

Prevalence and Risk of Latent Tuberculosis Infection in Primary Health Care Workers at La Lisa Municipality, Havana, Cuba

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Abstract

Background: Tuberculosis transmission is a risk to health care workers (HCW) **Objectives:** To determine the prevalence of latent tuberculosis infection (LTBI), the annual risk of infection and its possible association with some predictive variables. **Methods:** A cross-sectional study in 1063 HCW at La Lisa municipality policlinics, Havana, was carried out during 2009-2011; a Tuberculin Skin Test (TST) was applied, along with a structured questionnaire exploring general and on exposition data. The reading was performed in 905 HCW at 72 hours, defining as positive ≥ 10 mm induration and tuberculin conversion as ≥ 10 mm increasing in the second TST of those previously negative. To prove the possible influence of predictive variables on the presence of infection, a bivariate analysis and a multivariate model were applied. **Results:** The prevalence of LTBI was 15,2%, with 3,7% of AIR. The highest prevalence in Berovides Policlinic (19,3%) and the lowest in Fernández (10,5%). The highest annual risk of infection was in Labra (6,4%) and the lowest in Fonseca (1%). The variables possibly associated to LTBI were: belonging to Labra and Berovides policlinics, having contact with tuberculosis patients, being ≥ 20 years working there and belonging to the following occupational groups: administrative, nurse, maintenance staff and health technicians. **Conclusions:** The transmission of tuberculosis infection, even in low levels, is possibly associated to the labor environment; so it would be advisable to value the application of preventive chemotherapy in these personnel and to maintain the appropriate measures of infection control in the institutions.

Keywords

Tuberculosis, Latent Tuberculosis Infection, Prevalence, Primary Health Care

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1. Background

Transmission of *Mycobacterium tuberculosis* is a risk in health-care settings. The magnitude of risk varies by setting, occupational group, the prevalence of tuberculosis (TB) in the community, the population served and the effectiveness of TB infection control measures. The risk may be higher in areas where patients are treated before diagnosis and initiation of TB treatment.¹

In Cuba, TB incidence rates are among the lowest in the region. The national crude incidence rate in 2013 was 6,4 per

100 000 population and it has maintained below 7 during the last ten years, with the lowest in 2009 (5,9 per 100 000 population).²

The National TB Control Program (NTCP) takes actions to eliminate the disease as a public health problem, based on a differentiated intervention on the most vulnerable groups of acquiring the disease, including health care workers (HCW).³

Havana is the capital and most densely populated province, with the higher economic importance in Cuba, where main TB generating outbreaks are concentrated. That behavior largely determines the results of the country, notifying about

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a quarter part of the national incidence.²

La Lisa municipality, as part of strengthening of the NTCP, is immersed in an active screening for early detection of TB and other respiratory diseases. Despite this, even 60% of cases are diagnosed in secondary health care level.³ In 2008 the municipality was ranked as high risk in the stratification performed to execute the actions derived of the strengthening of the NTCP funded by The Global Fund.⁴ After that, a decreasing in the incidence from 12 cases during 2009 (8,6 x 100 000 population) to 9 cases during 2010 (6,2 x 100 000) and 6 cases during 2011 (3,9 x 100 000) was observed, with a decrease of about 3 cases per year and 4,7% annual in the incidence rate. (Martínez D. Un-published data)

In Cuba there have been some recent studies evaluating the TB risk in hospital workers of different categories,⁵⁻⁷ but have not been any studies on workers of Primary Health Care level, which is currently diagnosing around 40% of TB cases and gives medical treatment and monitoring to 100% of the cases under Directly Observed Treatment Short-course (DOTS).

As part of the TB risk assessment in HCW from primary health care of La Lisa, in this study the prevalence of latent tuberculosis infection (LTBI), the annual risk of infection and the possible association with predictor variables was determined.

2. Methods

Setting: La Lisa municipality is located at southwest of Havana province; with a geographical area of 37,1 Km². The total population varied from 133,255 inhabitants in 2009 to 133,520 in 2011 and the population density ranged from 3588 inhabitants per km² in 2009 to 3595 in 2011.⁸ It is divided into seven People's Councils (spatial administrative division of the municipal government), that are served by five health areas (territorial health units)⁹: Aleida Fernández, Cristóbal Labra, Elpidio Berovides, Pulido Humarán and Pedro Fonseca.

Design: A cross-sectional study was conducted during the period 2009-2011.

Study population: Of the 1294 HCW available (working at the time of the study), all those who agreed to participate were included once did not have any of the following exclusion criteria: pregnancy, acute infectious disease. The total number of participants was 1063.

Procedures: In 2009 they underwent a Tuberculin Test (TST) and those negative, were tested again a year later to assess tuberculin conversion. The TST was performed according to WHO standard technique¹⁰ by two trained and standardized

nurses, using 2 Tuberculin Units (0.1 ml) of PPD RT-23 from Evans. The reading was performed at 72 hours, considering as positive those indurations ≥ 10 millimeters. Individuals without response (0 mm) were considered as non-reactors, and those with ≥ 15 mm in diameter as hyper-reactors. The increasing in ≥ 10 mm in the second TST in those patients previously negative was considered tuberculin conversion.

In addition, we applied a structured questionnaire to explore the possible association with the presence of infection of the independent variables: age, sex, occupational category (administrative, nurses, doctors, maintenance personnel, services, health technicians and not health technicians), departments, working time in the center, history of contact with TB patients and presence of BCG vaccination scar. The history of contact with TB patients was considered exposure to TB; workers with BCG vaccination scar were considered vaccinated. The departments were grouped into six areas: Medical Family Clinics, Consulting Specialties, Diagnosis and Treatment, Maintenance, Clerk, Services and Leader's cabinets.

Statistical analysis: LTBI prevalence rates for each variable were calculated and homogeneity tests using Kruskal-Wallis for samples and Levene for variances were applied. The induration diameter average was analyzed according to the presence or not of BCG scar, taking into account five categories: nonreactors (0 mm), negative reactors (1-9), negative (0-9), positive (≥ 10 mm) and hyper-reactors (≥ 15 mm). The Annual Risk of Infection (ARI) was estimated using the direct method, by calculating the tuberculin conversion during a year (% of individuals who converted in the second TST up to the total of those negative in the first one).

To test the possible influence of the independent variables on the presence or absence of infection, bivariate analysis between each of the independent covariates and the response variable (presence of infection) using Prevalence Risk Ratio (PRR)¹¹ was initially performed, with reference to the lower prevalence for each covariate. The PRR > 1 was considered significant with CI- 95% and $p < 0.05$.

A multivariate binary logistic regression model by backward method (Wald) was then applied introducing in the model the results with $p < 0.05$ in bivariate analysis. Calculations were performed with the statistical software EpiInfo 2002 (Centers for Disease Control and Prevention, Atlanta, GA, USA), tests of homogeneity in XLSTAT 2009 and logistic regression in SPSS 11.5 (SPSS Inc., Chicago, IL).

Ethical considerations: informed consent from all study participants was obtained. This research was approved by the Ethics Committee of the Pedro Kourí Institute (IPK), Havana, Cuba.

3. Results

Up to 905 read TST, 15.2% were positive. The higher prevalence of reactors was at the Berovides polyclinic (19.3%), and the lowest in Fernández (10.5%), with statistically significant difference between groups ($p = 0.02$). The mean diameter of induration (including non-reactors) was 3.8 mm (SD 5.5) for the municipality, and ranged from 3 mm in Fernández and Fonseca to 5 mm in Berovides; 45.5% were non-reactors, figure ranged from 37.4% in Berovides to 53% in Fonseca. (Table 1)

Most HCW (91.3%) are vaccinated and comparing the results of TST with a history of BCG vaccination (Table 2), no significant differences for non-reactors, nor for total negative or positive were found, including hyper-reactors between vaccinated and unvaccinated.

From 821 workers (90.7%) that were negative, 30 (3.7%) converted to positive in the second TST. The lowest rate of tuberculin conversion was in the polyclinic Fernández (1%) and the highest in Labra (6.4%). (Table 3)

In bivariate analysis of possible factors that might be related to the presence of LTBI in HCW of La Lisa, values for sex, previous BCG vaccination and age were not significantly greater than one, depending groups used to compare these variables. Working in polyclinics Labra (RRP=1.74; $p=0.027$) and Berovides (RRP=1.84; $p=0.017$) were found with a statistically significant RRP, with reference to Fernández which had the lowest prevalence of LTBI. (Table 4)

Workers who reported previous contact with TB cases had a prevalence 2.76 times higher than those who did not report such a contact ($p=0.000$). Also significant was the fact of having been working for more than two years in the primary health care of La Lisa, compared with those who worked less than two years.

The administrative staff (PRR=2.75; $p=0.010$), nurses (PRR=2.62; $p=0.001$), maintenance personnel (PRR=3.50; $p=0.000$), and health technicians (PRR = 2.06; $p=0.023$) had significantly higher prevalence than physicians, occupational group with the lowest prevalence of reactors (7.6%).

Grouping HCW by work areas, PRR was significantly higher in Medical Family Clinics (PRR = 2.38; $p=0.021$) and maintenance workers (PRR=3.91; $p=0.009$) compared with leaders cabinets that had the lowest PRR.

In multivariate analysis, the best model found also included as variables associated with the presence of LTBI: work in the polyclinics Labra and Berovides, referred contact with TB cases, working more than 20 years in the institution, and belonging to the following occupational categories: administrative, nurses, health technicians and maintenance

workers (Table 5).

4. Discussion

The prevalence of LTBI and the tuberculin conversion as measure of ARI in primary health care workers of La Lisa is much lower than that found in some hospitals in the province. However, it was higher than that reported by the municipality in all risk groups.

The transmission of *M. tuberculosis* in primary health care workers may be associated with risk of exposure to patients seen, the prolonged work in this sector and some occupational categories and work areas where workers are more exposed to *Mycobacterium tuberculosis*.

TST was used to diagnose ITBL in this research, because the Interferon Gamma Release Assay (IGRA) is not yet in use by the Cuban NTCP since the high costs of this modern test. Even that, the recently published WHO Guidelines for management of LTBI recommends the use of both test, taking in account the advantage and disadvantage of them.¹²

In this research all TST were performed by two nurses who were kept constant until the end of it, which is a strength that increases the reliability of the results. It is useful to repeat the TST two weeks after the first survey to study the "Booster" phenomenon.¹³ It is a limitation of this study not having made it to those not reactors cases for logistical reasons; but considering that a high cut-off point was used, it is expected that most individuals with reactions due to BCG or non-tuberculous mycobacteria don't react more than 9 mm with the booster.¹⁴

The prevalence of TST reactors among primary health care workers in La Lisa is higher than that found in the risk population surveyed in the municipality during 2009-2011, in which positivity of 6.4% on average has been reported up to the total TST conducted by the NTCP. (Unpublished data: Indicators to Strengthen NCTP, Municipal Unit of Hygiene and Epidemiology, La Lisa, 2010.) They were similar in the five health areas, with values between 5.2% in Labra and 7.3% in Fernández.

During the national research in vulnerable groups, the TST positivity found was 2.9%; while in Havana province and its high-risk municipalities were 3.3 and 5.4% respectively. (Unpublished data: Ministry of Public Health. Indicators of Strengthen PNCTB Cuba, 2010.)

However, both LTBI and tuberculin conversion are well below those reported in hospitals HCW in the province. Pedro Kourí Institute (IPK), also located in La Lisa, has reported LTBI prevalence from 33.5% to 55.2% in HCW, with 14.6% of tuberculin conversion.^{5,15} This is logical

considering that in IPK more than 40 TB patients are hospitalized in average during a year, besides the National TB Reference Laboratory is located inside its facilities. Therefore, the exposure risk is higher to its staff, while in the whole La Lisa municipality were handled only 34 TB cases during the period 2007-2011, averaging 7 cases per year. Desegregating by health areas, this average drops to 1-2 cases per year in Fernández and Humarán, and less than one case in Fonseca. (Unpublished data: Municipal Unit of Hygiene and Epidemiology, La Lisa. Indicators of the National TB Control Program, 2009-2011.)

Another published study of the Pneumology Hospital in Havana, reports 50.8% of LTBI in the staff, with 35.9% of tuberculin conversion, the highest among the studies performed in the country. This is consistent with the higher risk level of exposure to their HCW, as this is the national reference center for the treatment of complicated TB cases.¹⁶

However, our figures are similar to those found in a surgical teaching hospital of Santiago de Cuba with 15.4% of TST reactors in their staff.⁶ Despite this is a provincial hospital, in the lower prevalence of LTBI and tuberculin conversion rate also might influence the TB incidence in the general population, which is lower in Santiago de Cuba province (about 5×10^5) compared with Havana, which contributes about 25% of the country's cases annually and has kept rates above 8×10^5 in the last five years.²

Most LTBI prevalence studies published in the world are in hospital workers, and a systematic review by Joshi R et al. found that the LTBI prevalence in HCW was 54% in average;¹⁷ in another review by Menzies et al. of 42 papers a LTBI prevalence of 63% in low/middle-income countries and 24% in high-income countries was found.¹⁸

Significantly higher were the PRR in two health areas, Berovides and Labra, where more TB cases were treated in the period analyzed (10 cases each), and where only TB cases were found in HCW (one in each polyclinic). Berovides and Labra are the polyclinics that serve the most densely populated areas of the municipality, the council of St. Augustine by Berovides, and the councils Alturas de La Lisa and Versalles-Coronela by Labra.

In this study we found higher LTBI prevalence in maintenance personnel, administrative and nurses, which partially differs from other studies published. Nurses usually are among the highest risk, which is consistent with studies published in both national⁶⁻⁷ and international literature.¹⁹⁻²³ Surprisingly, we found doctors with the lowest prevalence of LTBI, what could be explained because in practice, nursing staff is in daily and close contact with patients on treatment application, while doctors evaluate patients twice a month.

In a study in primary health care workers in Russia a higher positivity was found in nurses (32.8%) and physicians (25.5%), although a high positivity in administrative and other support staff was also found.²⁰ In another study in Portugal a high LTBI positivity in employees with functions that are not supposed to involve risk, as administrative and assistants, was also found.²²

Regarding workspaces, surprisingly, the maintenance personnel, who perform tasks unrelated directly with patients, appears associated with LTBI. Much of maintenance personnel are workers with low educational and social level who could have habits such as alcoholism,²³ which involves greater risk than to healthy people. Furthermore, the higher prevalence in workers with occupations involving less risk may be related to infection in the community or in other health facilities where they have worked before.

However, the areas of diagnosis and treatment were not associated. This may be because in these polyclinics, despite around 2335 sputum smears were tested in 2007-2011, only 0.08% were positive, and both the perception of risk and the implementation of preventive infection control measures are generally higher in these areas.

Another area associated to LTBI was Medical Family Clinics (MFC), where monitoring and strictly supervised care is given to all TB patients, specifically by nurses, which precisely had one of the highest LTBI prevalence, not like that in physicians who had the lowest numbers. It is necessary to note that a large number of doctors and nurses in the MFC have been in internationalist health missions in countries with high TB burden, so it is also possible that many of these nurses have become infected during those stays and no in their MFC.

The incidence of LTBI in HCW is related to TB incidence in the general population of the area. A study published by Vries et al. reported in the Netherlands that 42% had acquired the infection in the hospital, 28% in the community and 30% abroad.²⁴ The risk of infection is more related to the contact proximity to the infection source than with time of exposure.²⁵⁻²⁹

We found association between a very long working time (over 20 years) in the areas and the presence of LTBI, which is consistent with national¹⁶ and international^{21,29} literature reviewed about the influence of prolonged exposure on HCW.

In Cuba, BCG vaccination coverage is nearly 100% at birth, and until 1992 a reactivation dose was applied to 9 years old scholar children³, so it is justified that a high percentage of respondents have BCG scar. Nevertheless, a high percentage of vaccinated were not reactors.

Because the post-vaccination allergy declines over time³⁰⁻³¹,

and in Cuba it was 3-4 mm in children under 15 years more than 30 years ago³²⁻³³, a high cut-off point could provide a high likelihood to differentiate with minimal error, a large proportion of natural allergies (including cross non-tuberculosis mycobacterial infections) an post-vaccination allergies.

In a compilation of international data of 1980-2005 on the effect of BCG vaccination on TST results in general population found a mediocre performance of TST in people of all ages and from vaccinated countries with low TB incidence³⁴, but it was a good way of detecting LTBI in vaccinated adults from countries with intermediate and high incidence of TB. However, a recent study in Sweden³⁵ on health students, the specificity of TST with different cut-offs points were estimated, and for ≥ 10 mm this was 97.5%, while for ≥ 15 mm was 99.3%.

In our study, despite most workers are vaccinated, no difference for both cut-offs points (≥ 10 and ≥ 15 mm) between vaccinated and unvaccinated were found, and BCG vaccination was not predictor of tuberculosis infection in multivariate analysis, reinforcing the idea that using a high

cut-off point does differentiate infected from uninfected. More than 30 years have elapsed since BCG vaccination for most of the HCW studied. Taking in account that BCG only protect against severe TB in infants, this protection is no longer active for the studied population.

In conclusion, the prevalence of Latent TB Infection and the Annual Risk of Infection in Primary Health Care workers of La Lisa are higher in areas where more cases of TB are served, but lower than in other health care levels in Havana province. The transmission of tuberculosis infection in workers of Primary Health Care in La Lisa, although at low levels, is possibly associated with the work environment, so we suggested assessing the implementation of preventive chemotherapy to the infected personnel at higher risk and maintaining appropriate infection control in the institutions. Even that is recommended by the NTCP³, infection control and TB surveillance plans in HCW at primary health care are not yet applied. This should be a priority to implement by the NTCP in the next years to reach the TB elimination as is planned.

Table 1. Results of the tuberculin survey in Health Care Workers of five Primary Health Care Areas at La Lisa Municipality, 2009-2011.

Health Areas	N	No reactors (PDT=0 mm)		positive TST (≥ 10 mm)		Induration	
		n	%	n	%	Mean	ED
Aleida Fernández	191	99	51.8	20	10.5	3.0	4.5
Cristóbal Labra	208	96	46.2	38	18.3	4.1	5.9
Elpidio Berovides	171	64	37.4	33	19.3	5.0	7.0
Pulido Humarán	220	92	41.8	33	15.0	3.7	4.9
Pedro Fonseca	115	61	53.0	14	12.2	3.0	4.7
Municipality	905	412	45.5	138	15.2	3.8	5.5

Source: Surveys performed.

Table 2. Distribution of induration diameter according to BCG scar presence in Health Care Workers of five Primary Health Care Areas at La Lisa Municipality, 2009-2011.

Diameter average (mm)	With BCG Scar		Without BCG Scar		Total		P values
	No.	%	No.	%	No.	%	
0	350	24.2	29	21.2	379	23.9	0.42
1 a 9	282	19.5	31	22.6	313	19.8	0.37
0 a 9	632	43.7	60	43.8	692	43.7	0.98
≥ 10	124	8.6	11	8.0	135	8.5	0.82
≥ 15	58	4.0	6	4.4	64	4.0	0.83
Total	756	91.4	71	8.6	827	100.0	

Source: Surveys performed.

Table 3. Tuberculin Conversion in Health Care Workers of five Primary Health Care Areas at La Lisa Municipality, 2009-2011.

Health areas	Previous TST negative	Tuberculin Conversion	
		n	%
Aleida Fernández	183	7	3.8
Cristóbal Labra	188	12	6.4
Elpidio Berovides	149	3	2.0
Pulido Humarán	197	7	3.6
Pedro Fonseca	104	1	1.0
Municipality	821	30	3.7

Source: Surveys performed
TST- Tuberculin Skin Test.

Table 4. Risk factors associated to LTBI (TST positive defined as ≥ 10 mm) in Health Care Workers of five Primary Health Care Areas at La Lisa Municipality, 2009-2011: Bivariate analysis.

Variables		TST positive	%	TST negative	%	PRR	P value
Health Areas	A. Fernández	20	10.5	171	89.5	Reference	
	C. Labra	38	18.3	170	81.7	1.74	0.027
	E. Berovides	33	19.3	138	80.7	1.84	0.172
	P. Humarán	33	15.0	187	85.0	1.43	0.646
	P. Fonseca	14	12.2	101	87.8	1.16	
Sex	Male	20	13.0	134	87.0	Reference	
	Female	117	15.6	634	84.4	1.20	0.413
BCG scar	Yes	123	16.3	632	83.7	1.05	0.861
	No	11	15.5	60	84.5	Reference	
TB Contact	Yes	11	42.3	15	57.7	2.76	0.000
	No	122	15.3	673	84.7	Reference	
Age (years)	16-49	106	14.5	624	85.5	Reference	
	50-59	31	19.7	126	80.3	1.36	0.100
	≥ 60	0	0.0	17	100.0		
	≤ 2	19	8.3	209	91.7	Reference	
Working time (years)	3-5	36	16.5	182	83.5	1.98	0.013
	6-10	45	16.8	223	83.2	2.01	0.007
	11-20	23	15.3	122	84.7	1.90	0.038
	> 20	15	31.9	32	68.1	3.83	0.000
	Administrative	10	20.8	38	79.2	2.75	0.010
Occupational Category	Nursing	39	19.9	157	80.1	2.62	0.001
	Physicians	11	7.6	134	92.4	Reference	
	Maintenance	17	26.6	47	73.4	3.50	0.000
	Services	17	11.3	134	88.7	1.48	0.281
	Health Technics	34	15.6	184	84.4	2.06	0.023
	No health Technics	9	10.8	74	89.2	1.43	0.403
	MFC	29	19.3	121	80.7	2.38	0.021
	Specialized medical office	14	15.2	78	84.8	1.87	0.144
	Diagnostic y Treatment	39	15.9	206	89.1	1.96	0.073
	Working areas	Maintenance	7	31.8	15	68.2	3.91
Office workers		8	8.8	83	91.2	1.08	0.876
Services		34	15.5	185	84.5	1.91	0.089
Leaders cabinets		7	8.1	79	91.9	Reference	

Source: Surveys performed.

TST- Tuberculin Skin Test, MFC- Medical Family Clinics.

Table 5. Risk factors associated to LTBI (TST positive defined as ≥ 10 mm) in Health Care Workers of five Primary Health Care Areas at La Lisa Municipality, 2009-2011: Multivariate analysis.

Variable	p-values	OR	C.I. 95,0% OR
Polyclinic C. Labra	0.027	2.04	1.1-3.8
Polyclinic E. Berovides	0.003	2.62	1.4-5.0
TB contact	0.001	4.62	1.9-11.2
Working time > 20 years	0.011	8.52	1.6-44.1
Administrative	0.003	4.70	1.7-12.9
Nursing	0.002	3.24	1.5-6.8
Health Technics	0.021	2.48	1.1-5.3
Maintenance staff	0.000	5.82	2.4-13.9

Source: Surveys performed.

OR: Odds Ratio , CI: Confidence Interval

Abbreviations

ARI: Annual Risk of Infection

DOTS: Directly Observed Therapy Short-Course

HCW: Health Care Workers

IPK: Pedro Kouri Institute

LTBI: Latent Tuberculosis Infection

NTCP: National Tuberculosis Control Program

TB: Tuberculosis

TST: Tuberculin Skin Test

MFC: Medical Family Clinics

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