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High prevalence and risk factors associated with latent tuberculous infection in two Colombian prisons

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SUMMARY

SETTING: Two prisons in Medellín and Itagüí, Colombia.

OBJECTIVE: To determine the prevalence of tuberculin skin test (TST) positivity in prisoners and the annual risk of tuberculous infection (ARTI), to identify risk factors associated with a positive result, and to describe progression to active disease.

DESIGN: Cross-sectional study. Inmates were included if time of incarceration was ⩾1 year and excluded if subjects had had previous or active tuberculosis (TB), or conditions that could hamper TST administration or interpretation.

RESULTS: We screened 1014 inmates. The overall prevalence of TST positivity was 77.6%. The first TST administration resulted in 66% positivity, and the second TST an additional 11.6%. In Prison One, the ARTI was 5.09% in high TB incidence cell blocks and 2.72% in low TB incidence blocks. In Prison Two, the ARTI was 2.77%. Risk factors associated with TST positivity were history of previous incarceration and length of incarceration. Among all those included in the study, four individuals developed active pulmonary TB.

CONCLUSION: Prevalence of TST positivity in prisoners and the ARTI were higher than in the general population, but differed between prisons; it is important to apply a second TST to avoid an overestimation of converters during follow-up.

KEY WORDS: latent tuberculous infection; tuberculin test; prisons; prevalence; risk factors

LATENT TUBERCULOUS INFECTION (LTBI), defined as infection with *Mycobacterium tuberculosis*, manifests as pre-defined tuberculin skin test (TST) reaction and/or as a positive interferon-gamma release assay (IGRA) test result with no clinical or radiological evidence of active disease.[1] The median estimated annual incidence rate ratio for LTBI in six prisons in the United States and one prison in Brazil was 26.4 compared to the general population.[2] Diagnosis of LTBI is important to initiate preventive treatment and reduce the risk of developing active tuberculosis (TB), benefiting both infected and susceptible inmates inside prisons. The incidence of recent TST conversion reported in Maryland prisons was 6.3 per 100 person-years; the use of broader coverage levels of isoniazid (INH) prophylaxis reduced the risk of infection by 50%.[3]

Two methods are used to detect LTBI, the TST and IGRAs; however, both are imperfect.[4–7] In developing countries, the use of TST is not often recommended for three main reasons: the priority for TB control programmes in these areas is to detect and treat infectious cases, the prevalence of TB disease is high, and bacille Calmette-Guérin (BCG) vaccination is used extensively.[1,8–11] The role of IGRA in the early detection of LTBI is controversial due to within-subject test result variability,[5] and the fact that IGRA conversion is not associated with any indicator of recent infection or exposure and may thus represent unexplained variability on serial testing.[6] Prisons in Colombia do not apply TST at the time of entry into prison, IGRA is available for research purposes only, and in the local guidelines the treatment of LTBI is not recommended for immunocompetent adults.

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Pai et al. recently suggested that to maximise the positive predictive value of existing tests, LTBI screening should be reserved for those who are at sufficiently high risk of progressing to active disease.[12] Prison inmates are considered a high-risk population due to high TB incidence, with the overcrowding, close contact with infectious TB and other risk factors for progression to active TB disease that are more common among prisoners. The annual risk of tuberculous infection (ARTI) reported in New South Wales, Australia, among those detained continuously between 1996 and 2001 was 3.1%, while among recidivists it was 2.7%,[13] in contrast to the general population (0.04%).[14] In Cali, Colombia, the ARTI during the 1970s, 1980s and 1990s was respectively 1.24%, 0.93% and 0.85% in the general population.[15]

With the high risk of TST conversion and progression to active TB, and the significant overcrowding in the Colombian prison system, we sought to estimate the prevalence of positive TST and ARTI in two prisons in Colombia. We also wanted to identify risk factors associated with a positive TST, and to describe progression to active TB to identify individuals most likely to become infectious and to prioritise diagnostic and preventive measures for those most at risk.

STUDY POPULATION AND METHODS

Study settings

This was a cohort study conducted between 26 November 2012 and 10 December 2013 in two male prisons in Medellin (prison capacity 2424, maximum number incarcerated 7585) and Itagui (prison capacity 328, maximum number incarcerated 749).

Inclusion criteria

At the time of enrolment, eligible participants were projected to remain in the prison for at least 1 more year to allow for follow-up; individuals voluntarily agreed to participate in the study and provided signed consent.

Exclusion criteria

Exclusion criteria were as follows: previous or current active TB, severe adverse event with previous TST administration, immunosuppressive treatment and administration of live vaccines (measles, mumps and rubella, varicella or the live attenuated influenza vaccine) in the 4 weeks before TST application.

Sample and selection of participants

Due to the high number of prisoners incarcerated in Prison One, we screened those confined in cell blocks with high ($\geqslant$300 cases/100 000 prisoners) and low (0 cases/100 000 prisoners) TB incidence. In Prison Two, we screened those incarcerated in the maximum-security cell blocks.

Procedures

Two nurses visited the selected block cells in each prison from Monday to Friday during the study period and identified individuals who met the inclusion criteria. The information was collected for all individuals as previously described.[16] The TST (tuberculin purified protein derivative RT-23, 2 tuberculin units/0.1 ml, Statens Serum Institut, Copenhagen, Denmark) was administered according to US Centers for Disease Control and Prevention (CDC) recommendations.[17] Reading was performed within 48–72 h of administration and measured and recorded in mm induration. A second TST was applied in the case of a negative result in the first application.

To evaluate inter-reader agreement, two nurses read the TST result for the same 75 patients. Each nurse was randomly assigned the order of TST reading for each patient. The inter-reader variability of results had an intra-class coefficient correlation of 0.97 (95% confidence interval [CI] 0.96–0.98), with a mean difference between two readers of 0.813 ± 0.811.

A positive result was defined as an induration of $\geqslant$10 mm diameter for non-human immunodeficiency virus (HIV) infected persons, and $\geqslant$5 mm for HIV-infected subjects. To account for inter-observer variation for the TST with a standard deviation (SD) of 0.811, we took a 2 SD difference in reading as representing true variation between the first and second reading. Based on this definition a $\geqslant$10 mm induration and an increase of $\geqslant$2 mm between the first and second application was deemed a positive test.

Individuals were followed for a year to observe whether they developed active TB. The health care service at each prison used sputum smear microscopy for the diagnosis of pulmonary TB. HIV testing was not performed, as the HIV prevalence in four prisons recently studied was 2.1%.[16]

Ethics statement

Approval for the study was obtained from the Ethics Committee of the Facultad Nacional de Salud Pública, the Universidad de Antioquia, the Instituto Nacional Penitenciario y Carcelario (INPEC), and the director of each prison. Written consent forms were explained and signed in the presence of two witnesses (prisoners).

Analysis

We estimated the overall point prevalence of a positive TST, and stratified the results by prison. To determine factors associated with a positive TST result, we performed a bivariate analysis to estimate the prevalence ratio (PR) and the 95%CI. Any variables with a P value < 0.25, as well as the presence of BCG scar, were included in a binomial regression. The PR and 95%CIs are reported and adjusted for age, previous incarceration, period of

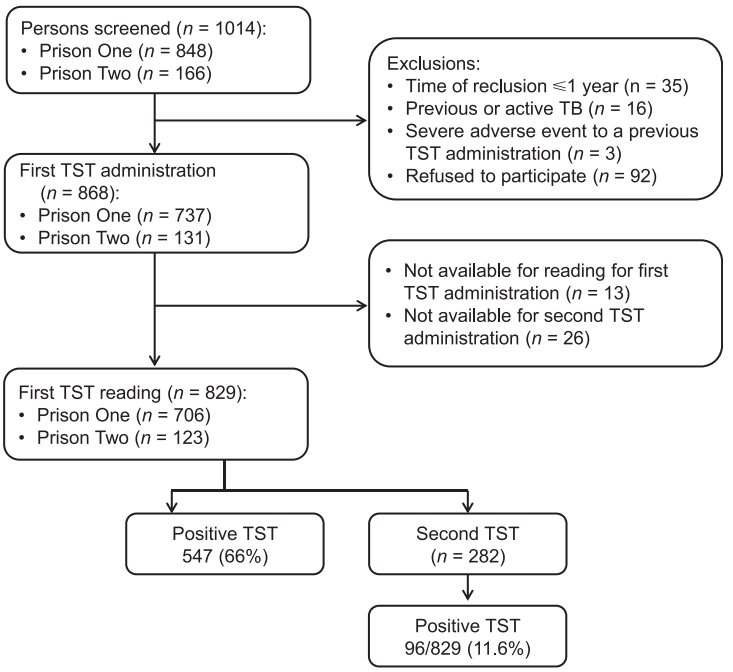

Figure Flow chart of persons screened and included in the study. TB = tuberculosis; TST = tuberculin skin test.

current incarceration, contact with a TB case and BCG scar. As we found a difference in the prevalence of a positive TST result between the two prisons, standard errors were adjusted by the cluster effect for each prison for bivariate and multivariate analyses. Finally, the ARTI was estimated using the formula $R = 1–(1–P)^{1/a}$, where P is the prevalence of positive TST, and a is the mean age of the cohort.[18] Analyses were performed using STATA®, version 11.0 (Stata Corp, College Station, TX, USA) and SPSS®, version 20.0 software (Statistical Product and Service Solutions, Chicago, IL, USA).

RESULTS

Among 8334 prisoners, 1014 were screened and 829 were included in the study; 66% were TST-positive in the first test (97.3% read within 72 h and 2.7% at 48 h after administration), and an additional 11.6% were positive in the second test (88% read within 72 h and 12% at 48 h) (Figure).

The overall point prevalence of TST positivity was 77.6%. In Prison One, the ARTI was 4.25% per year; stratified by cell blocks with high and low incidence, the ARTI was respectively 5.09% and 2.72%/year. In Prison Two, the ARTI was 2.77%/year (Table 1). The median age was 32 years, and history of contact with a TB case was elicited in 30.4% (76.6% were inmates). Among TST-positive inmates, 32.3% had a history of previous incarceration, 50% had had contact with a TB case in the last 11.5 months, and 40.1% came from neighbourhoods with a TB incidence of >100 cases/100 000 (Table 2).

Risk factors associated with higher prevalence of TST positivity were history of previous incarceration and time of current incarceration of 13–24 months (Table 3). Among the 580 participants included in the study, four developed active pulmonary TB. All were TST-positive. Two had respiratory symptoms and one

Table 1 Prevalence of positive TST and ARTI in two prisons in Colombia

	Prevalence of positive TST		ARTI of persons without BCG scar	ARTI all subjects
Prison	Persons without BCG scar *n/N* (%)	All subjects *n/N* (%)	% (95%CI)	% (95%CI)
Prison One	158/202 (78.2)	563/706 (79.7)	3.22 (0.78–5.63)	4.25 (2.76–5.73)
Cell blocks with low TB incidence	79/102 (77.5)	132/168 (78.6)	2.40 (0–5.37)	2.72 (0.26–5.18)
Cell blocks with high TB incidence	79/100 (79.0)	431/538 (80.1)	4.77 (0.59–8.95)	5.09 (3.23–6.95)
Prison Two	17/35 (48.6)	80/123 (65.0)	1.8 (0–6.13)	2.77 (0–5.66)
Total	175/237 (78.3)	643/829 (77.6)	2.9 (0.77–5.05)	3.96 (2.63–5.29)

TST = tuberculin skin test; ARTI = annual risk of tuberculous infection; BCG = bacille Calmette-Guérin; CI = confidence interval; TB = tuberculosis.

Table 2 Baseline characteristics of prisoners with positive and negative TST results

Variable	Positive TST *n* (%)	Negative TST *n* (%)
Age, years, median [IQR]	32 [25–46]	29 [24–42]
Time of current incarceration, months, median [IQR]	14 [6–30]	10 (4–27)
Time since the last contact with a TB case, months, median [IQR]	11.5 [5–24]	6 [3–24]
History of previous incarceration	173 (32.3)	37 (24.2)
Comorbidities		
COPD	30 (16.3)	14 (18.9)
Diabetes mellitus	11 (6.0)	4 (5.4)
HIV	1 (0.5)	1 (1.4)
Others	87 (47.3)	33 (44.6)
Current smoking	209 (32.5)	53 (28.5)
Current alcohol use	106 (16.5)	21 (11.3)
Current illicit drug use	261 (40.6)	73 (39.2)
BCG scar	432 (71.2)	111 (64.2)
History of contact with a TB case		
No contact	443 (68.9)	134 (72.0)
Contact inside the prison	154 (24.0)	39 (21.0)
Contact outside the prison	42 (6.5)	12 (6.5)
Contact outside and inside the prison	4 (0.6)	1 (0.5)
TB incidence in areas where subjects lived before incarceration, cases/100 000 population*		
<50	71 (19.8)	21 (23.9)
50–100	144 (40.1)	41 (46.6)
>100	144 (40.1)	26 (29.5)

* Includes those living in Medellin before incarceration.
TST = tuberculin skin test; IQR = interquartile range; SD = standard deviation; TB = tuberculosis; COPD = chronic obstructive pulmonary disease; HIV = human immunodeficiency virus; BCG = bacille Calmette-Guérin.

had a history of contact with a TB case. The intervals between TST administration and TB diagnosis were 56, 131, 153 and 177 days, respectively.

DISCUSSION

The main findings of this study were 1) the high prevalence of TST positivity, which was higher than in the general population in Prison One, Medellin, while in Prison Two the prevalence was similar to that in household contacts (HHCs) of pulmonary TB patients in Medellin;[19] 2) the importance of a second TST to identify additional cases of LTBI and to avoid overestimation of converters during follow-up; 3) the high ARTI in prisons compared to the general population,[15] and the variation between prison blocks; and 4) although in Colombia and other high-burden settings, INH treatment for LTBI is not recommended for immunocompetent adults with a positive first TST result, the importance of clinical follow-up, particu-

Table 3 Risk factors associated with the prevalence of a positive TST in prisoners

	Prevalence of positive TST	Crude prevalence ratio (95%CI)	Adjusted prevalence ratio (95%CI)*
Age, years			
18–24	72.0	1	1
25–64	79.4	1.10 (0.97–1.25)	1.10 (0.98–1.23)
⩾65	76.4	1.06 (1.05–1.07)	1.10 (0.93–1.32)
History of previous incarceration			
No	75.7	1	1
Yes	82.4	1.09 (1.01–1.17)	1.08 (1.00–1.17)
Time of current incarceration, months			
⩽12	73.6	1	1
13–24	83.2	1.13 (1.07–1.20)	1.09 (1.01–1.18)
⩾25	80.1	1.09 (0.86–1.38)	1.03 (0.83–1.29)
BCG scar status			
No	73.8	1	1
Yes	79.6	1.08 (0.94–1.23)	1.12 (0.96–1.30)
Time since last contact with a TB case, months			
No contact	76.8	1	1
1–12	79.4	1.03 (0.91–1.18)	1.00 (0.81–1.24)
⩾13	81.0	1.05 (0.99–1.12)	1.00 (0.95–1.05)

* Adjusted for all other variables listed.
TST = tuberculin skin test; CI = confidence interval; BCG = bacille Calmette-Guérin TB = tuberculosis.

larly in high-incidence blocks and among individuals with respiratory symptoms, is highlighted.

The prevalence of TST positivity among HHCs of pulmonary TB patients in a study conducted in Medellin between 2005 and 2006 was 65.9%; in the source population, this was 42.7%.[19] Our results demonstrate a higher prevalence of TST positivity in prisons than in the general population. In Prison Two, the prevalence of TST positivity was similar to that among HHCs, which is again significantly higher than in the general population, illustrating the variability between facilities.

It is known that some of the risk factors contributing to LTBI in prisons are the high TB incidence in these settings, the degree of overcrowding and the close contact between prisoners. In this case, TB incidence in Prison One ranged between 353 and 500/100 000 prisoners,[16] while in Prison Two, it was 1335/100 000 in 2013 (information provided by health care authorities). These figures are both higher than in the general population in Colombia (25/100 000). The magnitude of overcrowding at both sites during the study was 212% in Prison One and 128% in Prison Two (actual population compared to capacity). In a study from Maryland, USA, the most significant variable associated with TST conversion was the density of the prison population.[3] In our study, two risk factors were associated with the prevalence of positive TST: previous incarceration and length of detention; this is in line with previous studies.[20,21]

In contrast to our results, prevalence of TST positivity reported in high-income countries is lower: 26.8% in Spain,[22] 17.9% in Italy,[20] 12–14% in Australia,[13] 18% in the United States,[3] and 46.9% in Switzerland.[23] In low-middle-income countries, TST prevalence ranges between 48% in Pakistan,[24] 52.4% in Nigeria,[25] 60.8% in Brazil[26] and 88.8% in Malaysia.[21] One possible explanation for the high percentage of positive TST in our study compared to the above-mentioned studies is that two-step testing was performed according to CDC recommendations. Our results showed that 34% (96/282) of persons who were TST-negative at first administration had a positive TST on the second administration 1–3 weeks later, adding an overall 11% positivity to the entire study population. This finding has significant implications for follow-up and for estimating LTBI incidence in prisons, as 6 or 12 months after the first TST these individuals would have been considered TST converters. The lack of application of a two-step TST thus leads to an overestimation of the ARTI, and the administration of INH for presumed LTBI among these 'converters'. Another reason contributing to the high TST positivity in our study is the large number of patients whose reactions were read 72 h after administration. Singh et al. showed that the TST reaction is significantly larger at 72 h than at 48 h, which may lead to false-negative results.[27] In this study, TST positivity was 48.9% for those read at 48 h compared to 79.2% at 72 h. Again, settings in which indurations are read at 48 h may lead to false-positive reactions of subsequent TST conversion at 6 or 12 months.

Although LTBI screening is not recommended in high TB incidence settings, it is important to study the impact of both initial and annual LTBI testing in prisons for prisoners and correctional workers. The LTBI incidence rate ratio in prisons compared to the general population ranges between 5.03 and 83.74 in the United States and 61.76 in Brazil;[2] the annual incidence rate of TST converters among correctional officers reported in the United States was 1.3%,[28] 1.9%[29] and 3.8% in low TB incidence states, 4.9% in medium TB incidence states, and 8.3% in high TB incidence states.[30] The estimated ARTI in the present study reflects the higher risk of infection among incarcerated individuals than among the general population.[15]

As the high TST prevalence prohibits broad treatment of LTBI, identification of recent conversion or high risk for active TB is critical for the prevention of forward transmission within prisons and to the general population. In this study, four patients with a positive TST developed active pulmonary TB. Among these, two had respiratory symptoms at the time of enrolment and one had a close TB contact. The presence of symptoms and the relatively rapid progression to active TB suggests that active disease may have been present at the time of incarceration. In these individuals, INH would have been inappropriate. It is conceivable that with a short questionnaire, TST administration and complementary testing to identify active TB, the risk of transmission within these facilities can be reduced. Based on these observations and our previous study,[16] we propose TST screening at entry to prison. A positive result on the first TST combined with assessment of risk of exposure, history of incarceration, contact with a TB case, history of previous TB and/or body mass index <18 kg/m^2 should lead to clinical follow-up and investigations for TB in the presence of respiratory symptoms. A negative TST on entry to prison should be followed every year by a TST so as to be able to administer LTBI treatment for converters.

The main limitation of this study was the lack of chest X-rays, making it impossible to distinguish active TB from LTBI among TST-positive cases. Another limitation of the TST could be variability due to genetic factors. A genetic study among household contacts of smear-positive TB case patients from Medellin showed that the co-dominant major gene (aa, Aa and AA) explains ~65% of TST variability; ~35% of the population carried the AA genotype and were predisposed to low TST reactivity, whereas ~17% of those with the aa genotype were predisposed to high TST reactivity.[31]

In conclusion, TST positivity prevalence and ARTI

among prisoners were higher than in the general population, and differed between and within prisons. Application of a two-step TST and reading at 72 h are important to avoid misinterpretation during follow-up. The ability to screen individuals with a combination of TST and a risk assessment questionnaire may allow for targeted imaging in a subset of patients. This approach has the potential to prevent entry of individuals with active disease into crowded prison blocks where transmission would be inevitable.

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RESUME

CONTEXTE : Deux prisons à Medellín et Itagüí, en Colombie.

OBJECTIF : Déterminer la prévalence des tests cutanés à la tuberculine (TST) positifs chez les détenus ainsi que le risque annuel d'infection tuberculeuse (ARTI), identifier les facteurs de risque associés à un résultat positif et décrire la progression vers la maladie active.

SCHÉMA : Etude transversale. Les détenus ont été inclus si le temps de détention était ⩾1 an et exclus s'ils avaient des antécédents de tuberculose (TB) ou une TB active ou d'autres pathologies qui pourraient entraver l'administration ou l'interprétation du TST.

RÉSULTATS : Nous avons dépisté 1014 détenus. La prévalence d'ensemble des TST positifs était de 77,6%. Le premier TST a abouti à 66% de positivité et le deuxième à 11,6% de plus. Dans la première prison, le taux d'ARTI était de 5,09% dans les quartiers de cellules à incidence élevée de TB et de 2,72% dans les quartiers à faible incidence. Dans la deuxième prison, le taux d'ARTI était de 2,77%. Les facteurs de risque associés à un TST positif étaient un antécédent de détention ainsi que la durée de la détention. Parmi tous les détenus inclus dans cette étude, quatre ont développé une TB pulmonaire active.

CONCLUSION : La prévalence des TST positifs et l'ARTI étaient plus élevés que dans la population générale et ils différaient d'une prison à l'autre. L'étude a montré qu'il était important de faire un deuxième TST afin d'éviter de surestimer le nombre de conversions pendant le suivi.

RESUMEN

MARCO DE REFERENCIA: Dos prisiones en Medellín e Itagüí, Colombia.

OBJETIVO: Determinar la prevalencia de tuberculina positiva (TST) en prisioneros, el riesgo anual de infección tuberculosa (ARTI), identificar los factores de riesgo asociados con un resultado positivo y describir la progresión a enfermedad activa.

METODO: Estudio transversal. Se incluyeron prisioneros si tenían una condena ⩾1 año y excluidos si tenían tuberculosis (TB) previa o activa o condiciones que pudieran dificultar la administración o interpretación de la TST.

RESULTADOS: Se tamizaron 1014 prisioneros. La prevalencia general de TST fue 77,6%. La primera administración fue positiva en el 66% de prisioneros, y 11,6% adicional con la TST de refuerzo. En la Prisión Uno, el ARTI en las celdas de alta incidencia de TB fue 5,09% y en celdas de baja incidencia 2,72%. En la Prisión Dos el ARTI fue 2,77%. Los factores de riesgo asociados con TST positiva fueron historia de reclusión previa y duración de la reclusión. Entre todas las personas incluidas cuatro desarrollaron TB pulmonar activa.

CONCLUSIÓN: La prevalencia de TST en prisioneros y el ARTI es alto comparado con la población general, y esta difiere entre prisiones. Es importante aplicar TST de refuerzo para evitar la sobreestimación de los convertores durante el seguimiento.