
CLINICAL AND EPIDEMIOLOGICAL FEATURES OF AIDS/TUBERCULOSIS COMORBIDITY

Alice Tung Wan Song, Denise Schout, Hillegonda Maria Dutilh Novaes and Moisés Goldbaum

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Considering the relevance of AIDS/tuberculosis comorbidity worldwide, especially in Brazil, this study was developed to describe the clinical and epidemiological features of the comorbid cases identified from 1989 to 1997 by the epidemiology service of the Hospital das Clínicas of the Universidade de São Paulo.

METHODS: Databases containing information on all identified AIDS/tuberculosis cases cared for at the hospital were used to gather information on comorbid cases.

RESULTS: During the period, 559 patients were identified as presenting with AIDS/tuberculosis comorbidity. Risk behavior for AIDS was primarily heterosexual contact (38.9%), followed by intravenous drug use (29.3%) and homosexual/bisexual contact (23.2%). Regarding clinical features, there were higher rates of extrapulmonary tuberculosis when compared to tuberculosis without comorbidity. There was an increase in reporting of AIDS by ambulatory units during the period. Epidemiologically, there was a decrease in the male/female ratio, a predominance in the 20 to 39 year-old age group, and a majority of individuals who had less than 8 years of schooling and had low professional qualifications.

CONCLUSIONS: High rates of AIDS/tuberculosis cases at our hospital indicate the need for better attention towards early detection of tuberculosis, especially in its extrapulmonary form. Since the population that attends this hospital tends to be of a lower socioeconomic status, better management of AIDS and tuberculosis is required to increase the rates of treatment adherence and thus lower the social costs.

DESCRIPTORS: AIDS. Tuberculosis. Comorbidity. Epidemiology. Epidemiological Surveillance.

During the past few years, explosive growth has occurred in emerging and reemerging diseases, such as AIDS and tuberculosis, due to multiple factors, including environmental changes, insufficient public health systems, and social and economic changes.

The dynamics of tuberculosis have changed since the start of the AIDS epidemic in 1981. The disease has reappeared at unexpected levels in developed countries where the incidence used to be low. Rates have also increased significantly in developing countries where the disease was already considered a public health problem.

Despite the new and efficient antiretroviral therapy protecting patients from opportunistic infections, tuberculosis remains a significant problem with HIV infection¹.

The increased incidence of AIDS/tuberculosis comorbidity is primarily due to the following: HIV can easily reactivate a latent mycobacterial infection, acquired tuberculosis infection rapidly progresses in an HIV-infected

individual, and exogenous re-infection occurs¹. A study conducted in New York² found that 30.0% of seronegative individuals acquired *Mycobacterium tuberculosis* infection after exposure; 3.0% became infected in the first year after exposure.

Seropositive patients face higher risks of developing tuberculosis. The risk of reactivation of a latent mycobacterial infection increases from approximately 0.07 to 0.1 cases per 100 patients for seronegative individuals compared to with 9.7 to 10.4 cases per 100 patients for the HIV seropositive group².

Tuberculosis is the most important

From the Department of Preventive Medicine, Epidemiology Service, Hospital das Clínicas, Faculty of Medicine, University of São Paulo.

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opportunistic infection for HIV-infected individuals³. In the recent AIDS epidemic in sub-Saharan countries with efficient reporting systems, tuberculosis cases doubled or even tripled in a short period of 10 years⁴. In these countries, 60.0% of children and 70.0% of adults are seropositive for HIV; the average death rate is 50.0% in 18 months⁵. The AIDS/tuberculosis association has also been observed throughout the world. In New York, tuberculosis patients are found to be seropositive for HIV more frequently than in the general population; in Asia, incidence of tuberculosis has increased due to the rapid HIV dissemination, and it is estimated that approximately 1.3 million adults are coinfecting by both agents⁴.

The epidemiology of AIDS in Brazil shows high rates of association with tuberculosis. Annual tendencies indicate a statistically significant decline of all AIDS related opportunistic complications, including candidiasis, tuberculosis, pneumocystosis, pneumonia, cerebral toxoplasmosis, Kaposi's sarcoma, cryptococcal meningitis, and protozoal infections⁶; however, an increased incidence of tuberculosis has been noticed in the Northeast and Centrowest regions of the country.

From 1980 to 1997, oral candidiasis was the most prevalent AIDS-related opportunistic infection in the State of São Paulo (59.9%), while tuberculosis represented 32.5% of opportunistic infections. The pulmonary form of the disease was found in 19.2% of the patients, while disseminated, extrapulmonary or noncavitary tuberculosis were found in 13.3% of the cases⁷.

HIV infection modifies the epidemiological and clinical manifestations of tuberculosis. Seropositive individuals present an atypical pattern with uncommon radiologic findings, and in many cases diagnosis is only made at necropsy⁸. Moreover, tuberculosis in-

creases the susceptibility to other opportunistic infections as well as mortality rates⁹.

Given the relevance of the AIDS/tuberculosis comorbidity worldwide and in Brazil, this study was conducted to describe the clinical and epidemiological features of these cases identified from 1989 to 1997 at our hospital.

METHODS

Hospital das Clínicas of the Universidade de São Paulo is the largest medical center in Latin America and is considered a tertiary center of reference for the health system of the metropolitan São Paulo area. Since 1988, the hospital's epidemiology service has been responsible for the investigation of reportable diseases identified at the hospital. Data from reported cases produced by this service made this study possible.

Confirmed AIDS/tuberculosis cases were analyzed according to the case definitions standardized by the "Ministério da Saúde"^{10, 11} (Health ministry)

The study was based on 2 data banks containing information on all the reported AIDS/tuberculosis cases cared for at the hospital. A specific data bank was created to analyze the subgroup of patients found in both original banks. Information registered in the epidemiological reporting forms that populated the data banks included name, gender, street address, district and city of residence, hospital admission date, hospital unit that reported the case, clinical form of tuberculosis, case development, and hospital discharge date.

The period of 1989 to 1997 was selected to avoid the influence of the changes in AIDS case definition criteria introduced by CRT-AIDS in 1998.

Additional information was added

to the original data banks from notification files and computerized laboratory data to enhance the clinical and epidemiological description of AIDS/tuberculosis comorbidity.

The additional information included occupation, educational level, date of AIDS and tuberculosis diagnosis, diagnostic criteria for both diseases, result of PPD (purified protein derivative of tuberculin) test, previous treatment for tuberculosis, associated diseases, date of initiation of treatment for tuberculosis, results of laboratory tuberculosis diagnostic tests (direct bacilloscopy - acid fast smear microscopy, mycobacterial culture and immunohistochemistry), date of the beginning of symptoms, and risk factors for HIV transmission. A special form was created to collect the complementary information. However, some newly gathered information was incomplete due to lack of recording of the information on the epidemiological reporting forms. Therefore, pieces of information such as PPD, associated diseases, outcome, and date of beginning of symptoms were excluded from the study.

RESULTS AND DISCUSSION

From 1989 to 1997, 559 AIDS/tuberculosis comorbidity patients were found. These cases represented 19.5% of the total of tuberculosis cases and 20.7% of the total of AIDS cases in this period. The number of AIDS cases increased until 1995 (Table 1), followed by a decrease in 1996 and 1997. The numbers did not match the expected increasing tendencies, and this can be explained by inadequate reporting from ambulatory units during these years.

The main limitations of this project involved the use of preexistent data banks. The results may not express the universe of cases cared for in the hospital during the period, be-

cause information was extracted from data containing only the reported cases and was subject to routine assessment problems. Furthermore, changes in the form of assistance may also have produced nonmeasurable variations due to inadequate control. The standardized tuberculosis reporting form used in 1989 and 1990 gathered only information about patient identification and some laboratory results.

Regarding risk behavior for HIV infection, 71.2% of the patients were heterosexuals, 20.8% were homosexuals, and 8.0% were bisexuals. Thirty-three percent mentioned intravenous drug addiction, and 7.9% had blood transfusions after 1981. The use of intravenous drugs is associated not only with HIV infection, but also with tuberculosis, according to a study conducted in Amsterdam¹², which found a 6-fold increase in risk of acquiring tuberculosis for HIV seronegative intravenous drug users, while a 13-fold increase was found for seropositive drug users.

The risk factors for HIV among heterosexuals (Table 2) were intravenous drug use (20.2%), an HIV seropositive or AIDS patient as sexual partner (13.7%), multiple sexual partners (12.3%), promiscuous sexual partner (7.9%), and intravenous drug-addicted sexual partner (4.3%).

Many individuals had multiple risks for HIV infection; thus, a hierarchical sequence of the manner of HIV transmission was adopted, according to UNAIDS (The Joint United Nations Programme on HIV/AIDS)¹³. The risk factors that presumably led to HIV infection were distributed as seen in Figure 1: 38.9% acquired the infection through heterosexual contact, 29.3% through intravenous drug use, 23.2% through homosexual or bisexual contact, 5.0% through blood transfusion, and 3.6% through vertical transmission.

Three hundred and sixty-seven cases were identified on admission at the hospital; the death rate for these

patients was 30.5%. These cases represented 65% of comorbid cases diagnosed at the time of hospital admission, indicating failure of early detection of the diseases.

The distribution of reported cases of AIDS by source of identification and selected periods (1989 to 1991, 1992 to 1994, and 1995 to 1997) is shown in Figure 2. The significant increase in cases reported by ambulatory units (4.0% in 1989-1991, 56.0% in 1992-1994, and 58.0% in 1995-1997) is due to the initiation of a specialized ambulatory unit for AIDS (“Casa da AIDS”) and to the enhanced information-gathering routine developed by the hospital epidemiology service. Hospital assistance routines may influence the information-gathering needs

(especially from ambulatory units) and the overall reporting process.

Gender distribution (Table 1) showed a male predominance during the whole period. When comparing

Table 1 - Aids/tuberculosis comorbidity cases by gender - HCFMUSP, 1989 to 1997.

Year	Gender		M/F ratio	Total
	F	M		
1989	6	23	3.8	29
1990	10	31	3.1	41
1991	8	33	4.1	41
1992	8	51	6.4	59
1993	13	46	3.5	59
1994	20	43	2.2	63
1995	21	96	4.6	117
1996	33	62	1.9	95
1997	17	38	2.2	55
Total	136	423	3.1	559

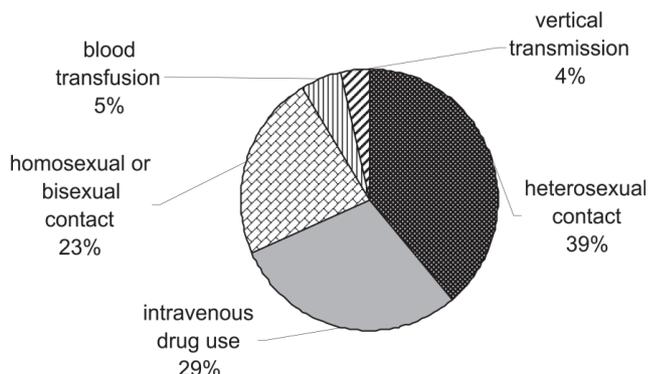


Figure 1 - Comorbidity cases by risk factor for HIV infection - HCFMUSP, 1989 to 1997.

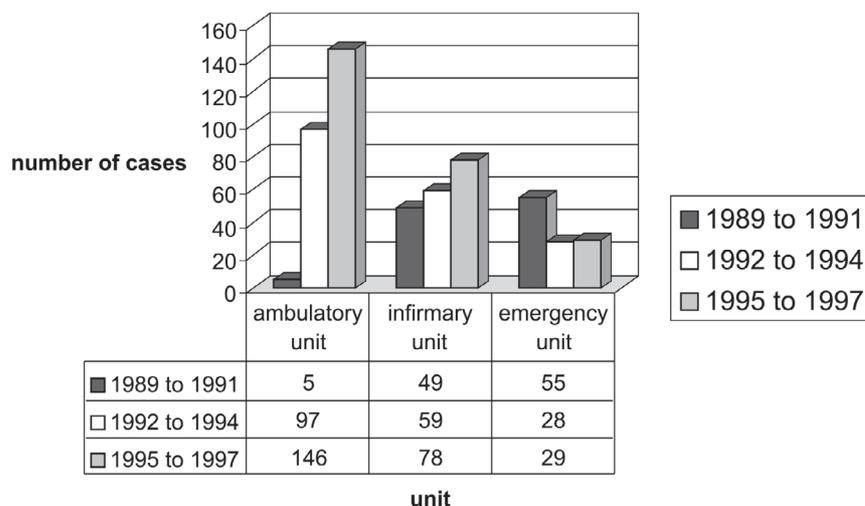


Figure 2 - Aids comorbidity cases by source of notification - HCFMUSP, 1989 to 1997.

the median of the male:female ratio during the first 5 years with that during the last 4 years, the results are 4:1 and 2:6, respectively. This variation could be attributed to the changes in AIDS epidemiological scenario in the State of São Paulo, where higher rates of infection of women led to an increased incidence in the heterosexual population¹⁴. This occurrence has also been found in other countries, such as Puerto Rico, where the proportion of HIV-infected women doubled during the 1980s and the 1990s.

Regarding age (Table 3), 72.5% of the patients were 20 to 39 years old, the prime working age. This pattern reflects that observed in other studies, such as one conducted in Africa¹⁶, where the majority of the comorbid cases occurred from ages 20 to 40 years. A peculiar finding was that children from 0 to 4 years old accounted for 2.9% of cases (1.6% in the 0- to 1-year-old age group), surpassing the next age groups up to the 19-year-old group, thus demonstrating the importance of vertical transmission. This finding is an indicator of the increasing occurrence of AIDS in women. These findings match the data from the State of São Paulo¹⁷, where the same age group accounted for 2.9% of cases during the same period.

Regarding educational level, 56.8% had less than 8 years of schooling, and only 7.2% had a college degree (Table 4). This finding may either reflect the increasing tendencies of pauperism observed among the affected patients, frequently mentioned in literature¹³, or the usual demand of our hospital. In another study conducted in Brazil (Belo Horizonte)⁶, a higher incidence of AIDS/tuberculosis comorbidity was observed in individuals who spent less than 8 years in school; the author related this finding to more difficult access to antiretroviral therapy and chemoprophylaxis for this segment of the population.

Regarding occupation, 36.8% of the patients (210/559) had service-related jobs, such as maids, drivers, general helpers, hairdressers, waiters, or construction workers, showing a lower professional qualification, which matched the amount of schooling (data not shown).

Most patients (81.6%) lived in the

City of São Paulo, and 15.9% lived in the metropolitan area surrounding the city. Among those living in the city, about 18.0% lived out of the hospital coverage area as defined by the Emergency Medical Assistance Integrated Program developed for the São Paulo metropolitan area.

Table 2 - Aids/tuberculosis comorbidity cases by heterosexual risky behavior - HCFMUSP, 1989 to 1997.

Risky behavior	N	%
none	90	35.4
intravenous drug use	56	22.0
sexual partner with HIV/AIDS	38	15.0
multiple sexual partners	34	13.4
promiscuous sexual partner	22	8.7
intravenous drug addict sexual partner	12	4.7
bisexual sexual partner	1	0.4
all	1	0.4
Total *	254	100.0

* 23 heterosexual patients with unknown risky behavior

Table 3 - Aids/tuberculosis comorbidity cases by gender and age - HCFMUSP, 1989 to 1997.

Age	Gender		N	Total	%
	F	M			
0 a 4 years	8	8	16		2.9
5 to 9 years	2	2	4		0.7
10 to 14 years	-	4	4		0.7
15 to 19 years	2	6	8		1.4
20 to 24 years	21	46	67		12.0
25 to 29 years	33	84	117		20.9
30 to 34 years	31	103	134		24.0
35 to 39 years	15	72	87		15.6
40 to 44 years	12	48	60		10.7
45 to 49 years	3	28	31		5.5
50 to 54 years	4	14	18		3.2
55 to 59 years	3	3	6		1.1
>= 60 years	2	5	7		1.3
Total	136	423	559		100.0

Table 4 - Aids/tuberculosis comorbidity cases by gender and schooling level - HCFMUSP, 1989 to 1997.

Schooling level	Gender		N	Total	%
	F	M			
illiteracy	3	3	6		1.5
less than 8 years	55	167	222		56.8
8 years	16	59	75		19.2
9 to 11 years	9	30	39		10.0
more than 11 years	3	25	28		7.2
minor	10	11	21		5.4
Total *	96	295	391		100.0

* 168 patients with unknown schooling level

The pulmonary form of tuberculosis accounted for 73.0% of all forms of tuberculosis cases (ranging from 63.3% in 1991 to 81.1% in 1995) and 63.4% of tuberculosis in seropositive patients (ranging from 50.0% in 1992 to 74.4% in 1993) (Table 5). Meanwhile, the extrapulmonary form represented 27.0% of the cases of tuberculosis without AIDS (ranging from 18.9% in 1995 to 36.7% in 1991) and increased to 36.6% in the comorbid group. Although statistical analysis was not applied to the numbers, extrapulmonary tuberculosis appears to occur more frequently in seropositive individuals. A greater involvement of extrapulmonary structures in HIV-positive tuberculosis patients due to hematogenous mycobacterial dissemination is described in the literature¹⁸. The lymph nodal and disseminated forms accounted for 36.7% and 30.5% of extrapulmonary tuberculosis, respectively.

Of 559 patients, 14 (2.3%) presented 2 episodes of tuberculosis during the period of study: 7 individuals developed pulmonary disease in both episodes; 2 developed extrapulmonary tuberculosis twice; and 5 presented both forms, 1 in each episode.

Thirty-five patients reported prior treatment for tuberculosis, which could indicate re-infection, reactivation of a latent infection, or inadequate treatment. Approximately one-third of these patients abandoned treatment on

the first diagnosis, possibly due to the low educational and social level, despite the controversy of the influence of social and economical status on treatment adherence¹⁹.

Regarding diagnosis of tuberculosis, direct bacilloscopy was performed in 76.8% of the cases and was found positive in 63.0%. The choice for direct bacilloscopy may reflect the characteristics of a university hospital where investigation follows a systematic path, or it may reflect an attempt to prevent nosocomial transmission. In another study conducted in Brazil²⁰, direct bacilloscopy was performed in 72.9% of the cases and was positive in only 23.9% of them.

Although negative direct bacilloscopy in seropositive patients may look like a lower risk of transmission, these individuals are generally more immunocompromised and have higher mortality rates²¹. These findings could be related to subdiagnosis of tuberculosis following a negative test and leading to erroneous differential diagnosis, such as pneumocystosis and Kaposi's sarcoma.

Diagnosis of tuberculosis was accomplished first through direct bacilloscopy (39.5%), and second through specimen culture (29.9%) (Table 6). Specimen culture was undertaken for 209 patients (36.0%) and was positive in 68.4%. Although less specific than specimen culture, direct bacilloscopy is a reliable test with a

high positive predictive value (98.4% in sputum samples and 96.4% in bronchoalveolar lavage samples) for tuberculosis infection²². Despite the challenges at our hospital, only 3.5% of tuberculosis cases had the diagnosis clarified at necropsy (data found in notification forms). Findings of 50.0% of cases diagnosed postmortem may reflect an inferior investigation⁸.

Diagnosis of AIDS was reached according to the Caracas criteria in 51.2% of the cases and according to the Centers of Disease Control criteria in 39.0%; in 9.8% of the cases the diagnostic criteria were unknown. The findings following the use of Caracas criteria for diagnosis of AIDS are supported by the findings of oral candidiasis and tuberculosis, since the diseases are most frequently related to AIDS in Brazil.

CONCLUSIONS

Comorbid cases of AIDS/tuberculosis have a higher rate of extrapulmonary clinical manifestation, probably due to the immunosuppression inflicted by HIV. Further studies are needed to describe the immune status (lymphocytes, viral load, etc.) that accompanies mycobacterial infection.

Although atypical, tuberculosis in association with AIDS is still a transmissible, treatable, and preventable disease. Therefore, early diagnosis and

Table 5 - Aids/tuberculosis comorbidity cases by clinical form of tuberculosis - HCFMUSP, 1989 to 1997.

year	Extrapulmonary		Pulmonary		Total N
	N	%	N	%	
1989	13	33.3	26	66.7	39
1990	19	45.2	23	54.8	42
1991	15	36.6	26	63.4	41
1992	28	50.0	28	50.0	56
1993	11	25.6	32	74.4	43
1994	15	40.5	22	59.5	37
1995	44	35.5	80	64.5	124
1996	15	30.6	34	69.4	49
1997	50	35.2	92	64.8	142
Total	210	36.6	363	63.4	573

Table 6 - Aids/tuberculosis comorbidity cases by diagnosis exam of tuberculosis - HCFMUSP, 1989 to 1997.

Exam	N	%
direct bacilloscopy	186	39.5
specimen culture	141	29.9
clinical/radiologic	90	19.1
pathological	30	6.4
necropsy	20	4.2
immunohistochemistry	4	0.8
Total *	471	100.0

* 102 patients with unknown diagnostic exam

treatment of AIDS patients also infected by *M. tuberculosis* can lead to lower mortality rates. The complex treatment, leading to poor adhesion, may be one of the factors contributing to the maintenance of high rates of incidence of the AIDS/tuberculosis comorbidity. A study conducted by the Brazilian National Health Department¹⁹ identifies the lowest social class as at risk for nonadherence to medical treatment. This is the same social class that frequently attends at our hospital's medical facilities and is at

risk for AIDS/tuberculosis comorbidity. The low schooling level and professional qualification of this group reinforces the need for a multiprofessional team and a special project to enhance early diagnosis and adherence to established medical treatment. The study is based on reported files and computerized laboratory data research. The investigation files of the hospital epidemiology service provided adequate data for the clinical and epidemiological description of comorbid AIDS/tuberculosis cases. Access to computer-

ized patient information and laboratory data offered additional information. The survey was conducted without consultation of the patient clinical files, demonstrating the viability of studies developed through research of routine data collected by hospital epidemiological surveillance services.

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RESUMO

SONG ATW e col. - Aspectos clínicos e epidemiológicos da comorbidade AIDS/tuberculose. **Rev. Hosp. Clín. Fac. Med. S. Paulo** 58(4):207-214, 2003.

Frente à importância da comorbidade AIDS/tuberculose no mundo e especialmente no Brasil, este estudo foi realizado para descrever os aspectos clínicos e epidemiológicos dos casos

de comorbidade notificados pelo Serviço de Epidemiologia do Hospital das Clínicas of the Universidade de São Paulo identificados de 1989 à 1997.

MÉTODOS: Foram utilizados bancos de dados contendo informações de todos os casos notificados de AIDS/tuberculose assistidos pelo hospital.

RESULTADOS: Durante o período estudado, foram identificados 559 pacientes com a comorbidade. Os fatores

de risco para AIDS incluíam principalmente contato heterossexual (38,9%), seguido por uso de drogas endovenosas (29,3%), e contato homossexual/bissexual (23,2%). Quanto aos aspectos clínicos, houve maiores índices de tuberculose extrapulmonar em comparação com tuberculose isoladamente. As unidades ambulatoriais mostraram aumento das notificações de AIDS durante o período. A descrição epidemiológica mostrou um declí-

nio na relação masculino/feminino, predomínio do acometimento da faixa etária de 20 a 39 anos e de indivíduos com escolaridade menor que 8 anos de estudo, com baixa qualificação profissional.

CONCLUSÃO: As altas taxas de

casos de comorbidade AIDS/tuberculose indicam a necessidade de melhor atendimento desses pacientes, objetivando a detecção precoce da comorbidade. Tendo em vista as más condições sócio-econômicas da maioria da população deste hospital, uma melhor

atenção visa ao aumento da aderência ao tratamento, e por consequência, menores custos sociais.

DESCRITORES: AIDS. Tuberculose. Comorbidade. Epidemiologia. Vigilância epidemiológica.

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