

**ORIGINAL ARTICLE**

**Epidemiological profile of tuberculosis infection and disease among cocaine users admitted to hospitals of the Greater São Paulo city\***

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**ABSTRACT**

**OBJECTIVE:** To evaluate the prevalence and the risk factors for tuberculosis (TB) infection and disease among hospitalized cocaine users.

**METHOD:** A cross-sectional study performed on a sample of 440 addicts over 18 years of age, admitted to hospitals of the metropolitan area of the Greater São Paulo city, whose clinical conditions allowed them to answer a standard questionnaire, and who agreed to participate in the study. The prevalence of TB infection was assessed through positive tuberculin testing (PPD), and of TB disease by the finding of *M. tuberculosis* in the sputum of patients with respiratory symptoms.

**RESULTS:** Respiratory symptoms were present in 21% of the patients, the most frequent being weight loss and cough, which disappeared when cocaine use was discontinued. The general prevalence of TB infection was 28%. The prevalence of TB disease was 0.6%. The factors which were associated with positive PPD were: age, color/race, time spent in prison, and drug use in prison.

**CONCLUSION:** No increased prevalence of TB infection and disease was found in these patients. Older addicts had a higher probability of having TB infection, and so had those who had been in prison.

**Key words:** Tuberculosis, epidemiology. Inpatients. Cocaine-related disorders.

**Acronyms and abbreviations used in this paper**

TB – Tuberculosis

PPD – Positive tuberculin test  
HIV – Human immunodeficiency virus  
ANEP – National Association of Research Companies (Associação Nacional de Empresas de Pesquisa)  
BCG – Bacillus Calmette-Guérin  
ELISA – Enzyme-linked immunosorbent assay  
AIDS – Acquired immunodeficiency syndrome

## Introduction

Tuberculosis (TB) and drug use are both older than history itself. Only in the second half of the 20<sup>th</sup> century the first studies were published showing an association between these morbidities.<sup>(1,2)</sup> The environment in which addicts live, whether to purchase or to use the drug, is highly favorable for the transmission and progress of the disease. It consists of clandestine places, without ventilation, poorly lightened, and with an intense flow of people which, if they are infected, will spread the TB bacilli by coughing.<sup>(3,4)</sup> Among the forms cocaine is presented, crack causes the greatest dependence, the greatest danger and the severer consequences. As its users have a more intense criminal life;<sup>(5,6)</sup> prisons work as TB reservoirs.<sup>(7,8)</sup>

Studies on the prevalence of TB associated with the use of inhaled (powder) and/or smoked (crack) cocaine are scarce. The existing researches deal fundamentally with issues regarding HIV infection, usually taking into account only the population of intravenous drug users. As a rule, several important issues regarding morbidity and mortality due to mycobacterioses are unknown to addicts. The main factors responsible for the lack of studies on the prevalence of TB in substance abusers are: failure in disease notification, lack of standardization of screening methods, and mainly the impossibility of correctly determining their number and their exposure to the infectious agent, because they live as outcasts of society and of the law.

Thus, our objective is to show the prevalence of TB infection and disease, and the risk factors associated with this morbidity, among inhaled and/or smoked cocaine addicts who seek medical attention.

## Methods

Our purpose was to perform a cross-sectional study, with a convenient sample, regarding both selection and time. Our aim was to determine the prevalence and the risk factors for TB infection and disease among inhaled (powder) and/or smoked (crack) cocaine users, aged 18 years or over, of both genders, residents of the the Greater São Paulo city, with social and psychological problems resulting from cocaine use, admitted to six selected hospital units in the metropolitan area, so as to be representative of the population of addicts who seek health services. Patients were excluded if they were somnolent, confused or aggressive, or if they had been admitted exclusively due to use of marijuana and solvents. The study protocol was approved by the Ethics Committee of Escola Paulista de Medicina, Federal University of São Paulo (Unifesp). All patients were informed about the objectives of the study, and a consent form was previously obtained from each one of them.

Six psychiatric hospitals of the metropolitan area were chosen, which met the following selection criteria: a) to receive patients from both the public network and health insurance holders and private patients, who came spontaneously or were brought in by the police and/or relatives; b) to have a specific ward and protocol for the treatment of addicts; c) to admit patients from all areas of the Greater São Paulo city; d) to give the team free access to the hospital premises for the interviews. The exclusively private hospitals did not agree to participate.

The expected prevalence of infection by the tuberculosis bacillus among Brazilians of the same age is 20 to 30%.<sup>(9)</sup> For an estimated prevalence of tuberculosis infection among addicts of 35%, with a sample error of 5%, a confidence interval of 95%, and expected losses of 10%, the calculated sample size was 385 patients.

After several discussions with a team of psychiatrists, psychologists, and social workers experienced in assisting drug using patients, and after an initial pilot instrument had been applied, a questionnaire was worked out to obtain the following information from the patients: a) demographic features – gender, age, race, residence, place of birth; b) socioeconomic features – marital status, school education, occupation, type of home, and social class, the latter being evaluated according to the criteria of the National Association of Research Companies (Associação Nacional de Empresas de Pesquisa – ANEP);<sup>(10)</sup> c) patterns of cocaine use (powder or crack) – age when use started, time of use, quantity used and frequency, individual or collective use; d) concomitant consumption of alcohol, with the classification of mild, moderate and severe being made according to Laranjeira and Pinsky (1997);<sup>(11)</sup> e) use of other drugs, concomitantly or in the past – tobacco, marijuana, solvents, heroin, injected drugs; f) history of time in prison – number of times he/she was arrested, time in jail, drug use in jail; g) personal and family history of tuberculosis, BCG vaccination, current signs and symptoms.

All questionnaires were applied by a trained psychologist. The interviews were individual, in a closed room, in the presence of the interviewer, the patient being interviewed and a nurses aid. In order to ensure the veracity

of the obtained information, patients were interviewed only after release by the team responsible for their treatment or when, after submitting them to simple memory and reasoning tests, the interviewer felt that they were not affected by the use of illegal drugs or under sedative medication, besides their addict behavior.

Diagnoses of tuberculosis infection and disease were made according to the rules of the Ministry of Health,<sup>(12)</sup> considering as positive those patients who presented an induration of 10mm or more. Patients with PPD= 0mm were encouraged to have a second test done after 15 to 21 days, in order to analyze their secondary immune response.

All patients who complained during the interview of productive cough for over three weeks were observed during the first days as inpatients. If no improvement of the symptoms occurred after discontinuation of cocaine use, sputum was collected for bacterioscopy and culture, to search for mycobacteria.

All participating addicts had blood samples collected for HIV testing. Whenever two ELISA tests were positive, a confirmation test was run using the Western Blot technique. Positive-testing addicts were considered infected by the tuberculosis bacillus if they had an induration of 5mm or more.

## Statistical Analysis

Information entry was performed by means of a program created in *Microsoft Access* – a relational data management system for *Windows 95*.

For data analysis, the *Epi-Info 6.04* software was used. The results of the observations made regarding the sociodemographic variables, the drug use patterns, and the TB-related parameters are presented in tables, represented by mean values for numerical variables and by percentages for category variables. For comparison between the mean values of two groups of variables, Student's *t* test was used. For comparison between the category variables of two groups, the chi-square test was used. Two-tail tests were used, with the a probability set at 5%.

## Results

During the study period, from 12/01/97 through 09/15/98, 458 patients were analyzed. In 18 addicts (3.9%) the PPD reading was impossible (13 patients requested discharge, three were discharged on disciplinary grounds, and two escaped). So, 440 users of inhaled and/or smoked cocaine were enrolled in the study. Of these, 131 (29.8%) used inhaled cocaine, 169 (38.4%) were dependent on crack, 133 (30.2%) used both forms of the drug (powder and crack), and seven (1.6%) claimed to be also users of the injected form. The mean age was  $27.5 \pm 6.9$  years. Only 18 (4%) addicts were women.

Only a few individuals had contact with a person known to have tuberculosis. The positive skin test reaction to the BCG vaccine was present in 88.0% of the substance abusers in this sample. The great majority of the addicts (71.8%) had no symptoms and, when they had, their most frequent complaints were weight loss and cough. All symptoms disappeared with the interruption of drug use.

PPD was positive in 93 patients (21.1%). In 131 addicts (30.0%) whose initial PPD value was zero, a second tuberculin test could be performed after 15 to 21 days. Eighty-one of them (61.8%) remained with the value zero, 21 (16.0%) became weakly reactive (PPD < 9mm), and 29 (22.2%) became positive. So, the final prevalence of positive tuberculin tests was 27.7% (93 patients positive at start, and 29 after the second test).

[Table 1](#) shows the prevalence of TB infection according to the demographic aspects and their level of statistical significance. No significant statistical difference was shown by the following parameters: place of birth (Greater São Paulo city or another place), school education, marital status (with or without a partner), source of income, social class, and a history of homelessness.

**TABLE 1**  
**Presence or absence of TB infection according to demographic aspects**

	No		Tuberculosis infection		<i>p</i>
	Number	%	Yes Number	%	
Age (years)					
18-25	168	82.3	36	17.7	
> 25	150	63.5	86	36.5	0.0000
Color/race					
White	243	75.9	77	24.1	
Non-white	75	62.5	45	37.5	0.0072
Place of birth					
Greater São Paulo city	255	73.1	94	26.9	
São Paulo State	20	66.7	10	33.3	
Other states	43	70.5	18	29.5	NS
School education					
Incomplete high school	270	73.0	100	27.0	
Complete high school	48	68.6	22	31.4	NS
Marital status					
Without a partner	246	74.8	83	25.2	
With a partner	72	64.9	39	35.1	NS
Source of income					
Yes	158	71.5	63	28.5	
Unemployed	160	73.1	59	26.9	NS
Social class					
A	17	73.9	6	26.1	
B	73	66.4	37	33.6	
C	112	74.2	39	25.8	
D	76	74.5	26	25.5	
E	40	74.1	14	25.9	NS
History of homelessness					
Yes	76	65.6	40	34.4	
No	242	74.7	82	25.3	NS

Two hundred and thirty-four patients (52.7%) had never been hospitalized before, whereas 37 (8.4%) had previously been admitted to a hospital three or more times. The number of previous hospitalizations had no influence on the PPD result.

[Table 2](#) discloses the influence of the kind of drug consumed (illegal or not) on the PPD values. Exclusive users of crack had a higher probability of having a positive tuberculin test than non-users ( $p = 0.0265$ ). The exclusive use of inhaled cocaine or its concomitant use with crack was not associated with a statistically significant increase of the probability of a positive PPD. The concomitant use of cocaine and alcohol and/or tobacco and/or marijuana showed no statistical significance.

**TABLE 2**  
**Presence or absence of TB infection according to the kind of drug used**

	Tuberculosis infection				<i>p</i>
	No		Yes		
	Number	%	Number	%	
Alcohol (units/week)					
Do not drink	99	72.8	37	27.2	
< 22	56	78.6	15	21.4	
22-50	37	64.9	20	35.1	
> 50	127	71.8	50	28.2	NS
Marijuana					
Yes	174	70.7	72	29.3	
No	144	74.2	50	25.8	NS
Tobacco					
Yes	273	72.0	106	28.0	
No	45	73.8	16	26.2	NS
Kind of drug					
Inhaled cocaine					
Yes	102	77.9	29	22.1	
No	216	69.9	93	30.1	NS
Crack					
Yes	112	66.3	57	33.7	
No	206	76.0	65	24.0	0.0265
Both					
Yes	104	74.3	36	25.7	
No	214	71.3	86	28.7	NS

We found no statistical significance for the time of drug use, the number of times a week it was used, the number of persons with whom the drug was used, the quantity used (g/day) (Table 3). The mean age at the beginning of drug use among the patients with TB infection was  $24.0 \pm 7.2$  years; among those who were not PPD-positive, it was  $21.4 \pm 6.7$  years ( $p = 0.0004$ ). The patients with positive PPD started drug use at an older age.

**TABLE 3**  
**Presence or absence of TB infection according to drug use pattern**

	Tuberculosis infection				<i>p</i>
	No		Yes		
	Number	%	Number	%	
Age at onset of use					
Mean	21.4		24.0		
Standard deviation	6.7		7.2		0.0004
Time of use (years)					
< 2	50	83.3	10	16.7	
2-5	145	72.1	56	27.9	
6-10	97	69.8	42	30.2	
> 10	26	65.0	14	35.0	NS
Number of times/week he/she uses the drug					
< 1	10	52.6	9	47.4	
1-3	77	72.6	29	27.4	
4-6	22	64.7	12	35.3	
Every day	209	74.4	72	25.6	NS
Number of persons with whom he/she uses drug					
Alone	52	73.2	19	26.8	
1-5	178	72.4	68	27.6	
> 5	88	71.5	35	28.5	NS
Quantity (g/day)					
Up to 2	162	74.3	56	25.7	
3-5	116	69.0	52	31.0	
> 5	40	74.1	14	25.9	NS

Table 4 shows the influence of prison on the prevalence of tuberculosis infection. The fact that the addict had been in jail or not, and the number of times he/she was in jail did not show any statistical significance, but the time spent in jail did. Those who spent less than 24 hours in prison had a lower rate of positive tests. Yet, those who stayed longer than six months had a higher frequency of tuberculosis infection ( $p = 0.0409$ ). Drug use in prison, besides being of relevant clinical importance, also showed a statistical difference. Those who used drugs while in jail had a higher rate of positive tests ( $p = 0.0037$ ).

**TABLE 4**  
Presence or absence of TB infection according to history of imprisonment

	Tuberculosis infection				<i>p</i>
	No		Yes		
	Number	%	Number	%	
History of imprisonment (n = 439)*					
Yes	174	69.0	78	31.0	NS
No	143	76.5	44	23.5	
Number of arrests (n = 252)					
1	86	69.4	38	30.6	NS
2-5	68	71.6	27	28.4	
> 5	20	60.6	13	39.4	
Time (days) spent in jail (n = 252)					
Less than 24 hours	80	77.7	23	22.3	0.0409
1-30	49	65.3	26	34.7	
31-180	30	66.7	15	33.3	
> 180	15	51.7	14	48.3	
Time (months) elapsed since last arrest					
< 1	12	92.3	1	7.7	NS
1-6	31	70.5	13	29.5	
7-12	21	61.8	13	38.2	
> 12	110	68.3	51	31.7	
Drug use in jail					
Yes	44	56.4	34	43.6	0.0037
No	130	74.7	44	25.3	

\* One patient did not answer this question

The fact that the addict shared the material for drug use did not interfere with the test result. Thirty-two patients (7.3%) were HIV-positive on the ELISA blood test. Only 18 (4.1%) of them were confirmed by Western Blot. Although the cutoff value for serum-positive patients was set at 5mm, none of the patients had a PPD between 5mm and 9mm; all values found were either zero or over 10mm. The patient being HIV-positive was not related to the kind of drug used.

## Discussion

We found a higher rate of crack users and a small prevalence of injected drug addicts in our sample. The prevalence of TB infection was not higher than expected for the general population of the same age. The TB disease rate was low, and persistent respiratory symptoms were not frequent in this group of individuals.

The problems resulting from the use of convenience samples are well known. The characteristics of drug users who are in contact with a health care service are very different, and may not represent the community they came from. There is a filter in the selection of patients that makes some users seek medical attention while others do not. If the approach is correct, the results not only inform about the existence of the problem, but give also an idea of its magnitude and importance, providing the grounds for the work of other health professionals who experience similar conditions and whose patients resemble those included in these samples. (13-15) Another major problem is the veracity of the information obtained by the questionnaire, since cocaine has the characteristic of benumbing the reality of facts. Kokkevi *et al.*<sup>(16)</sup> (1997) studied the reliability of the answers of substance abusers, and showed that they were reliable, depending on some factors, such as: short time of interview, simplicity of the questions, and training of the interviewer. Our questionnaire was simple and objective, with a majority of "yes" and "no" answers, performed by an experienced and trained psychologist, and the time of interview was about 20 minutes. All patients were interviewed only after being released by the team assisting them, and only if they gave coherent answers and showed a good memory for dates and situations. Whenever an individual was found not to be apt to answer the questionnaire, he/she was either not included or the interview was postponed to the following week.

Another point to be considered is the fact that we analyzed hospitalized addicts. The possibility of hospital TB transmission is well known, and the best way of preventing it is early diagnosis and proper isolation of the bacilliferous patient.<sup>(17)</sup> Before admission to specialized hospitals, addicts were screened in general hospitals, in search for comorbidities. Whenever present, they kept the substance abusers in general hospitals until they were treated. There were no records on addicted patients with TB in the history of the visited hospitals.

The tuberculin test is not 100% sensitive and specific. However, there is currently no better method to diagnose tuberculosis infection.<sup>(8,18)</sup> It is known that crossreactions may occur with other, non-tuberculosis mycobacteria, and that BCG vaccination may interfere, leading to false-positive results. However, these factors do not contraindicate the test.

In this study, no TB disease diagnosis was made. The literature<sup>(19-22)</sup> shows a TB disease prevalence varying from 6% to 30%, but the reports concern the association of this morbidity with injection drug users and, consequently, with AIDS. Since we had a very small number of intravenous drug addicts, this may be an explanation of our findings. Other important factors were: the little contact with tuberculosis patients – 14.1% of the addicts claimed to have met and had contact with an individual known to have the disease, but this contact had occurred a long time ago. In 1997, Melo<sup>(23)</sup> reported that, for the disease to be transmitted in the general population, the contact has to be of at least 200 to 300 hours with a bacillus-carrying patient. This number of hours decreases, if the patients immune status is compromised. We did not evaluate in our sample the time spent in the houses where drugs were sold and used. Thus, we do not know if this contact between addicts was momentary or long-lasting. A positive skin test reaction to the BCG vaccine was present in 88% of the addicts, which might show vaccine protection, although, in their age bracket, the vaccine was expected to have already lost its protective effect.

The great majority (71.8%) of addicts showed no symptoms consistent with TB. Since most patients stayed in the hospital for 30 days on the average, their evolution could be followed-up. All addicts which manifested some kind of symptoms presented a major improvement in their complaint within one week from admission and, consequently, of not using cocaine. Those with a productive cough had a decrease in expectoration production, and the grayish color (peculiar of crack users) became whitish. Whenever the improvement was not as pronounced, it was the result of the association with smoking, a common fact in inpatients. Patients who were admitted with weight loss gained their weight back within a few days. Upon medical discharge, they were more dynamic and virtually without any respiratory symptoms. Many of the typical symptoms of substance abuse are similar to those found in TB disease. We observed this mainly in patients who were re-admitted due to relapse. Such addicts came back with extreme weight loss, productive cough with blackened sputum, a few with blood streaks and a worsening of their general conditions. However, this exuberant symptomatology soon disappeared, as the drug use was discontinued.

We found a 27.7% prevalence of TB infection. The rate found in Brazilian draftees and the one expected for the general population is around 30%<sup>(9)</sup>. This means that we did not find a higher frequency of PPD-positive subjects in this population either, since the values found were similar to those expected for a sample of the general population of the same age. We stress the importance of the secondary immune response for the interpretation of the tuberculin test. The first PPD was positive in 21.1% of the cases. Of those whose PPD could be repeated after 15 to 21 days, 22.2% became positive, whereas these individuals would have been considered non-reactive if only a single test had been performed. For logistic reasons, we did not study the cellular immunity of these patients in more detail. We do not know precisely the anergy rate of this group of individuals. Zoloth *et al.*<sup>(24)</sup> (1993) found a high anergy rate among drug-using prisoners. Therefore, they suggested that the tuberculin test should not be the only parameter for tuberculosis screening in this population, since chest X-rays could be more useful. Other authors analyzed a program for TB screening in the general population, and showed that 5.6% of the individuals had radiological lesions consistent with the disease, 65% of them being PPD-negative. However, a diagnosis of active disease was made in patients with both a positive tuberculin test and a radiological lesion suggestive of TB, which led to the conclusion that there is no ideal test for this diagnosis.<sup>(25)</sup>

Older age and color/race were demographic factors with a statistically significant association with positive PPD, similar to other reports, which showed that the most affected age bracket was from 20 to 40 years of age, and that non-white subjects had a 7 to 20 times higher probability of having TB infection.<sup>(26,27)</sup>

Social class and housing antecedents did not interfere with the test result. This is probably due to the fact that the social level recorded may not reflect reality, considering that the user could belong to a higher level, if he had not disposed of his possessions to buy drugs. A great majority of patients lived in a house or apartment. Few of them lived in slums or in the streets. However, it is well known that TB is strongly related to poverty and distress.<sup>(27)</sup>

The age of onset of drug use revealed that those who started consumption later were more likely to have TB infection. As mentioned earlier, older age was a major factor in increasing positive tuberculin testing, thus representing a confusing factor regarding this association.

We found only 4.8% of HIV-positive patients, and their positive status had no influence on PPD. The low frequency of virus-infected individuals probably resulted from the fact that we found no injection drug users,

which are those more frequently exposed to HIV. An analysis of the induration size in HIV-positive patients who were injection drug users showed that 15% of them had a tuberculin test > 10mm, and that they did not differ in nodule size from HIV-negative individuals.<sup>(28)</sup> Daley *et al.*<sup>(29)</sup> (1998) studied a group of injection drug users from San Francisco, and found 30.5% of HIV-positive patients, 28% of which had a positive reaction at the tuberculin test, as compared to 44% of those who were HIV-negative.

A history of imprisonment was more pronounced in crack users, and the main parameters related to PPD were the number of arrests, the number of days spent in jail, the time elapsed since the last arrest, and drug use in prison. Other authors<sup>(23)</sup> stated that the risk for TB was 4.3 times higher in prisoners who were drug users than in those who were not. They also showed, by multivariate analysis, that individuals who stayed in jail for over one year had a 2.2 times higher risk of developing the disease.

Thus, older non-white addicts are more likely to present TB infection, and so are those who stayed in jail longer and used drugs there. Although we did not observe an increased prevalence of TB infection and disease in this sample, we saw patients who were physically and mentally wasted, using one or more drugs, living in a clandestine environment. All these factors are closely related to this lung disease. Maybe an active search for addicts approached in the streets or in places used for drug consumption could increase the proportion of infected and sick individuals. An X-ray study performed on suspected patients could help early detection of those affected by the disease, but the presence of symptoms alone is not a good parameter for testing, since they virtually disappear with the interruption of drug use.

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