Burden of HIV and tuberculosis co-infection in Montreal, Quebec

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ABSTRACT

OBJECTIVE: Define the burden of HIV-TB co-infection and predictors of HIV screening among incident TB cases.

METHODS: Analysis of surveillance data on TB incident cases reported to Montreal's Public Health Department from 2004 to 2009. Among all reported TB cases, proportions of cases with HIV testing and HIV infection were calculated by patient characteristics. A test for linear trends was performed on the annual proportions of HIV-tested and HIV-positive cases. Adjusted odds ratios (AOR) for HIV testing at time of TB diagnosis were computed.

RESULTS: A total of 778 incident TB cases were included in the analysis. HIV testing was reported for 50.8% (n=395) of cases. The proportion of HIV-tested cases increased significantly from 43% in 2004 to 70% in 2009. HIV-TB co-infection was found in 9.3% of patients with reported HIV status or in 4.2% of the overall cohort. HIV prevalence was high in men, individuals aged 40-59, those originating from Sub-Saharan Africa and the Caribbean, and the homeless. Multivariate analysis revealed that HIV testing at time of TB diagnosis was performed mainly for subjects born in the Caribbean, Central or South America, or Sub-Saharan Africa, those with pulmonary disease, and injection drug users.

CONCLUSIONS: Although reporting of HIV testing among incident TB patients increased, targeted HIV testing still occurs. HIV prevalence in TB cases remained stable during the study period; however, it may be underestimated due to missed opportunities for HIV testing and under-reporting.

KEY WORDS: HIV screening; comprehensive care; universal testing; tuberculosis; surveillance

La traduction du résumé se trouve à la fin de l'article.

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Early initiation of antiretroviral therapy in HIV-infected individuals can improve survival outcomes[1,2] and reduce HIV transmission.[3,4] Unfortunately in North America, there is a reported tendency for late first presentation for HIV care.[5] In addition, a French multicentre study asserted that 82% of HIV-positive patients who contacted health care facilities with HIV-related conditions[6] prior to their HIV diagnosis were not offered HIV testing at that time. Globally, tuberculosis (TB) is the most common, potentially fatal opportunistic infection affecting HIV-positive individuals.[7-9] HIV increases morbidity and mortality in patients with latent and active TB.[10-12] Failure to recognize HIV infection in TB patients in a timely fashion leads to inadequate clinical case management. The World Health Organization (WHO) considers HIV surveillance among TB patients as a critical component of comprehensive HIV/AIDS care.[13]

In Canada, universal HIV testing of TB cases has been recommended since 2002.[14,15] However, despite these recommendations, HIV-testing report rates remain low. Thus, in 2009, there were 1,658 new active and relapsed TB cases reported to the Canadian Tuberculosis Reporting System (CTBRS) with a corresponding incidence rate of 4.9 per 100,000 population. HIV status was known for 650 of those cases (39%) and 9.8% were positive.[16]

Montreal, the major Quebec census metropolitan area, accounts for 70% of all new TB cases[17] and 65% of all newly diagnosed HIV cases[18] reported in the province.

In the current study, we quantified the proportion of TB patients in Montreal who were tested for HIV, evaluated the burden of HIV-TB co-infection, and examined the predictors of HIV testing at time of TB diagnosis.

METHODS

Data source

In Quebec, it is mandatory to report incident TB cases. In Montreal, each case is assigned to the nurse case manager at the public health department (Direction de santé publique, DSP) and standardized information on clinical, epidemiological, and socio-demographic characteristics is collected. The nurse also ensures that adequate treatment is initiated according to baseline drug sensitivities of the *Mycobacterium tuberculosis* (MTB) isolate, verifies patient adherence to treatment and initiates contact investigation.

All incident cases reported from January 1, 2004 to December 31, 2009, confirmed by culture or diagnosed on the basis of clinical and radiological signs were retrieved for analysis. Data were also extracted on demographic characteristics, clinical information, HIV

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Table 1. Characteristics of TB cases, proportion tested for HIV infection and factors associated with HIV testing, Montreal, 2004-2009

Characteristic	Number (%)	% tested for HIV	OR (95% CI)‡	AOR (95% CI)‡
Sex				
Male	422 (54.2)	53.6	1.2 (0.9-1.7)	1.0 (0.7-1.4)
Female	356 (45.8)	47.5	**Reference**	**Reference**
Age group* (years)				
0-18	34 (4.4)	55.9	0.8 (0.4-1.8)	0.6 (0.3-1.7)
19-29	183 (23.5)	56.3	0.8 (0.5-1.3)	0.7 (0.4-1.1)
30-39	186 (23.9)	64.0	**Reference**	**Reference**
40-49	119 (15.3)	61.3	0.6 (0.4-1.1)	0.6 (0.3-1.001)
50-59	84 (10.8)	46.4	**0.4 (0.2-0.8)**	**0.4 (0.2-0.7)**
60 and over	172 (22.1)	24.4	**0.2 (0.1-0.4)**	**0.2 (0.1-0.3)**
Region of birth*				
Asia	274 (35.2)	46.7	1.6 (0.9-2.6)	1.6 (0.9-3.0)
Caribbean	102 (13.1)	58.8	**2.4 (1.3-4.5)**	**2.6 (1.3-5.5)**
Central/South America	28 (3.6)	67.9	**4.8 (1.9-12.1)**	**3.7 (1.3 -10.7)**
Europe	66 (8.5)	43.9	1.4 (0.7-2.9)	2.1 (0.9-4.9)
Middle East/North Africa	46 (5.9)	47.8	1.5 (0.7-3.3)	1.2 (0.5-2.9)
Canada	108 (13.9)	39.0	**Reference**	**Reference**
Sub-Saharan Africa	120 (15.4)	70.0	**3.4 (1.9-6.3)**	**2.5 (1.2-5.3)**
Unknown/Other	34 (4.4)	32.4	1.2 (0.5-2.8)	1.4 (0.5-4.0)
TB status†				
Positive culture	701 (93.2)	50.8	1.7 (0.9-3.4)	
Negative culture	51 (6.8)	47.1	**Reference**	
Infection site*				
Pulmonary	550 (70.7)	57.6	**3.7 (2.5-5.4)**	**4.5 (2.9-6.9)**
Other	228 (29.3)	34.2	**Reference**	**Reference**
Alcohol use	37 (4.8)	62.2	1.3 (0.6-2.8)	
IV drug use*	25 (3.2)	80.0	**3.7 (1.3-10.7)**	**4.0 (1.2-13.4)**
Incarceration	10 (1.3)	50.0	0.6 (0.1-3.1)	
Homelessness	10 (1.3)	70.0	1.5 (0.3-7.5)	
Recent TB exposure	65 (8.3)	58.5	1.4 (0.8-2.4)	
Co-morbidities*	90 (11.6)	36.7	**0.5 (0.3-0.8)**	1.0 (0.5-1.8)
Total	778 (100)	50.8		

* $p<0.05$.
† 26 values were missing.
‡ Number of cases in the analysis is 675.

testing and HIV status, as well as on medical and socio-behavioural HIV or TB risk factors.

Statistical analysis

The outcome variables were reported HIV testing, HIV testing at the time of TB diagnosis, and HIV status. For this analysis, site of TB infection was classified as pulmonary if any part of the lungs was affected, including miliary TB. Patients' countries of birth were grouped according to geographical region. If patient data were missing on any HIV or TB risk factor of interest (alcohol abuse, intravenous drug use (IV drug use), history of incarceration and/or homelessness, close contact with an active TB case and co-morbidities such as cancer, diabetes, silicosis, and renal insufficiency), the patients were classified as not having this risk factor.

Descriptive summary statistics were presented as median and interquartile range (IQR) for continuous variables, and as frequencies and percentages for categorical variables. Chi-square, Fisher's exact tests and Student's t-test were used to evaluate univariate associations according to level of measurement.

For the HIV prevalence analysis, rates with 95% confidence intervals (CI) were estimated for TB cases with reported HIV status and for all incident TB cases. Among the latter, patients for whom information on HIV testing was missing were assumed to be HIV negative.

Unconditional logistic regression was performed to examine the effects of various patient characteristics on likelihood of HIV testing at time of TB diagnosis. Variables that showed statistical significance at $p<0.05$ in the univariate analysis were included in the final model (region of birth, site of infection, IV drug use, year of TB diagnosis, and reported co-morbidities). The variables sex and age were included in the final model irrespective of their strength of association. Crude odds ratios (OR) and adjusted odds ratios (AOR) with 95% CI were estimated. HIV testing at time of TB diagnosis was defined as testing done in a time interval from one month before to six months after date of TB diagnosis, that is, HIV testing done around the time of initial clinical investigation for TB and at any time throughout the standard TB treatment period. Ninety-six cases with reported HIV testing but for whom information on the date of the test was missing, as well as seven cases known to be HIV-positive prior to TB diagnosis were excluded from the analysis.

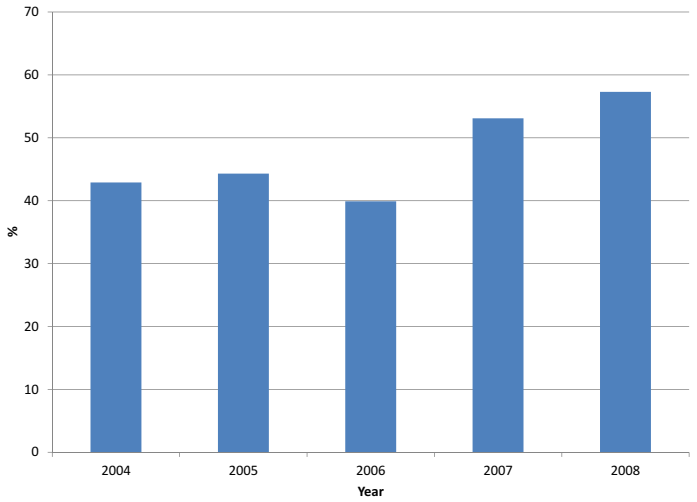

Figure 1. Proportion of TB incident cases with reported testing for HIV, Montreal, 2004-2009

Table 2. Incident TB-HIV co-infected cases by year, Montreal, 2004-2009

	2004	2005	2006	2007	2008	2009	p*
N	5	5	4	7	8	4	–
% among TB cases with reported HIV testing	9.8	10.2	7.7	12.3	11.0	5.4	0.60
% among all TB cases	3.8	3.8	2.9	5.5	6.1	3.4	0.60

* Chi-squared test for trend.

Table 3. Rates of HIV seroprevalence among TB cases, Montreal, 2004-2009

Characteristic	Cases with reported HIV status	HIV positive	HIV positive among cases with reported HIV status	HIV positive among all incident TB cases
	N	N	% (95% CI)	% (95% CI)
Sex				
Female	147	7	4.8 (1.3-8.2)	2.0 (0.5-3.4)
Male	209	26	12.4 (7.9-17.0)	6.2 (3.9-8.5)
Age group (years)				
0-29	108	7	6.5 (1.8-11.2)	3.2 (0.9-5.6)
30-39	107	10	9.3 (3.7-15.0)	5.4 (2.1-8.6)
40-49	66	9	13.6 (5.1-22.1)	7.6 (2.7-12.3)
50-59	35	6	17.1 (4.0-30.3)	7.1 (1.5-12.8)
60 and over	40	1	2.5 (0.0-7.6)	0.6 (0.0-1.7)
Region of birth				
Asia	113	3	2.7 (0.0-5.7)	1.1 (0.0-2.3)
Caribbean	54	9	16.7 (6.4-26.9)	8.8 (3.2-14.4)
Central/South America	18	0		
Europe	26	0		
Middle East/North Africa	18	0		
Canada	39	4	10.3 (0.3-20.2)	3.7 (0.1-7.3)
Sub-Saharan Africa	80	17	21.3 (12.1-30.4)	14.2 (7.8-20.5)
Unknown/Other	8	0		
TB status*				
Positive culture	320	30	9.4 (6.2-12.6)	4.3 (2.8-5.8)
Negative culture	22	0		
Infection site				
Pulmonary	287	28	9.8 (6.3-13.2)	5.1 (3.2-6.9)
Other	69	5	7.3 (1.0-13.5)	2.2 (0.3-4.1)
Alcohol use	21	3	14.3 (0.0-30.6)	8.1 (0.0-17.3)
IV drug use	18	3	16.7 (0.0-35.7)	12.0 (0.0-25.7)
Incarceration	4	1	25.0 (0.0-100.0)	10.0 (0.0-32.6)
Homelessness	6	3	50.0 (0.0-100.0)	30.0 (0.0-64.6)
Recent TB exposure	35	1	2.9 (0.0-8.7)	1.5 (0.0-4.6)
Co-morbidities	30	7	23.3 (7.3-39.4)	7.8 (2.1-13.4)
Total	356	33	9.3 (6.2-12.3)	4.2 (2.8-5.7)

* 26 values were missing for all patients and 14 for those with reported HIV test results.

A chi-squared test for trends was performed on the annual proportions of HIV-tested and HIV-positive cases over the study period. Data were analyzed using SAS software (version 9.3, SAS Institute, Cary, NC).

This evaluation of the DSP's surveillance program did not require ethics approval.

RESULTS

A total of 778 incident TB cases were reported to Montreal's DSP during the study period, 54.2% of whom were male. Median age was 38.0 (IQR: 28.0-57.0). There were 104 Canadian-born non-Aboriginal and 4 Canadian-born Aboriginal TB cases. Cases born in Canada made up 13.9% of the study population. The majority of TB cases were foreign-born and came from Asia (35.2%), Sub-Saharan Africa (15.4%), the Caribbean (13.1%), Europe (8.5%), the Middle East and North Africa (5.9%), Central or South America (3.6%), or other regions (4.4%). Among all cases, 93.2% of TB diagnoses were confirmed microbiologically, 70.7% of cases had pulmonary disease and 14.5% had at least one recorded HIV or TB risk factor (Table 1).

Overall, HIV testing was reported for 50.8% (n=395) of TB incident cases. The proportion of HIV-tested cases significantly increased from 43% in 2004 to 70% in 2009 ($p<0.001$) (Figure 1). Information on HIV status was available for 90% of those for whom HIV testing was reported. Of 39 HIV-tested cases but for whom information of HIV status was missing, 35 (85.9%) were immigrants and 22 (56.4%) female, the median age was 33.0 years (IQR: 25.0-47.0).

Of the 356 TB cases for whom HIV status had been reported, 33 (9.3%; 95% CI: 6.2-12.3) had HIV infection, that is, 4.2% (95% CI: 2.8-5.7) of the overall cohort. There was no significant change in the annual prevalence of HIV-TB co-infected cases among all new TB patients over the study period ($p=0.6$) (Table 2). The median age of HIV-positive individuals was 39.0 years (IQR: 32.0-48.0), and there were 3.7 times more men than women. Among the overall cohort of incident TB cases, HIV prevalence was higher in those originating from high HIV burden countries: 14.2% (95% CI: 7.8-20.5) of individuals from Sub-Saharan Africa and 8.8% (95% CI: 3.2-14.4) from the Caribbean were HIV positive. HIV prevalence in Canadian-born incident TB patients was 3.7% (95% CI: 0.1-7.3). There were no HIV-positive TB cases among Aboriginals, and those originating from Central or South America, Europe, the Middle East and North Africa, or those from the group of countries classified as unknown/other (Table 3).

A total of 675 incident TB cases were included in the analysis on predictors of HIV testing at time of TB diagnosis (Table 4). The 96 cases with reported HIV testing but with missing values on the date of the test were compared to the cases for whom information on the date of HIV test was available. There were no significant differences in distribution by age, sex and ethnicity between the groups.

Table 4. Partition of reported incident TB cases for the analysis of predictors of HIV testing at the time of TB diagnosis, Montreal, 2004-2009

	Reported HIV testing at the time of TB diagnosis		Excluded from the analysis
	Yes	No	
HIV testing done from 1 month before to 6 months after TB	270		
HIV (+) cases with HIV testing more than 1 month before TB			7
HIV (-) cases with HIV testing more than 1 month before TB		17	
HIV testing more than 6 months after TB		5	
Reported HIV testing, but missing information of the date of the test			96
No reported HIV testing		383	
Total	270	405	103

Estimated crude odds ratios for likelihood of HIV testing at time of TB diagnosis were significant for age, region of birth, site of infection, reported history of IV drug use and reported presence of co-morbidities (Table 1).

Adjusted regression analysis revealed that the likelihood of being tested for HIV at time of TB diagnosis declines with increasing age. Thus, compared with those aged 30-39, cases aged 50-59 years and 60 years or older were 2.5 and 5 times less likely, respectively, to have been tested for HIV (adjusted odds ratio (AOR) = 0.4; 95% CI: 0.2-0.7 and AOR = 0.2; 95% CI: 0.1-0.3, respectively) (Table 1). Subjects born in the Caribbean (AOR = 2.6; 95% CI: 1.3-5.5), Central or South America (AOR = 3.7; 95% CI: 1.3-10.7) and Sub-Saharan Africa (AOR = 2.5; 95% CI: 1.2-5.3) were more likely to be tested for HIV than Canadian-born cases. Cases with pulmonary TB had a higher likelihood of being tested than cases with extrapulmonary TB (AOR = 4.5; 95% CI: 2.9-6.9). Injection drug users were 4 times more likely to undergo HIV testing than non-users (AOR = 4.0; 95% CI: 1.2-13.4) (Table 1).

DISCUSSION

In 2004-2009, an average of 50.8% of incident TB cases had reported HIV testing in Montreal. The proportion of cases with reported HIV testing rose significantly during the study period and reached 70% in 2009. However, the actual proportion of TB cases tested for HIV may differ: in our study no medical file reviews were performed by the case managers, who had to rely on information given by various sources (e.g., treating physicians, TB clinic nurses or the patients themselves). Furthermore, information on the date of the test was missing for 24% of individuals tested, and information on HIV test results had not been recorded for 10% of HIV-tested TB cases. Case managers should direct more efforts towards the immigrants as this group had the most missing data. Since 2002, Citizenship and Immigration Canada (CIC) has required mandatory HIV testing as a part of the Immigration Medical Examination for immigrants and refugees.[19] However, during our study period, the transfer of information from CIC to the Montreal DSP was not effectuated and thus our figures on HIV prevalence are likely underestimated.

Based on the information available, HIV prevalence among the overall cohort of incident TB cases was 4.2% (95% CI: 2.8-5.7) with no significant change from 2004 to 2009, a figure substantially higher than the estimated national HIV prevalence (208.0 per 100,000).[20] There were almost 4 times more men than women among HIV-infected TB cases, which is consistent with Canadian estimates.[5]

In 2004-2009, HIV prevalence among all incident TB cases was positively correlated with patient age up to 60 years, after which it fell significantly. Although patients aged 50-59 were less likely to be tested, the age-specific HIV prevalence was high in this group. This is consistent with the results of the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) study, which demonstrated that from 1997 to 2007 there was an increase in the proportion of newly diagnosed HIV-infected individuals over 50 years old.[21] In our study, burden of infection remains high in vulnerable populations, that is, those who reported alcohol abuse, history of IV drug use, homelessness and detention at a correctional facility. HIV prevalence was higher among foreign-born cases originating from the HIV-endemic regions of Sub-Saharan Africa and the Caribbean. Of the 33 HIV-positive TB cases, 29 (87.9%) were immigrants. Among the latter, 7 cases had a known positive HIV status before TB diagnosis. Although we were unable to get information on clinical management of their HIV infections, these cases could be regarded as missed opportunities for TB prevention.

Our study shows that despite likely improvements in physician compliance with Canadian standards, targeted HIV testing remains. At the time of TB diagnosis, physicians are more likely to order an HIV test if a patient reports a history of IV drug use or originates from Sub-Saharan Africa, the Caribbean, South or Central America. Although reporting requirements in Montreal do not differ according to site of TB, case managers carry out less extensive follow-up procedures in terms of contact investigation and detailed clinical management, including HIV testing and HIV status, for extrapulmonary forms of TB. Thus, missing information could introduce a potential misclassification of non-HIV-tested extrapulmonary TB patients; it could also partially explain why patients with pulmonary disease had higher odds of being tested for HIV compared to those with extrapulmonary TB, which contradicts what has been reported elsewhere.[22]

Patient selection was similar in a study analyzing screening practices for TB among HIV-infected patients in a Montreal HIV clinic. Despite acknowledging HIV patients as a target group for universal latent TB screening, clinicians were more likely to test those originating from WHO-recognized high-burden TB countries or HIV-endemic countries.[23]

Overall, knowledge of HIV status of TB cases has risen in Montreal over the period 2004-2009. This may be due to continual improvement in screening practices and surveillance (better data entry, collection of information from TB patients, reporting of HIV status by clinicians). However, screening rates are most likely still below target values. Although it may be desirable to promote universal HIV screening of TB patients, our data tend to indicate that the current targeted testing seems to identify most of the TB-HIV co-infections as the rates of overall co-infected cases remained stable regardless of a notable increase in reported screening. Nonetheless, enhanced reporting of information concerning TB cases, including information on HIV status, is essential to efficiently monitor the burden of dual infection and to plan and evaluate programs for control and prevention.

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RÉSUMÉ

OBJECTIFS : Estimer le fardeau de la coinfection par le virus de l'immunodéficience humaine (VIH) et la tuberculose (TB) et les facteurs prédictifs du dépistage du VIH chez les cas incidents de TB.

MÉTHODES : Les données de surveillance de la TB chez les cas incidents déclarés à la Direction de santé publique de Montréal de 2004 à 2009 ont été analysées. Parmi l'ensemble des cas de TB déclarés, la proportion de cas dépistés pour le VIH et la proportion des cas infectés par le VIH ont été calculées en fonction des caractéristiques des patients. Le test du χ^2 pour les tendances linéaires a été utilisé pour évaluer l'évolution des proportions annuelles des cas qui étaient testés et des cas qui étaient séropositifs. Des rapports de cotes pour le dépistage du VIH au moment du diagnostic de la TB ont été calculés après ajustement.

RÉSULTATS : Un total de 778 cas de TB ont été inclus aux fins d'analyse. Le résultat du dépistage du VIH était disponible pour 50,8 % (n=395) des cas. La proportion des cas dépistés pour le VIH a augmenté de façon significative passant de 43 % en 2004 à 70 % en 2009. La coinfection VIH-TB était présente chez 9,3 % des patients dont le résultat du dépistage du VIH était disponible ou chez 4,2 % de l'ensemble des patients. La prévalence du VIH était plus élevée chez les personnes de sexe masculin, chez les personnes âgées de 40 à 59 ans, chez les personnes nées en Afrique sub-saharienne et dans les Caraïbes et chez les personnes sans-abri. L'analyse multivariée a montré que le dépistage du VIH au moment du diagnostic de la TB était plus fréquent chez les cas nés dans les Caraïbes, en Amérique centrale ou du Sud et en Afrique sub-saharienne, chez les patients atteints de TB pulmonaire et chez les utilisateurs de drogues injectables.

CONCLUSION : Bien que le dépistage du VIH parmi les cas incidents de TB augmente, il reste influencé par le profil du patient. La prévalence du VIH parmi les cas de TB est restée stable pendant la période à l'étude; cependant, cette prévalence pourrait être sous-estimée par les occasions de dépister manquées et la sous-déclaration des résultats du dépistage lorsqu'il est fait.

MOTS CLÉS : dépistage du VIH; soins globaux; dépistage systématique; tuberculose; surveillance