

## PREVALENCE OF HIV1 IN LEPROSY PATIENTS IN RIO DE JANEIRO, BRAZIL

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**SUMMARY:** The purpose of this study was to learn if HI V1 infection was associated with leprosy in South America, Rio de Janeiro, Brazil by comparing the prevalence rates of 1,016 leprosy patients tested on a voluntary basis and 78,482 blood donors. A cross-sectional survey of anti-HIV1 antibodies was conducted in Rio de Janeiro, from 1990 to 1992 for this purpose. HIV1 prevalence found among leprosy patients was (three cases) 2.9 per 1,000, and among blood donors was (282 cases) 3.8 per 1,000. Such difference was not significant (OR = 0,79,  $p = 0.69$ ). Since HIV1 cases were only found among male leprosy patients, further analysis excluded females. Male leprosy patients showed a slightly higher prevalence of HIV1 than blood donors before and after age adjustment. However, this result was not statistically significant (adjusted odds ratio = 1.38, 95% CI 0.35-4.5,  $p = 0.83$ ). These data do not provide evidence that leprosy and HIV1 infection are associated in the State of Rio de Janeiro. This is consistent with similar investigations conducted elsewhere.

**Key words:** Cross-sectional survey; HIV1 infection; AIDS; Leprosy; Epidemiology, Blood donors.

### 1. INTRODUCTION

Association between Human Immunodeficiency Virus (HIV) and mycobacteria has been frequently described with relevant implications. In developed countries mycobacteria from Avium Intracellulare complex (MAIC) has been responsible for severe infection in individuals with AIDS<sup>(7,9,14)</sup>. In Third World countries, mycobacteria other than *M. leprae* such as *M. tuberculosis* and *M. avium* are common pathogenic bacteria found in HIV1 seropositive persons<sup>(7,9,12,14)</sup>. With these facts in mind; several studies have been proposed to observe possible implications between leprosy and AIDS. However, most of them were unable to find an important association<sup>(2,4, 5, 9, 3, 10, 11, 13, 15)</sup>

Changes in the time trend of a disease incidence, especially toward the lepromatous form, increasing lack of response to specific leprosy

treatment; frequency of reactional episodes; and frequency of leprosy relapses may indicate a relationship to a new concomitant condition that could be HIV1/AIDS. It is also important to study how fast HIV1 infection develops in leprosy patients, differences in the clinical picture, and the role of specific drugs, like Dapsone, Clofazimine and Rifampicin in the prevention of opportunistic infections among patients with leprosy and HIV1 infection,

The present study relates to HIV1 infection in leprosy patients and compares it with a large sample of blood donors by age and gender.

### 2. MATERIAL AND METHODS

A total of 1,016 leprosy patients, from 1990 to 1992, under treatment and surveillance had their sera tested on a voluntary basis. All of

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them were managed in four out-patient health care units of the Metropolitan region of Rio de Janeiro: Curupaiti State Hospital, Duque de Caxias, Nova Iguaçu, and Itaboraí Health Centers. All leprosy patients visiting the clinic, willing to collaborate were included in the study. Since the study was conducted anonymous only age and gender was allowed to be obtained from the participants by the Institutional Review Board of the Secretary of Health.

A 10 ml sample of venous blood was collected from all leprosy patients. HIV1 antibodies were demonstrated using first recombinant Elisa (ABBOT). Positive samples were re-tested with Virostika ELISA (ORGANON) and with the indirect immunofluorescencetest (IFI-K37/3). All laboratory procedures were conducted using standard techniques at the Noel Nutels State Central Laboratory, Rio de Janeiro.

A volunteer (not paid) blood donor group was selected for comparison purposes. This may not be the most representative group for the source population. However, HIV1 results are easy to obtain and its voluntary nature resembles that of the leprosy patients that were asked to participate. This study was designed to confirm previously published reports that used blood donors as a comparison group<sup>(6,8)</sup>. Most of the blood donors in Brazil are being asked to donate to cover the potential need for a surgical procedure or medical emergency in a relative or friend. The data base file from the State Institute of Hematology (SIH) was used to identify 78,727 blood donors during the same recruitment period as for the leprosy patients (1990-1992).

At the State Institute of Hematology are routinely collected data from a self-administered questionnaire and clinical inspection of all potential blood donors. Patients are excluded if they report any evidence of infectious disease such as hepatitis (any type), malaria, HIV1/AIDS, tuberculosis, leprosy, Chagas disease (American Trypanosomiasis), or are suspected to belong to a behavioral high risk group such as homosexuals, prostitutes, and tattooed people. Any donor with a history of leprosy or tuberculosis is therefore excluded from blood donation. Routine blood testing for a number of endemic diseases infection is carried out including Malaria, Chagas

Syphilis, Hepatitis B, Hepatitis C, and the presence of anti-HIV1 antibodies. Reactive sera to the HIV1 screening ELISA (ABBOT) are routinely confirmed by Western Blot (WB) test.

Data were collected by using standardized data collection forms. Study variables included age in years from 18 and older, gender, and date of diagnosis. This last variable was only used as part of the inclusion criteria. Frequencies, cumulative frequencies, percentages, and cumulative percentages were first used to examine the distribution of the variables under study between the two study populations. Student's test was used to assess the significance of the mean age differences. Ninety five percent confidence intervals based on Student's distribution were used for the mean age differences. Cross - tabulation was then used to assess the potential association between leprosy and HIV1 in a crude and age-adjusted analysis. The odds ratio was used as a measure of association, and the Yates-corrected chi square or Fisher exact tests were used to assess the statistical significance of the odds ratio. Confid or exact 95 percent confidence intervals were calculated for the odds ratio comparing leprosy cases with the blood donors that were used as a reference group. Prevalence rates were age-adjusted by the direct method.

### 3. RESULTS

The distribution of leprosy cases and blood donors by age and gender is shown in Table 1. About 50 percent of the leprosy patients were older than 40 years of age while only 28 percent of the blood donors were older than 40 years ( $p < 0.001$ ). The mean age among leprosy patients was 43 years while among blood donors was 31. Such a 12 years difference was found significant ( $p < 0.001$ ). A non-significant age difference was found between genders when leprosy patients and blood donors were combined. The male-female ratio was 1.4: 1 among leprosy patients and 10.4: 1 for blood donors. The blood group comprised 7.3 times more females than the leprosy cases ( $p < 0.001$ ).

A total of 11 HIV1 positive were found among the 1,016 sera examined from leprosy patients during the first screening (10.7 per 1,000),

**Table 1:** Distribution of leprosy cases and blood donors by age and gender. Rio de Janeiro. 1990-1992.

Leprosy cases						Blood Donors				
Age	Female n <sup>o</sup>	Male n <sup>o</sup>	Total n <sup>o</sup>	% cases	Cum.* %	Female n <sup>o</sup>	Male n <sup>o</sup>	Total n <sup>o</sup>	% cases	Cum.* %
18-25	60	80	140	13,78	13,8	1403	12670	17673	22,52	22,50
26-30	38	70	108	10,63	24,43	1159	12027	13186	16,80	39,30
31-35	54	74	128	12,60	37,03	1126	12272	13398	17,07	56,37
36-40	56	67	123	12,11	49,12	1065	11473	12538	15,98	72,35
41-54	33	42	75	7,38	56,52	745	8518	9263	11,80	84,15
46-50	45	63	108	10,63	67,15	628	5581	6209	7,91	92,06
51-55	45	46	91	8,96	76,1	486	3694	4180	5,33	97,39
56-60	33	54	87	8,56	84,67	255	1760	2015	2,57	99,97
61+	54	102	156	15,35	100,00	6	14	20	0,03	100,00
TOTAL	418	598	1016	100		6873	71609	78482	100	

Cum.\*, cumulative

but only 3 (2.9 per 1,000) were confirmed positive in the subsequent confirmatory tests. The blood donors testing resulted in 298 confirmed HIV1 positive individuals among 78,727 blood donors (3,8 per 1,000). The age and gender distribution of HIV1 positive tests for both study groups is shown in table 2, The three HIV1 positive tests were found among males between 36 and 50 years of age range for leprosy patients, while HIV1 positive cases among blood donors were found in both genders with a wider age spread. Table 3 shows that males have a borderline significant 60 percent more HIV1 positive individuals than females (age

adjusted Odds Ratio = 1.58,  $p = 0.073$ ) when leprosy patients and donors were combined. Male leprosy patients were 28 percent more likely to be HIV1 positive than the male blood donors (Crude Odds ratio = 1.28,  $p = 0.513$ ). After age adjustment, such difference slightly increased (Adjusted Odds Ratio = 1.38,  $p = 0.832$ ). In contrast, leprosy patients showed 33 percent less likelihood of being HIV1 positive as compared with blood donors when both genders were combined (age adjusted OR = 0.79,  $p = 0.687$ ),

#### 4. DISCUSSION

**Table 2:** Distribution of HIV1 positive individuals by age, gender, and group, Rio de Janeiro, 1990-1992.

Leprosy cases					Blood Donors			
Age	Female n <sup>o</sup>	Male n <sup>o</sup>	Total n <sup>o</sup>	Rate/ 1000	Female n <sup>o</sup>	Male n <sup>o</sup>	Total n <sup>o</sup>	Rate/ 1000
18-25	0	0	0	0	4	52	56	3,20
26-30	0	0	0	0	4	71	75	5,70
31-35	0	0	0	0	3	56	59	4,40
36-40	0	1	1	8,10	2	44	46	3,70
41-54	0	1	1	13,30	2	32	34	3,70
46-50	0	1	1	9,30	1	17	18	2,60
51-55	0	0	0	0	1	9	10	2,40
56-60	0	0	0	0	1	1	2	1,00
61+	0	0	0	0	0	0	0	0
TOTAL	0	3	3	2,95	18	282	300	3,81

Age adjusted rate for blood donors 2,89/1000 (leprosy cases were used as standard population)

**Table 3:** Analysis of the association with HIV1 seropositivity. Rio de Janeiro, 1990-1992.

variables	HIV(+)	HIV1(-)	Odds Ratio		95% confidence interval	p Value
			Crude	Adjusted*		
leprosy cases	3	1013	0,77	0,79	0.32-1.82	0.687
blood donors	300	78182				
(males only)						
leprosy cases	3	595	1,28	1,38	0.35-4.45	0,832
blood donors	282	71327				
leprosy cases	285	71922	1,6	1,58	0.96-2.63	0,073
blood donors	18	7273				

\* Adjusted by age

**Table 4:** Crude analysis of the association among selected variables. Rio de Janeiro, 1990-1992.

variables	Crude OR*	Mean	Mean Dif*	95% CI*	p*
<u>ages differences</u>					
leprosy cases	-	43,1	12,6	11.7-13.7	<0.001
blood donors	-	30,5			
(older than 40)					
leprosy cases	2,7	-	-	2.4-3.1	<0.001
blood donors					
<u>gender differences</u>					
leprosy cases blood donors	7,3	-	-	6.4-8.2	<0.001

\* OR, odds ratio; mean Dif, mean difference; p, pValue; CI, confidence interval

The results showed that HIV1 serum crude prevalence rate in leprosy patients from Rio de Janeiro was 2.9 per 1,000 patients while in blood donors was 3.8 per 1,000 donors. These findings accounts for a 1.3 per 1,000 difference in prevalence. Such difference was detected to be not statistically significant. Age standardized prevalence rate of the blood donors using as standard population the leprosy patients was found to be 2.8 per 1,000 which is practically the same as the one for leprosy cases (2,9 per 1,000). This last finding further supports the hypothesis of no association between HIV1 and leprosy as found in other countries. In this study, age distribution

seems to explain almost the entire difference found when crude rates were compared,

Confirmatory test for HIV1 was different in the two study groups. However, almost identical sensitivity and specificity are found in these two procedures (very close to 100 percent). In our study, Elisa test showed 11 positive cases among leprosy patients, and only 3 of them were confirmed. Leprosy may increase the false positive rate of HIV1 as was suggested in other studies<sup>(1, 5, 10, 13)</sup>

The prevalence of HIV1 infection among leprosy patients was found to be much lower (2.8 per 1,000) than expected (30 per 1,000) based upon previously reported prevalence rates from

emergency room visits due to all causes in Rio de Janeiro<sup>30</sup>. This fact importantly affected the power of the sample of this study. At the time of the study's preliminary analysis, it was impossible to continue recruiting leprosy cases in order to reach sufficient sample power (80 percent) because it was necessary to increase the sample of leprosy patients from 1016 to 25,400 which was far beyond the total number of active cases of leprosy in Rio de Janeiro that was about 11,000.

The lack of association between leprosy and HIV1 infection is consistent with other recent publications coming from areas where AIDS and leprosy occur simultaneously: Haiti<sup>(5)</sup>, Yemen, Congo, Ivory Coast, Senegal<sup>(11)</sup>, and Malawi<sup>(13)</sup>. These research projects studied both prevalent and incident cases of leprosy were unable to identify a clear association between HIV1/AIDS and leprosy. A publication from Zambia however, in 1989 found a higher prevalence of HIV1 positive individuals among hospitalized leprosy patients as compared to two control groups<sup>(8)</sup>. A case control study design was used in Zambian hospitalized patients comparing HIV1 prevalence rates in 33 leprosy in-patients (cases) and in 63 blood donor controls (OR=2.3, 0.6-8.9, p=0.197) as well as in 42 surgical patients that were used as a second control group within the same medical facility (OR=5.7, 0.9-61.0, p=0.049). The borderline significant association found in Zambia may be a reflection of an important selection bias. Leprosy patients are seldom hospitalized unless they are severely handicapped or suffer a concomitant disease. Such a concomitant disease may be AIDS. Therefore, a potential selection bias (Berkson's bias) may be present, that overestimates the association found. As pointed out by the authors of the Zambian study, patients under hospital attention, do not necessarily represent all leprosy patients nor does the control group representing the population in the community, specially when a rather small sample size is being studied and non-significant or borderline significant results are found.

A case-control study in Tanzania also showed a not statistically significant association between HIV1 and leprosy. A total sample of 93 leprosy patients (cases) was compared to 4,161 controls selected from a stratified cluster sample

from rural, urban, and roadside settlements. HIV1 was mostly found in urban areas while leprosy was found in rural areas<sup>(19)</sup>. The analysis showed 9 HIV1 positive cases among leprosy patients and 280 among 4,161 controls (OR = 1,5, p = 0.363). Among multibacillary leprosy cases the difference was larger and of borderline significance (OR = 3.1, 95% CI 1.0-8.4, p = 0.05). A small number of cases were found, and the analysis combined the urban-rural strata, potentially decreasing the precision in the calculation of the odds ratios and its corresponding standard errors.

Selection bias may be present in our study in Rio de Janeiro. Blood donors are screened for self-referred high risk behavior for HIV1 or history of any sexually transmitted disease. Therefore, these individuals were not included in the study. No such exclusion was applied to the leprosy patients group. This exclusion has an obvious impact of lowering the prevalence of HIV1 infection in the blood donor group. However, even with this potential bias possibly increasing the differences between the two groups, they showed a very similar HIV1 prevalence.

Cross-sectional and case-control studies on AIDS and leprosy in third world countries may be affected by an important survival bias. With all the difficulties in diagnosis and treatment of opportunistic infections, it is possible that a number of HIV1 positive patients do not survive long enough to develop clinical signs of leprosy which usually has a much longer incubation period than other mycobacterial infections such as *M. tuberculosis* or *M. avium*<sup>(14)</sup>.

It was expected to find a higher prevalence of HIV1 in leprosy patients (30 per 1,000) as compared to blood donors (3.5 per 1,000). However, no major differences were found in the present study. The prevalence of blood donors was slightly higher in spite of the potential selection bias lowering it. Therefore, it is clear that leprosy and HIV1 infections are not importantly associated in Rio de Janeiro.

Due to the small number of HIV1 reactive leprosy cases, we were unable to explore potential confounding variables such as clinical form, disease onset, and HIV1 high risk groups. Since the prevalence of leprosy and HIV1 infections were found to be low, it is difficult to conduct any

simple study design unless a 25 times larger sample size of leprosy patients can be studied. Only a combined design such as a nested case-control study in a HIV1 high risk cohort may

accomplish the goal of confirming or more firmly rejecting an association. Alternatively, meta analyses could be done.

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