

# Multi-centre study on the prevalence of latent TB infection among inmates in Spanish prisons

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## ABSTRACT

**Aims:** To study the prevalence of latent tuberculosis infection (LTBI) amongst inmates in Spanish prisons.

**Materials and Methods:** Multi-centre, cross-sectional study; two stage sampling. Socio-demographic, prison and clinical variables were gathered. A univariate, bivariate and multivariate analysis was carried out using logistic regression with the variables that showed statistical significance. The odds ratio was calculated with a confidence interval of 95%.

**Results:** 378 patients. The Mantoux test (PPD) assessable in 90.2% was available. 91.2% men, 37.8% foreigners with average age of 35.9±10.3 years. Average stay in prison: 2 years, 28.7% had been > 5 years in prison. 49.6% entered prison in 2006 or before. 24.5% had a history of intravenous drug use (IDU). 50.4% presented LTBI that was associated with: age > 40 years (63.2 vs. 43.8%; CI: 1.39-3.49; OR: 2.20; p=0.001); stay of > 5 years in prison (71.2 vs. 41.3%; CI: 2.13-5.75; OR: 3.50; p<0.001); in prison since 2006 or before (58.1 vs. 42.6%; CI: 1.22-2.88; OR: 1.87; p=0.004); infected with HCV+ (66.3 vs. 45.3%; CI: 1.40-4.0; OR: 2.37; p=0.001). The logistic regression model confirmed the independent association of LTBI with: a) age > 40 years (OR: 1.76; CI: 1.08-2.87; p=0.024); and length of prison stay > 5 years (OR: 2.50; CI: 1.41-4.43; p=0.002).

**Conclusions:** The prevalence of LTBI in prison is very high, especially amongst inmates over 40 and those who have been in prison for more than five years. To prevent the risk of progression to tuberculosis, treatment is recommended for those who require it along with the maintenance of control programmes for this pathology.

**Key words:** Latent tuberculosis; Prevalence; Prisons; Emigration and immigration; Tuberculin test; Multicenter study; Spain.

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## INTRODUCTION

Tuberculosis (TB) is an important healthcare concern with a worldwide rate estimated by the WHO of  $139 \times 10^5$  (139 cases for every 100,000 inhabitants<sup>1</sup>). In Spain, that rate is of  $18.3 \times 10^5$ , which places us among countries with a good control of the disease, but far from better results as those of the Netherlands<sup>2</sup>. Risk factors cluster in correctional facilities, therefore entailing a great vulnerability of TB for those housed within. Its incidence rates are about 52 times higher than those found among the general population<sup>3</sup>.

Latent TB infection is a condition which precedes TB disease and its treatment, highly effective, avoids the progression of the infection to the disease. Nevertheless, factors such as asymptomatic infection, long periods of time, and the fact that only a low percentage of progressions to the active disease occur, have led to fewer LTBI therapy prescriptions than recommended. This situation entails a risk and this risk is especially higher within a setting (such as prisons) where HIV-TB coinfection is frequent. This fact leads to highly recommend that LTBI treatment<sup>4</sup> be conducted and, in case of undiagnosed smear-positive patients, where *M. tuberculosis* transmission is easier, due to the closed nature of the setting. Therefore, LTBI diagnosis and treatment among inmates is a key tool in controlling the disease both inside and outside prison<sup>5,6</sup>, due to frequent mobility of inmates between facilities as well as between inside and outside prison settings.

In Spain, several studies on the prevalence of LTBI among inmates have been published<sup>6-10</sup>, but generally speaking, they are locally restricted and were conducted several years ago. Those studies do not depict the global situation of inmates in our country and may provide information which is no longer applicable to the current situation. That is why the main **objective** of this work is to know the prevalence of LTBI among inmates in Spanish prisons as well as the factors associated to the infection.

## MATERIAL AND METHOD

This sub-study is included in the PREVAHEP project, designed to measure the prevalence of infection by hepatotropic viruses, HIV and *M. tuberculosis* among inmates housed within Spanish facilities. It is a multi-centre, descriptive, cross-sectional study conducted in June 2008. Data was gathered from clinical histories of inmates under research, in view of the fact that serology and other tests are available for inma-

tes upon entry, including LTBI screening tests. It was estimated that the imprisoned population was about 62,000 people. For an estimated LTBI prevalence of 30%, the sampling size determined was of 364 inmates, assuming a variability of 5%, a  $\alpha$  error of 5% and a correction of 10% to compensate potential losses.

**Sampling method.** Two stage cluster sampling was used with probabilities proportional to unit size in the first stage (number of inmates per facility). 18 facilities were selected. The second stage consisted of randomized selection of 21 inmates per facility. Facilities selected were: Huelva, Córdoba, Almería, Sevilla I, Villabona (Asturias), Castellón I, León, El Dueso (Cantabria), Ponent (Lérida), Topas (Salamanca), Brians (Barcelona), Cáceres, Teixeira (La Coruña), Madrid II, Madrid VI, Murcia, Valencia y Fontcalent (Alicante I).

**Variables studied:** Data was gathered on: a) social and demographic variables (age, gender, race, nationality and injected drug use -IDU-); b) variables related to prison stay (total prison stay and year of last entry); and c) clinical and serologic variables (serology for HIV, HBV, HCV and PPD, which are all available for inmates upon entry in accordance with the TB Prevention and Control Program in Prisons; and presence or absence of previous TB disease). LTBI was considered for induration values measured after 48-96 hours were  $\geq 5$  mm in patients infected by HIV and  $\geq 10$  mm for those not infected<sup>11</sup>. Patients who had previously undergone TB disease and those whose PPD was not available were excluded.

**Statistic Analysis:** For the univariate analysis a description of the variables of the sample was done. For quantitative variables, the type of distribution was determined by means of the Kolmogorov-Smirnov test. For normal distributions, the arithmetic mean was used as a measure of central tendency (with a confidence interval of 95%) and the standard deviation (sd), as a dispersion measure. For other distributions, the median and the 25<sup>th</sup> and 75<sup>th</sup> percentiles (p25-p75) were used. Qualitative variables were expressed as absolute and relative frequencies, so that prevalence was determined as association indexes.

Bivariate analysis consisted of a comparison between variables. For quantitative variables, a homoscedastic assumption was valued when using the Lèvene test; the Student's T test was used for homogeneous variances, while the Mann-Whitney U test was used for heterogeneous variances. For qualitative variables, the comparison was made by means of Pearson's

chi-square test, except for those cases where any box of the fourfold (2x2) tables had a frequency under 5, in which case, Fisher's exact test was used. Mantel-Haenszel test was conducted to estimate the common odds ratio.

Within multivariate analysis, the dependent variable was defined as the presence or not of LTBI and the logistic regression model was readjusted with the independent variables which showed statistic significance or relevant importance for research. The degree of statistic significance of contrasting hypothesis was of  $p < 0.05$  and all data was analysed by means of SPSS v.15.

**Ethic and legal considerations:** Patients included were informed and their informed consent was required in order to use data. This was recorded in their clinical history. Compulsory administrative authorization was demanded to the Secretary General of Penitentiary Institutions and to Cataluña's *Secretaria de Serveis Penitenciaris, Rehabilitació i Justícia Juvenil de la Generalitat de Catalunya*. The study was evaluated and received approval by the Clinical Research Ethics Committee of the **Gol y Gorina** Institute in Barcelona.

## RESULTS

378 patients were included in the study, 8 of whom had a previous history of TB. Valid results for tuberculin skin testing (TST) were achieved in 341 (92.2%) patients of those included. No statistically significant differences were found between the whole sample and the patients with valid TST. Of those 341 patients researched, 311 were men (91.2%), and the average age was 35.7 (sd±10.3). 60.9% (n=226) was over 40 years old. The median value for prison stay was 2 years (p25-p75: 0.5; 169 (49.6%) had entered prison in 2006 or before having therefore completed at least one year and a half of continued imprisonment (see Table 1). 98 (28.7%) had spent over 5 years throughout their lives in prison.

LTBI was found in 172 patients (50.4%; CI95%:45.0-55.9%), and no differences were concluded between immigrant and Spanish inmates (see Table 2). By means of bivariate analysis, LTBI was associated to: a) being ≥40years old [72 (41.9%) vs. 42 (24.9%); OR: 2.20; CI95%: 1.39-3.49;  $p=0.001$ ]; b) having spent over 5 years in prison [74 (43.8%) vs. 30 (17.8%); OR: 3.50; CI95%: 2.13-5.75;  $p < 0.0001$ ]; c) last entry date ≤ 2006 [100 (58.1%) vs. 72 (41.9%); OR: 1.87; CI95%: 1.22-2.88;  $p=0.004$ ]; and d) pre-

senting a positive serology for HCV[53 (66.3%) vs. 27 (33.7%); OR: 2.37; CI95%: 1.40-4.00;  $p=0.001$ ]. Other variables were not significantly associated (see Table 2). Prevalence for infections by HCV, HIV and HBV (HbsAg +) were of 22.7% (CI95%: 18.3-27.1); 11.1% (CI95%:7.35-1.4) and 2.6% (CI95%:0.8-4.5) correspondingly. There were 5 patients (1.5%) who simultaneously presented HIV-HCV-HBV infections; 29 (8.5%) with HCV-HIV coinfection and 1 (0.3%) with HCV-HBV coinfection (see Table 2).

Multivariate analysis confirmed the existing independent association between LTBI and having spent over 5 years in prison. (OR: 2.50; CI: 1.41-4.43;  $p=0.002$ ) and being over 40 years old (OR: 1.76; CI: 1.08-2.86;  $p=0.024$ ). The association with the rest of variables was ruled out (see Table 3).

Among the 172 LTBI patients, the Spanish inmates were generally older: 58 (54.7%) were 40 or over, while only 14 (21.5%) of the immigrant inmates were that age (OR: 4.402; CI95%: 2.177-8.902;  $p < 0.0001$ ); and, on the whole, had spent over five years throughout their life in prison: 66 (61.7%) among the Spanish patients and 8 (12.3%) among the immigrant group (Or: 11.470; CI95%: 4.970-26.471;  $p < 0.0001$ ). On the other hand, the Spanish patients had spent less time under continued imprisonment: 36 (55.4%) immigrants had entered prison after 01-01-2007, while only 36 (33.6%) of the Spanish inmates had done so (OR: 0.408; CI95%: 0.217-0.769;  $p=0.006$ ) (see Table 4).

Table 1: Comparison of characteristics between total population and valid LTBI group

Variable	Total sample n=378	Valid TST n=341	p
Age	35.7 (±10.3)	35.9 (±10.4)	NS
Gender			
Male	347 (91.8%)	311 (91.2%)	NS
Female	31 (8.2%)	30 (8.8%)	
Years in prison (median (p25-p75))	2 (0-5)	2 (1-5)	NS
	14 (3.7%)	13 (3.8%)	NS
	57 (15.1%)	44 (12.9%)	NS
	23 (6.1%)	22 (6.5%)	NS
Not Spanish	149 (39.4%)	129 (37.8%)	NS
Previous IDU	87 (23.2%)	83 (24.5%)	NS
Year of last entry	≤2006 82 (48.1%)	169 (49.6%)	NS
	≥2006 196 (51.9%)	172 (50.4%)	

TST: tuberculin skin testing; (sd): standard deviation; (p25-p75): percentiles 25 and 75; IDU: injecting drug use; NS: not significant

Table 2: LTBI associated variables. Bivariate analysis

Variables		LTBI		p	OR	CI95%
		Yes	No			
Gender	Male	161 (93.6%)	150(88.8%)	0.119	1.86	0.85-4.03
	Female	11 (6.4%)	19 (11.2%)			
Age	≥40	72 (41.9%)	42 (24.9%)	0.001	2.20	1.39-3.50
	<40	99 (58.1%)	127(75.1%)			
Duration of stay	≥5	74(43.8%)	30(17.8%)	<0.0001	3.50	2.13-5.75
	<5	98 (56.2%)	139(88.2%)			
	Yes	6 (3.5%)	7 (4.1%)	0.753	0.84	0.28-2.54
	No	166 (96.5%)	132(94.9%)			
	Yes	28 (16.3%)	16 (9.5%)	0.063	1.86	0.97-3.58
	No	144 (83.7%)	153(90.5%)			
	Yes	13 (7.6%)	9 (5.3%)	0.404	1.45	0.60-3.50
	No	159 (92.4%)	160(94.7%)			
Nationality	Immigrant	66 (51.2%)	63 (48.8%)	0.835	0.96	0.62-1.48
	Spanish	106 (48.8%)	108(41.2%)			
IDU	IDU	49 (28.8%)	34 (20.0%)	0.063	1.61	0.97-2.66
	Not IDU	121(71.2%)	135(80.0%)			
Year of last entry	2006 or before	100(58.1%)	72 (41.9%)	0.004	1.87	1.22-2.88
	2006 or later	72 (42.6%)	97 (57.4%)			
Ab. HCV	Positive	53 (31.1%)	27 (15.8%)	0.001	2.37	1.40-4.00
	Negative	117 (69.9%)	141(84.2%)			
Ab. HIV	Positive	24 (41.1%)	14 (8.2%)	0.096	1.81	0.90-3.63
	Negative	146 (85.9%)	154(91.8%)			
HBsAg	Positive	6 (3.7%)	2 (1.1%)	0.185	2.98	0.59-15.00
	negative	152(92.3%)	151(98.9%)			

Table 3: Variables associated to LTBI. Multivariate analysis

Variable	CI95%			
	Odds Ratio	lower	upper	"p"
Gender	1.40	0.63	3.13	0.410
Age>40	1.76	1.08	2.86	0.024
>5 years of imprisonment	2.50	1.41	4.43	0.002
HCV+ serology	1.32	0.73	2.40	0.363

Table 4: Patient LTBI comparison according to nationality

		Immigrants	Spanish	"p"	O.R.	CI95%
Age	<40	51 (78.5%)	48 (45.3%)	<0.0001	4.402	2.177-8.902
	≥40	14 (21.5%)	58 (54.7%)			
Imprisonment duration	<5 years	57 (87.7%)	41 (38.3%)	<0.0001	11.470	4.970-26.471
	≥5 years	8 (12.3%)	66 (61.7%)			
Last entry	Up to 2006	29 (44.6%)	71 (66.4%)	0.006	0.408	0.217-0.769
	Since 2006	36 (55.4%)	36 (33.6%)			

## DISCUSSION

The results of our study conclude that half of inmates imprisoned in Spanish facilities present LTBI. Results achieved in social and demographic variables (age, gender, nationality, IDU, etc.) correspond to this year's official data ([www.institucionpenitenciarias.es](http://www.institucionpenitenciarias.es)). The prevalence is high, although it may be biased due to BCG vaccination, which is frequently found in inmates from developing countries who were found in this study although this was not considered, and due to booster response, occurred during repeated TST, which can lead to a false negative result of the first test<sup>12</sup>. Both facts were not considered in the calculation of the prevalence. Another limitation within the study is not considering the immune status of HIV-infected patients. Nevertheless, this effect is presumably less relevant because HIV patients represented slightly over 10% of the sample and their immunologic status was generally good (CD4:473±254/ml). Therefore anergic cases must have been very few or none, since anergy only develops in cases of severe immune unresponsiveness<sup>13</sup>.

It must be outlined that the prevalence rate found is similar to that concluded in a prevalence survey carried out ten years ago<sup>7</sup>, as well as to other prevalence rates stated in other studies published around those dates<sup>8,9</sup> and it is comparable to that observed in other studies recently published<sup>10</sup>. This high prevalence can be caused by poor social and economic conditions, which are highly prevalent among a great deal of the imprisoned population and traditionally associated to the risk of suffering LTBI. Other factors frequently associated are: a) age, since a longer exposure time is associated with a higher probability of infection; and b) physical proximity, sometimes enhanced by overcrowding in prisons. Both factors have been studied among the general population<sup>16-19</sup>, and among the imprisoned one<sup>20,21</sup>. Our study concludes that the factors independently associated to having LTBI are actually these two factors, among all those studied.

Despite the aforementioned limitations of our research, it can be affirmed that the prevalence of LTBI among Spanish inmates is clearly higher than the prevalence in the general population<sup>22</sup>. Among other countries' imprisoned population, LTBI is also frequent<sup>23</sup>, although the infection rates highly depend on the country and the facility where the study was carried out: prevalence rates of 20.1% and 17% have been found in North American facilities<sup>24,25</sup>, 61.5% in Brazil<sup>26</sup> or 48% in Pakistan<sup>20</sup>.

On the one hand, data achieved in this study suggests that numerous inmates enter prison when

they are already infected: many of these are immigrants. This fact has been already mentioned<sup>27</sup>, and it corresponds to the high infection rate found among alien populations, normally higher than the prevalence among the national population<sup>16</sup>. These patients frequently come from countries where TB is highly endemic. Nevertheless, this study has not found significant differences between the global prevalence of LTBI among Spanish and immigrant inmates. Although several studies have concluded a higher prevalence in the immigrant imprisoned population<sup>16,28,29</sup>, there are others which have similar results to us<sup>9</sup>. Probably we can explain this by the fact that the national population who normally enters prison has a higher prevalence of infection than other groups due to their origins and social conditions. Therefore the prevalence observed in this specific group is very close to that obtained in the immigrant population<sup>16</sup>.

Aside from the prevalence of LTBI upon entry, new infections must also be considered. These are more frequent in enclosed settings when contact with smear-positive patients occurs. Therefore, it is recommended that the TB control and surveillance programs be maintained and that LTBI treatment be instituted whenever indicated, since the risk of developing TB within the first two years of tuberculin conversion is especially high and affects approximately 5-10% of converters<sup>30</sup>.

Finally, it would be reasonable to think that a HIV infected cohort presented a higher prevalence of LTBI, as some studies carried out within correctional facilities have concluded<sup>31</sup>. Our study shows nonetheless a larger proportion of patients infected by HIV with LTBI, but with no statistical significance. Nevertheless, this data should be carefully considered since it can be conditioned by other factors which have not been considered such as immunodeficiency, cutaneous anergy, or booster response.

As a final point I would like to recall that TB is an important healthcare concern in Spanish prisons. The imprisoned population presents, as it has been shown in this study, a high prevalence for LTBI. The prescription of treatment is, therefore, a key element in reducing the risk of developing TB and preventing its transmission.

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