seek health services more often, enabling timely diagnosis and treatment of LTBI before it evolves into active TB disease [9,24]. Male individuals are more vulnerable to the occurrence of active TB and some studies have linked higher TST positivity in these individuals to sociocultural factors and biological differences [11,17,18,21,23,26,27].

Tobacco and alcohol consumption are considered as risk factors for TB [7,18]. In our study, there was a higher frequency of TST positivity among smokers at the two cut-off points analyzed. Studies carried out in Brazil have shown that being a smoker or ex-smoker is a risk factor for LTBI [9,20]. Regarding alcohol consumption, at both cut-off points, higher frequencies of TST positivity were recorded among non-alcohol drinkers, unlike a study carried out in China with 529 HCWs, which showed alcohol consumption as a risk factor for LTBI [18,29].

We also found that CHWs had a higher prevalence of TST positivity at the cut-off point ≥ 10mm. These HCWs are permanently in direct contact with the community and may neglect protective measures at work. Support service workers also had a higher frequency of positive results at both TST cut-off points. It is believed that this may be related to working in areas with high exposure and patient turnover, cleaning environments and disposing of waste without the proper use of PPE, as well as low payment and poor socioeconomic conditions [11,17]. A study conducted in Afghanistan with 3,686 HCWs showed a prevalence of LTBI of 35% among administrative and support service workers [17].

Higher education professionals also had a high frequency of TST positivity considering the lower cut-off point, as reported in a study in Vietnam, with a higher prevalence of TST positivity among medical and nursing professionals, workers directly involved in caring for TB patients [28]. This result may also reflect weaknesses in the training of these professionals in the management of TB cases, exposing them even more to the risks of infection. Early diagnosis, timely treatment and the correct use of PPE in the care of suspected and confirmed cases of active TB are therefore of the utmost importance [21].

A higher frequency of TST positivity was also found in participants aged between 40 and 49 years [18,23,24] and 50 years and over [9,18,19,22,29]. A study carried out in Peru found an association between older age and a higher frequency of positive TST results [24]. In addition, HCWs with more

than 10 years of professional experience [9,17,21,29] and working hours of 40 hours [29] also tested positive for LTBI more often, which may be related to permanent exposure at work, scarcity or inadequate PPE use.

Although the majority of HCWs works in high-risk environments and/or comes into contact with biological material, the scarcity or absence of PPE in health services is common [27]. In the abovementioned Peruvian study with 240 participants, 69.9% reported using N95 masks, but only 31.4% used this equipment throughout their working hours [24]. In a study carried out in Brazil, HCWs said they found it difficult to adapt and were even resistant to wearing masks at work, even though they are extremely important for protecting the health of this occupational group [9].

In addition to individual protection measures in health services, administrative and environmental control measures should also be implemented, including adjusting the attending schedules and movement flows of people with respiratory symptoms, prioritizing their care; training health teams to recognize the signs, symptoms, transmissibility and TB preventive measures, highlighting the importance of biosafety measures; encouraging the use and offering of protection masks when caring for patients with coughs and also when the HCW has respiratory symptoms and periodic occupational examinations (admission and periodic) including TST. Regarding environmental control, keeping work environments well ventilated and, when necessary, equipping rooms with exhaust fans, filters or ventilators [1,7,20,21] .

In our study, 100% of the participants reported not having been diagnosed with TB in the past and the majority reported not having had contact with TB patients in the last two years. However, among those who reported this contact, there was a statistically significant association with TST positivity at both cut-off points. In a study carried out in Kenya, with 1,005 participants, those who reported contact with active TB cases were twice as likely to have LTBI [21].

The only vaccine approved in Brazil for TB prevention is BCG, administered in a single dose, preferably at birth or up to 4 years, 11 months and 29 days of age, to protect against more severe forms of TB. In Brazil, BCG vaccination became compulsory in 1976 and is offered free of charge by the Brazilian Unified Health System (SUS) [1]. In our study and in similar studies [9,21,22], the majority of participants reported previous BCG vaccination and there was a statistically significant association with TST positivity.

A study carried out in Bangladesh with 449 HCWs found that among those vaccinated with BGC, the prevalence of TST positivity was 55% [22]. False-positive results for TST are possible among individuals vaccinated (or revaccinated) with BCG after the first year of life and/or when there is exposure to non-tuberculous mycobacteria. However, after 10 years of BCG vaccination, only 1% of positive TTs can be attributed to BCG [7]. Despite this possibility, TST has advantages for the diagnosis of LTBI, including high specificity (97%) and relatively low cost, which facilitates its use in developing countries with socioeconomic problems such as Brazil[1].

It was also possible to observe that most of the studied HCWs had not previously undergone TST, despite the recommendation to investigate LTBI in the admission and annual examinations of HCWs. It was also found that among the individuals who had previously undergone TST, only 5.3% tested positive for both cut-off points. Other factors can also be associated with TST positivity, including household contact with an infected person, comorbidities that cause immunosuppression such as HIV, use of immunosuppressive drugs or working in a high-risk biological environment [7,8,9].

Our study had strengths such as standardization in the application and reading of the TST and the potential to alert municipal managers to the need to carry out this testing periodically among HCWs. The cross-sectional study design is unable to identify causal relationships, and a longitudinal study is the most appropriate way to estimate the frequency of tuberculin conversion among HCWs, i.e., TST positivity 12 months after the previous test, with an increase of at least 6mm, in which case drug treatment is recommended [7]. In addition, the difficulty HCWs have in adhering to repeat TST one to three weeks after the first test made it impossible to assess the booster effect, which is indicated to check for reactivation of the immune response to tuberculin by memory cells, and may be associated with recent BCG vaccination or remote infection with M. tuberculosis, leading to an increase in false-positive rates [7]. Another important limitation refers to the fact that the estimated sample size was not reached, due to low adherence by the HCWs, which may have limited the statistical power to identify associations between exposure variables and the outcome.

In conclusion, this study showed a high prevalence of TST positivity in primary and medium-complexity HCWs. It is therefore necessary to strengthen effective environmental, administrative and individual protection measures to prevent infection in HCWs at high risk of exposure to Mycobacterium tuberculosis or with conditions that predispose to the development of active disease. The importance of carrying out admission and periodic occupational examinations with the TST should be emphasized. These measures are necessary to achieve the goals of global TB elimination, through early diagnosis of cases, including systematic screening and preventive treatment of population groups at high risk of LTBI, when necessary.

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