Prevalence of *Mycobacterium tuberculosis* infection among injection drug users in Toronto

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Abstract

Background: Injection drug users are at increased risk of *Mycobacterium tuberculosis* infection and active tuberculosis (TB). The primary objective of this study was to determine the prevalence of *M. tuberculosis* infection among injection drug users in Toronto, as indicated by a positive tuberculin skin test result. An additional objective was to identify predictors of a positive skin test result in this population.

Methods: A cross-sectional study was carried out involving self-selected injection drug users in the city of Toronto. A total of 171 participants were recruited through a downtown Toronto needle-exchange program from June 1 to Oct. 31, 1996.

Results: Of 167 subjects tested, 155 (92.8%) returned for interpretation of their skin test result within the designated timeframe (48 to 72 hours). Using a 5-mm cutoff, the prevalence rate of positive tuberculin skin test results was 31.0% (95% confidence interval 23.8% to 38.9%). Birth outside of Canada and increasing age were both predictive of a positive result.

Interpretation: There is a high burden of *M. tuberculosis* infection in this population of injection drug users. The compliance observed with returning for interpretation of skin test results indicates that successful TB screening is possible among injection drug users.

Résumé

Contexte : Les consommateurs de drogues injectées sont plus exposés à l'infection par *Mycobacterium tuberculosis* et à la tuberculose active. Cette étude visait avant tout à déterminer la prévalence de l'infection par *M. tuberculosis* chez les consommateurs de drogues injectées à Toronto, prévalence indiquée par un test cutané à la tuberculine qui donne un résultat positif. Elle visait aussi à identifier les prédicteurs d'un résultat positif à un test cutané à la tuberculine dans cette population.

Méthodes : On a réalisé une étude transversale portant sur des consommateurs de drogues injectées autosélectionnés de Toronto. Au total, on a recruté 171 participants dans le cadre d'un programme d'échange d'aiguilles au centre-ville de Toronto, du 1er juin au 31 octobre 1996.

Résultats : Sur les 167 sujets testés, 155 (92,8 %) sont revenus demander une interprétation du résultat de leur test cutané dans le délai prescrit (48 à 72 heures). Fondé sur une limite de 5 mm, le taux de prévalence des résultats positifs au test cutané à la tuberculine s'est établi à 31,0 % (intervalle de confiance à 95 %, 23,8 % à 38,9 %). La naissance à l'étranger et l'âge étaient deux facteurs prédicteurs d'un résultat positif.

Interprétation : Il existe un fardeau important d'infection par *M. tuberculosis* dans cette population de consommateurs de drogues injectées. La conformité observée chez les sujets qui reviennent demander une interprétation des résultats du test cutané indique qu'un dépistage de la tuberculose pourrait réussir chez les consommateurs de drogues injectées.

Tuberculosis (TB) in Canada is largely restricted to high-risk groups.[1] A targeted approach to TB control can be effective only after these high-risk populations are clearly identified.[2] As early as 1914, an association be-

tween drug use and TB was recognized.[3] The increased burden of TB among injection drug users has been attributed to both an increased prevalence of *Mycobacterium tuberculosis* infection and an increased likelihood of progression to active TB.[4] The prevalence of positive tuberculin skin test results among injection drug users in the United States has ranged from 10.3% to 45.8%.[5,6] In 1997 a study in Vancouver reported that 25% of injection drug users had a positive tuberculin skin test result.[7]

The population of injection drug users in Toronto may be distinct from such populations elsewhere in several regards. In particular, a lower prevalence of HIV infection among the estimated 8000 users in Toronto[8] may result in a lower burden of TB. We conducted this study to determine the prevalence of *M. tuberculosis* infection among injection drug users in Toronto, as demonstrated by a positive tuberculin skin test result, and to identify predictors for a positive result in this population.

Methods

A cross-sectional study was conducted from June 1 to Oct. 31, 1996, in the city of Toronto. The study design used a self-selected convenience sample to enroll injection drug users. The primary recruitment strategy involved direct contact with individuals who were using needle-exchange services. Subjects who were 16 years or older, had injected drugs in the last 6 months and were willing to return for interpretation of their skin test result were eligible to participate. One nurse administered all questionnaires and skin tests. A $10 financial incentive was provided to participants for undergoing the interview and skin test, plus an additional $15 for returning 48 to 72 hours later to have the test result interpreted. One-step TB testing was done using tuberculin purified protein derivative at a strength of 5 tuberculin units per 0.1-mL dose (Connaught Laboratories Ltd., Willowdale, Ont.). Simultaneous anergy testing measured delayed-type hypersensitivity to mumps (mumps skin test antigen; Connaught Laboratories) and *Candida* (*C. albicans* intradermal skin test solution, 1/100 dilution, Bencard Allergy Laboratories, Mississauga, Ont.). Tests were administered by the intradermal injection of 0.1 mL of antigen into the volar surface of the forearm. All test results were read using the palpation method, and the transverse diameter of induration was recorded.

The participants were all injection drug users whose current HIV status was not definitely known to the study investigators. Given the high risk of HIV infection in this population, an induration of 5 mm or greater for the tuberculin skin test was considered positive.[9] With respect to the anergy screen, failure to exhibit any induration at 48 to 72 hours was considered evidence of anergy.

Participants with a positive tuberculin skin test result or demonstrating anergy were referred to a TB clinic at a downtown teaching hospital for further medical assessment.

Confidentiality was assured, and unique identifiers were constructed for each participant. All participants were informed of the mandatory reporting system for TB. All subjects with a positive skin test result provided consent for the study coordinator to check the results of their medical assessment once they had been returned to the public health department. The study protocol was reviewed and approved by the University of Toronto Review Committee on the Use of Human Subjects.

The data were analysed using SPSS software (version 6.12; SPSS Inc., Chicago, 1996). Estimates of the prevalence of positive skin test results were calculated with 95% confidence intervals (CIs). Several independent variables were examined for their relation to a positive result. Bivariate analysis of these potential predictors of a positive result was carried out using χ^2 and Fisher's exact tests for categorical variables, and Student's *t*-test for continuous variables. A *p* value (two-tailed) of less than 0.05 indicated statistical significance.

Results

During the recruitment period 171 injection drug users were enrolled in the study. The flow of participants through the TB screening process is depicted in Fig. 1. Four of the subjects were excluded from skin testing: 3 had a history of active TB and 1 a history of completed prophylaxis for TB. A further 12 subjects were not compliant with returning for interpretation of their test result and were lost to follow-up.

The participants ranged in age from 20 to 61 years (median 37.5 years). Of the 171 recruited subjects, 160 (93.6%)
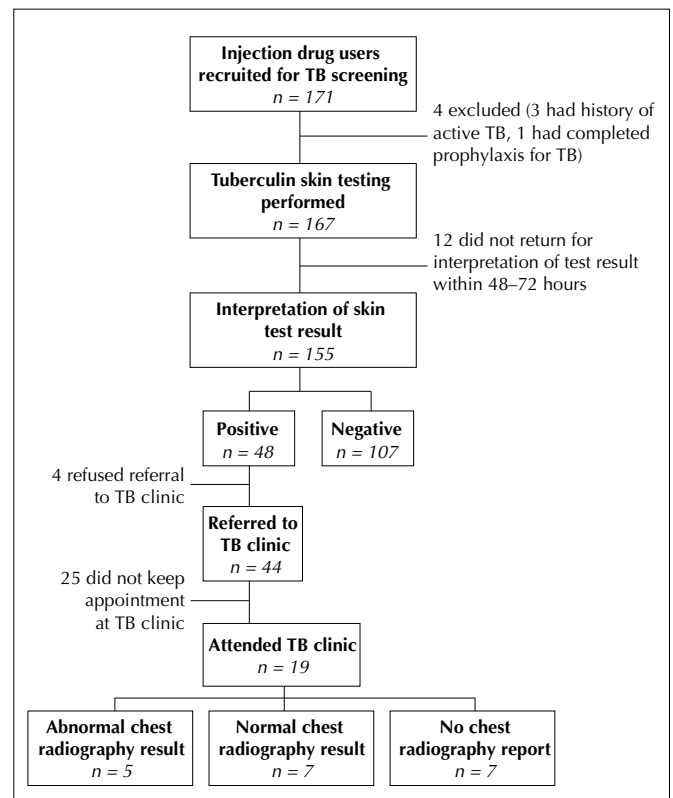

Fig. 1: Flow of study participants through tuberculosis screening and follow-up for medical assessment in a population of injection drug users in Toronto.

were men and 29 (17.0%) were born outside Canada. Ninety-eight (57.3%) reported injecting drugs at least once a day, with cocaine the drug most frequently used. A total of 107 (62.6%) of the participants had stayed in a shelter in the last year, and 145 (84.8%) reported being incarcerated at least once. Eight (4.7%) said that they were HIV positive.

Depending on the cut-off used (5 or 10 mm) the prevalence of positive tuberculin skin test results was 31.0% (95% CI 23.8% to 38.9%) for the 5-mm cut-off and 28.4% (95% CI 21.4% to 36.2%) for the 10-mm cut-off.

Table 1 presents sociodemographic characteristics, as well as exposure to prison or shelters, as predictors of a positive skin test result. Birth outside Canada and increasing age were both associated with a higher likelihood of a positive result. There were no significant associations between patterns of substance use (including alcohol use) and the prevalence of a positive result. There were also no differences in the prevalence of a positive result between subjects who had and those who had not been exposed to shelters or prison. Of the 8 participants who reported being HIV positive none had a positive tuberculin skin test result.

There were no anergic responses observed in the study population. Two subjects had marked reactions to the *Candida* antigen, which was subsequently removed from the skin test panel. All of the remaining participants who

were tested only with mumps antigen had a delayed type hypersensitivity reaction to this antigen.

A total of 48 participants with a positive skin test result were offered referrals to the TB clinic. In contrast to the 92.8% of subjects who returned for interpretation of the skin test results, only 19 (43.2%) of the 44 subjects who accepted referral to the TB clinic returned for the follow-up appointment. There were no confirmed cases of active TB among these 19 subjects.

Interpretation

The prevalence rate of 31% for a positive tuberculin skin test result in this population of injection drug users in Toronto represents a burden of *M. tuberculosis* infection in the range that has been cited in such populations elsewhere.[5,6] This rate is much higher than the rate of 0.4% to 16.4% reported in the general population.[10–12] This higher prevalence persists even when comparisons are made between specific segments of our study population and comparable subgroups of the Canadian population. For example, a positive skin test result was found among 38.1% of the subjects in our study aged 35 years and older, as compared with 28.3% among Ontario "chest clinic" patients older than 30 years.[12] As well, a positive result was found among 14.0% of the 50 Canadian-born subjects less than 35 years old in our study, as compared with 4.3% among young Canadian-born workers in a Montreal study reported in 1997.[10]

We used a 5-mm cut-off for the tuberculin skin test. However, because of the low prevalence of self-reported HIV seropositivity, we also examined the results using a more specific cut-off of 10 mm. Despite this doubling of the cut-off, 28.4% of the subjects were still found to have a positive skin test result. Using the estimated prevalence rate of 31.0% (95% CI 23.8% to 38.9%), it is conceivable that between 1900 and 3100 of the 8000 injection drug users in Toronto have *M. tuberculosis* infection.

As expected, increasing age and birth outside Canada were predictive of a positive tuberculin skin test result. The small number of female, aboriginal and HIV-positive injection drug users recruited into the study limited the power to detect a statistically significant association between these variables and *M. tuberculosis* infection. Similarly, the study probably lacked sufficient power to detect associations between substance use (including alcohol use) and *M. tuberculosis* infection.

The failure to detect a statistically significant association between shelter use or incarceration and *M. tuberculosis* infection may have been due to the small proportion of subjects who had not been exposed to these environments.

The absence of anergy in our study population contrasts with the rates of 9% to 46.5% reported among injection drug users in other populations.[13,14] The variability

Table 1: Predictors of a positive tuberculin skin test result among injection drug users in Toronto

Variable	No. (and %) of injection drug users n = 171	Prevalence of positive skin test result, %	p value
Age, yr			
< 35	58 (34.0)	19.0	0.01
≥ 35	97 (56.7)	38.1	
Sex			
Male	145 (84.8)	31.7	0.44
Female	10 (5.8)	20.0	
Country of birth			
Canada	130 (76.0)	25.4	< 0.001
Elsewhere	25 (14.6)	60.0	
Aboriginal status*			
Yes	8 (4.7)	37.5	0.42
No	122 (71.3)	24.6	
Education			
≥ grade 12	80 (46.8)	32.5	0.67
< grade 12	75 (43.9)	29.3	
History of shelter use			
Yes	100 (58.5)	33.0	0.46
No	55 (32.2)	27.3	
History of incarceration			
Yes	129 (75.4)	31.0	0.98
No	26 (15.2)	30.8	

*Status obtained only from Canadian-born subjects.

in the anergy results may be due to the lack of standardization of antigens, doses or interpretations of the skin test results.[15] Given the delayed type hypersensitivity responses to the mumps antigen observed, it is unlikely that the estimated prevalence of *M. tuberculosis* infection was affected by false-negative results.

Over 90% of the injection drug users in our study returned for interpretation of their skin test results within in the recommended timeframe. The relationship these people have with the needle-exchange program and the financial incentives we offered may have accounted for the observed compliance.

The lower compliance rate observed for medical follow-up may have been due to the hospital setting of the follow-up assessment, the early morning appointment times and the lack of additional financial incentives.

That skin test results were recorded for over 90% of the study subjects allows a confident estimation of the prevalence of *M. tuberculosis* infection in this study population. There is well-recognized variability in quantifying tuberculin skin test results.[16] However, the interpretation of all skin test results by one individual served to reduce this variability and further supports the estimated prevalence of *M. tuberculosis* infection.

The illicit nature of drug use in Canada hinders a true characterization of the population of injection drug users. The absence of subjects under the age of 20 and the small proportion of women recruited in our study limits the generalizability of our results to these groups.

A second limitation of the study design is the possible misclassification of injection drug user status. However, we controlled this by using a recruitment strategy that specifically targeted injection drug users, and we used strict eligibility criteria.

Implications for programs and policies

The high prevalence rate of *M. tuberculosis* infection in this population of injection drug users confirms their high-risk status for *M. tuberculosis* infection. Furthermore, our results suggest that compliance with screening is possible among injection drug users. However, TB screening of high-risk populations will be of little benefit without comprehensive follow-up and completion of treatment. Thus, strategies must be developed to ensure assessment and treatment of injection drug users with TB.

One way of overcoming some of the barriers to TB control in this population may be to have TB screening and possibly directly observed therapy conducted at needle-exchange sites and methadone clinics. In addition to the setting, factors such as flexible hours of access, transportation assistance and ensurance of short intervals between interpretation of skin test results and medical follow-up may

all serve to increase compliance in this population. Finally, the use of financial incentives for injection drug users to ensure their compliance with chemoprophylaxis and treatment of active TB should be considered.

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