Tuberculosis and AIDS Co-Morbidity in Brazil: Linkage of the Tuberculosis and AIDS Databases

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This study evaluated differences in AIDS patients with and without tuberculosis (TB) in Espírito Santo State, Brazil. Standard regional AIDS (SINAN, SISCEL, SICLOM and SIM) and tuberculosis (SINAN) databases were used. TB and AIDS databases were linked using Reclink software, version 3, with SPSS software support to identify co-infected cases. Data from July 2000 to June 2006 in Espírito Santo State were linked. The results showed 3,523 adult AIDS cases and 9,958 adult TB cases resulted in 430 co-infected patients, who were compared to 1,290 AIDS patients who never developed TB. Among 430 co-infected patients, TB was diagnosed first in 223 (51.9%), AIDS was first in 44 (10.2%), and AIDS and TB were diagnosed concurrently in 163 (37.9%). Median age did not differ between co-infected cases (36 years (interquartile range [IQR] 29-43) and non-co-infected cases (34 years; IQR 28-42). Pulmonary tuberculosis was diagnosed in 239 (55.6%); 109 (25.3%) had extra-pulmonary TB and 82 (19.1%) had both presentations. In the final logistic regression model, living in a metropolitan area [Odds Ratio (OR)=1.43 (95% Confidence Interval (CI) 1.05-1.95)], education ≤ 3 years [OR=3.03 (95%CI 1.56-5.88)] and CD4 counts ≤ 200/mm³ [OR=1.14 (95%CI 1.09-1.18)] were associated with co-infection. This report emphasizes the significance of tuberculosis among AIDS cases in Brazil, and highlights the importance of evaluating secondary data for purposes of improving data quality and developing public health interventions.
Key-Words: AIDS, tuberculosis, co-infection, secondary data.

HIV-infected patients are more likely to experience endogenous reactivation of a latent tuberculosis (TB) infection or rapidly progress from recent TB infection to TB disease than HIV-negative persons [1-3]. Thus, HIV-infected patients represent a source of potential TB index cases, which may increase incidence of TB disease and infection in the community [4,5].

There is often lack of communication between AIDS and TB programs and co-infected patients are often not detected until death, highlighting a failure of the health system to detect, diagnosis and treat these related diseases. Co-infection rates have been reported as high as 51% in mortality surveillance systems in Rio de Janeiro, Brazil [6], and more recently, an AIDS and TB database registry match found 18.5% of AIDS patients between 1995 and 2004 to be co-infected in Rio [7]. HIV-infected patients are at increased risk for reactivation of a latent TB infection [8] due to a deficient immunological response [9], while AIDS is a strong risk factor for death in TB patients [1,8]. Mortality in co-infected patients is commonly related to delays in diagnosis as HIV patients may postpone seeking health care to avoid receiving an AIDS diagnosis [10].

In Brazil, 506,499 cases of AIDS have already been reported through December 2007. Incidence increased through the mid-1990s with a peak of 19/100,000 in 1998. Approximately 80% of AIDS patients inhabit the South East and South regions of Brazil. The South East, where Espirito Santo State is located, is the most affected since the beginning of the epidemic but, despite the high incidence rate, the number of AIDS cases in the region remains stable at approximately 17,000 per year [11]. In 2007, 602 AIDS cases were reported in Espírito Santo State for an incidence of 7.2/100,000. TB incidence in the State was 56/100,000 in 2007, similar to the national average of 54.7/100,000 [11].

The objective of this study was to utilize and link existing TB and AIDS surveillance databases to evaluate the profile of TB-AIDS co-infected cases as defined by sex, age, immunity and death. These data provide an updated account of TB-AIDS co-infection in the State that will inform prevention and control programs for these two diseases.

Material and Methods
Study Design
A comparative study was designed to identify differences among AIDS patients with or without tuberculosis detected through linkage of regional comprehensive databases. These databases support the improvement of health care systems in Brazil by increasing the capacity of health care workers to make decisions based on accurate information.

Data Collection and Management Plan
Linkage of TB and AIDS databases was performed using Reclink software, version 3 [12], with SPSS software support to identify co-infected cases. Data from Espírito Santo State, July 2000 to June 2006, were linked. The AIDS database included data from SINAN (Morbidity Surveillance Database), SIM (Mortality Surveillance Database), SISCEL (AIDS

Laboratory Database) and SICLOM (Antiretroviral Control System Database).

Surveillance databases were compared using patient name, mother's name and date of birth with a math probability of 92% for names and 90% for dates. Block variables with patient's first and last names and gender were created to optimize the procedure and identify patients present in both databases. These data were checked individually to confirm co-infection, exclude duplicity and complete missing information. Any diagnoses of TB and AIDS within 90 days of each other were considered to be diagnosed at the same time. Patients < 14 years old were excluded. For each TB-AIDS co-infected case, the next three AIDS patients that were never reported to be co-infected with TB were chosen for comparison from the AIDS database.

Statistical Methods

Standard descriptive statistical analyses were performed, including frequency distributions for categorical data and calculation of medians and interquartile ranges for continuous variables. Prevalence of TB-AIDS co-infection was calculated for each risk factor of interest and odds ratios (OR) and 95% confidence intervals (CI) estimated the strength of associations. Variables significant at $p < 0.15$ in bivariate analyses, and additional variables based on known *a priori* associations, were considered in the multivariate analysis. The main risk factors were assessed by stepwise multiple logistic regression models, with 15% as the critical p-value for variable entry and 10% as the criterion for variable elimination.

Results

Three AIDS databases and the national mortality surveillance database were merged, cleaned and validated by the Brazilian Ministry of Health prior to our linkage with the tuberculosis database. This preliminary process added 887 AIDS cases to the 2,908 reported in the Morbidity Surveillance System (SINAN-AIDS). There were a total of 3,795 AIDS cases in the 4 databases from 2000 to 2006. After eliminating AIDS cases < 14 years of age, 3,523 AIDS patients remained for linkage with 9,958 TB cases in the State TB database. Among these 3,523 AIDS cases, TB-AIDS co-infection was found in 430 [12.2% (95%CI 11.1%-13.3%)] records. Among co-infected cases, TB was the first infection in 223 (51.9%), AIDS was first in 44 (10.2%) cases, and in 163 (37.9%) AIDS and TB were diagnosed at the same time. Regarding TB presentation in these patients, 239 (55.6%) were pulmonary, 109 (25.3%) extra-pulmonary and 82 (19.1%) had both presentations. Lymphatic TB was the most frequent extra-pulmonary presentation (23.2%). Approximately 90% of all co-infected cases were diagnosed with TB within one year of AIDS diagnosis.

Demographic variables of AIDS cases with and without TB are shown in Table 1. Median age in co-infected cases was 36 (interquartile range [IQR] 29; 43) years and 34 (IQR 28; 42) years among AIDS cases. Co-infected cases were more likely to be male, live in a metropolitan area, and be less educated in

bivariate analysis. Co-infected patients were also more likely to be reported in the AIDS database (SINAN-AIDS) compared to AIDS patients not co-infected with TB. Table 2 shows behavioral and clinical variables of AIDS cases with and without TB. Co-infected patients were more likely to have a CD4 count ≤ 200. No other behavioral or clinical factors were significantly different.

In the final logistic regression model, living in a metropolitan area [adjusted (a)OR=1.43 (95%CI 1.05-1.95)], lower education (up to three years) [aOR=3.03 (95%CI 1.56-5.88)] and lower CD4 counts [aOR=1.14 (95%CI 1.09-1.18)] were associated to co-infected cases.

Discussion

This study investigating the prevalence of co-infection of TB and AIDS in Espirito Santo State, Brazil found that 12.2% of AIDS cases between 2000 and 2006 were co-infected with TB, slightly less than recently reported in Rio de Janeiro, Brazil [7]. An increased association with TB-AIDS co-infection was seen among AIDS patients living in the metropolitan area, and those with less education and lower baseline CD4 counts. These results are in agreement with other studies in Brazil [13-16] and other areas [15,16].

It is important to use secondary data for assessing health programs and for implementing cost-effective health strategies. However, the data must be analyzed and interpreted appropriately [18] and there is an underlying assumption that data collection is relatively complete. The databases used in this analysis were developed to support the improvement of health care systems in Brazil by increasing the capacity of health care workers to make decisions based on accurate surveillance information. Previous investigators in Brazil have used these techniques to merge databases for improving surveillance information and implementing health strategies [12,19-21]. We found that 23% of all AIDS cases used to initiate our linkage process were not reported to the national AIDS database (SINAN-AIDS) and a large proportion of patients had missing data regarding behavioral risk factors and CD4 cell counts. Such underreporting of patients and patient data can have a dramatic impact on programs and interventions informed by these estimates.

Lower education was an important factor in TB-AIDS cases found in this study. In the last decade, the AIDS epidemic in Brazil has reached new population groups and cities where it had not been recorded previously, affecting the less privileged social segments in the country [16,22]. These populations have historically been plagued with high TB rates; thus, the introduction of the AIDS epidemic has worsened the TB problem. Our data suggests that TB-AIDS cases are poorer than AIDS cases without TB, using education as a proxy measure for poverty. Impoverished areas arise out of a socio-political context on differential access to power and resources. In this context, poverty is associated with little or no power, and extremely limited resources. Thus, poverty dramatically increases risk for HIV/AIDS and TB through increased

Table 1. Demographic data of AIDS cases with and without TB in Espírito Santo State, Brazil.

Variables	AIDS without TB N (%)	AIDS with TB N (%)	OR (95%CI)
Living in			
Metropolitan area	1,092 (76.0)	345 (24.0)	1.4 (1.03-1.80)[2]
Other	198 (70.0)	85 (30.0)	1
Surveillance at			
Metropolitan area	1,237 (74.8)	417 (25.2)	1.4 (0.74-2.54)
Other	53 (80.3)	13 (19.7)	1
Age (years)			
13-24	163 (79.5)	42 (20.5)	1
25-34	494 (75.9)	157 (24.1)	0.9 (0.49-1.65)
35-44	404 (74.7)	137 (25.3)	1.1 (0.64-1.65)
45-54	163 (68.5)	75 (31.5)	1.2 (0.68-2.03)
55 or more	66 (77.6)	19 (22.4)	1.6 (0.90-2.85)
Sex			
Male	711 (70.8)	293 (29.2)	1.7 (1.38-2.19)[1]
Female	579 (80.9)	137 (19.1)	1
Education (years)			
Illiterate	67 (64.4)	37 (35.6)	2.5 (1.24-5.25)[2]
1-3	237 (64.8)	129 (35.2)	2.5 (1.33-4.75)[2]
4-7	461 (74.1)	161 (25.9)	1.6 (0.86-3.01)
8-11	277 (83.7)	54 (16.3)	0.9 (0.46-1.75)
12 or more	60 (82.2)	13 (17.8%)	1
Missing values	188 (83.9)	36 (16.1%)	0.9 (0.44-1.78)
AIDS Surveillance			
SINAN	997 (73.6)	357 (26.4)	1.4 (1.08-1.91)[2]
Other databases*	293 (80.1)	73 (19.9)	1

* SISCEL, SICLOM, SIM; [1] $p<0.01$; [2] $p<0.05$.

exposure and greater vulnerability to infection [17,23,24]. Once infected, capacity to cope with the consequences of disease is diminished among poorer people because of barriers to access of preventive, diagnostic and curative services [17].

Efforts to prevent and control HIV/AIDS and TB in impoverished populations are not likely to succeed outside of an integrated approach that seeks to reduce the underlying social inequities. A challenge in addressing AIDS and TB in informal settlements is how to strategically utilize potential opportunities to create lasting improvements in urban areas with impoverished conditions so they are better equipped to reduce vulnerability to HIV/AIDS and TB, and to access the full range of health care services to prevent, treat and mitigate these diseases.

The present study also found an association between TB-AIDS co-infection and low CD4 cell counts, an association commonly observed in Brazil [25] and other areas [26]. TB patients who are HIV-infected with low CD4 cell counts frequently have chest radiographic findings that are not typical of pulmonary TB. In particular, they are more likely than TB patients who are not HIV-infected to have mediastinal adenopathy and less likely to have upper-lobe infiltrates and cavities [3,18]. Atypical radiographic findings increase the potential for delays in diagnosis, which increases transmission among patients and their contacts [27].

The most important limitation of this study is the definition of TB-AIDS co-infection, which includes patients diagnosed with TB prior to AIDS, AIDS prior to TB and patients diagnosed with both at the same time. By combining this group and comparing it to AIDS patients who never developed TB, we are not able to detect differences specific to one of these groups. Another limitation is that we only have dates for AIDS diagnoses, and not HIV-diagnoses. A TB diagnosis among an HIV-infected patient in Brazil is not an AIDS defining illness on its own. Thus, the timing of HIV, AIDS and TB is difficult to determine, which lead to the decision to combine these patient groups.

The most important strength of this study was the inclusion of four different databases that maximized the number of AIDS patients included in the linkage process. This approach revealed a significant underreporting problem of AIDS cases, in addition to a surprising number of individuals with missing data regarding behavioral risk factors and CD4 cell count data. These findings highlight the need for better surveillance procedures in AIDS patients, and further training and education of health care providers to ensure more complete and accurate data collection. These measures are a minimal expectation if surveillance databases are to be used for program development.

Table2. Behavioral and clinical data of AIDS cases with and without TB in Espírito Santo State, Brazil.

Variables	AIDS with TB	AIDS without TB	P value
Heterosexual			
Yes	241 (24.2%)	753 (75.8%)	0.481
No	97 (26.2%)	273 (73.8%)	
Unknown	92 (25.8%)	264 (74.1%)	
Bi/homosexual			
Yes	67 (25.0%)	201 (75.0%)	0.915
No	271 (24.7%)	825 (75.3%)	
Unknown	92 (25.8%)	264 (74.2%)	
IV Drug abuse			
Yes	38 (29.5%)	91 (70.5%)	0.400
No	300 (24.3%)	935 (75.7%)	
Unknown	92 (25.8%)	264 (74.2%)	
CD4 counts			
Up to 200	182 (25.6%)	526 (74.4%)	0.000
More than 200	133 (18.3%)	594 (81.7%)	
Missing values	115 (40.6%)	170 (59.4%)	
Death			
Yes	34 (20.0%)	136 (80.0%)	0.135
No	396 (25.5%)	1,154 (74.5%)	

This report emphasizes the significance of tuberculosis among AIDS cases in Brazil, and highlights the importance of evaluating secondary data for purposes of improving data quality and developing public health interventions. TB surveillance among HIV patients contributes to the development of more coordinated and collaborative approaches for controlling both epidemics. The combination of various surveillance components and data sources improves the knowledge of HIV and TB epidemics within groups at higher risk for both infections. TB-AIDS co-infection is a significant problem in our region that needs a targeted and informed plan of action.

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