

## Radiographic features of pulmonary tuberculosis in patients infected by HIV: is there an objective indicator of co-infection?

Características radiológicas da tuberculose pulmonar em doentes infectados pelo HIV: existe um indicador objetivo da co-infecção?

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**Abstract** This study aimed to compare the radiographic characteristics of patients with pulmonary tuberculosis (TB) and human immunodeficiency virus (HIV) infection with those of HIV-negative patients. In all, 275 TB patients attending the outpatients clinics at the University Hospital/UFPE, were studied from January 1997 to March 1999. Thirty nine (14.2%) of them were HIV<sup>+</sup>, with a higher frequency of males in this group ( $p=0.044$ ). Seventy-five percent of the HIV<sup>+</sup> patients and 19% of the HIV<sup>-</sup> had a negative tuberculin test (PPD) ( $p < 0.001$ ). The proportion of positive sputum smears in the two groups was similar. The radiological finding most strongly associated with co-infection was absence of cavitation ( $p < 0.001$ ). It may therefore be concluded that the lack of cavitation in patients with pulmonary TB may be considered a useful indicator of the need to investigate HIV infection. This approach could contribute to increasing the effectiveness of local health services, by offering appropriate treatment to co-infected patients.

**Key-words:** Tuberculosis. HIV/AIDS. Radiographic features.

**Resumo** Este trabalho objetivou comparar características radiológicas de doentes com tuberculose (TB) pulmonar, soropositivos para o vírus da imunodeficiência humana (HIV), com aquelas de doentes HIV<sup>-</sup>. Estudou-se, prospectivamente, 275 doentes com TB pulmonar, atendidos no Hospital das Clínicas da UFPE, entre janeiro de 1997 e março de 1999. Destes, 39 (14,2%) eram HIV<sup>+</sup>, com um predomínio maior de homens neste grupo ( $p=0,044$ ). Setenta e cinco por cento dos doentes HIV<sup>+</sup> e 19% dos HIV<sup>-</sup> apresentavam reação negativa ao teste tuberculínico (PPD) ( $p<0,001$ ). A proporção de baciloscopias positivas nos dois grupos foi semelhante. A característica radiológica mais fortemente associada à co-infecção tuberculose pulmonar/HIV<sup>+</sup> foi a ausência de cavidades ( $p<0,001$ ). Conclui-se que, diante de doentes com TB pulmonar, a ausência de cavidades na telerradiografia de tórax constitui-se num indicador útil da necessidade de se investigar a infecção pelo HIV. Esta conduta pode contribuir para aumentar a efetividade dos serviços locais de saúde, permitindo oferecer tratamento adequado a estes doentes.

**Palavras-chaves:** Tuberculose. HIV/AIDS. Achados radiológicos.

The pandemic of the Human Immunodeficiency Virus (HIV) has been pointed out as one of the major causes of the worldwide increase in tuberculosis cases. This is due to the fact that tuberculosis is one of the most common infections to occur in the course of HIV infection, either because of the reactivation of latent TB or as a result of new infection by the tuberculosis mycobacterium, with a faster progression towards the active disease. When tuberculosis is associated with HIV infection, the difficulty in establishing a diagnosis using traditional parameters contributes to the resurgence of this disease<sup>12</sup>.

In Brazil, as in most developing countries, the diagnosis of pulmonary tuberculosis depends on the clinical symptoms, chest radiography, tuberculin test and sputum smear examination for acid-fast bacilli (AFB). The culture for *M. tuberculosis* is not routinely performed due to the cost and delay in obtaining results<sup>11</sup>. In cases of pulmonary tuberculosis associated with HIV infection, the results of these examinations are often uncharacteristic, which delays the diagnosis<sup>15</sup>. At present, HIV testing is not routinely carried out on all tuberculosis patients<sup>8</sup>.

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However, the relatively high frequency of HIV infection among new cases of tuberculosis in some Brazilian cities (9.6%) indicates the need to investigate the presence of this association, in order to offer these patients appropriate treatment for both infections<sup>10</sup>. In 1996, it was estimated that in Brazil the greater number of individuals infected by HIV would result in a 20% increase in the incidence of tuberculosis by the end of the decade.

#### MATERIAL AND METHODS

All patients diagnosed as having pulmonary tuberculosis who attended the tuberculosis out-patients clinic at the University Hospital of the Federal University of Pernambuco (HC/UFPE) from January 1997 to May 1999, who had a chest x-ray taken and anti-HIV test performed were studied prospectively. All the patients had three sputum smear exams for acid-fast bacilli carried out using the Ziehl-Neelsen technique. The tuberculin test was performed with 0.1ml of PPD RT23, according to a standardized technique.

The chest radiographs were analyzed by a single radiologist of the HC/UFPE, a member of the research team, who filled out a standardized form. The radiographic features were summarized in categories previously discussed (as described in Table 2). The

Among the diagnostic tools traditionally used for the diagnosis of pulmonary tuberculosis, the chest x-ray plays a fundamental role, mainly because it is widely available within the public health system, even in poor areas. The study of the radiographic features of pulmonary tuberculosis associated with HIV infection is therefore justified in seeking objective indicators that may suggest a higher probability of the presence of co-infection.

radiologist was aware neither of the HIV status of the patient nor the previous radiographic reading, carried out by another radiologist from the hospital staff.

ELISA 1 and 2, immunofluorescence and Western-blot techniques were used for the diagnosis of HIV. When ELISA 1 and 2 tests were negative the result was considered as non-reagent. Those that were positive for ELISA 1 and 2 underwent an immunofluorescence test and when positive were considered as reagent.

The association between the clinical and radiographic characteristics and the result of the anti-HIV test was studied and the significance of this association was tested by the chi-square or Fisher test, when indicated, and the p-value.

#### RESULTS

Two hundred and seventy-five (275) patients with a diagnosis of pulmonary tuberculosis met the inclusion criteria. Thirty-nine (14.2%) of these were HIV<sup>+</sup>, with a significantly larger proportion of men among HIV<sup>+</sup> patients than among HIV<sup>-</sup> ( $p=0.044$ ), whilst the age distribution of the two groups was similar (Table 1).

Seventy-five percent (75%) of the HIV<sup>+</sup> patients had a negative tuberculin test (PPD=0mm), compared with 19% (36 out of 189) of the HIV<sup>-</sup> patients ( $p < 0.001$ ). There was no statistically significant association between the result of the sputum smear examination and the result of the HIV test ( $p=0.188$ ).

Table 1- Demographic and clinical characteristics of 275 pulmonary tuberculosis patients HIV<sup>+</sup> and HIV<sup>-</sup>, Hospital das Clínicas - UFPE, January 1997 to March 1999.

Characteristics	HIV <sup>+</sup>		HIV <sup>-</sup>		P-value
	n	%	n	%	
Sex					
Male	30	76.9	138	58.5	0.044
Female	9	23.1	98	41.5	
Total	39	100.0	236	100.0	
Age group (years)					
0-14	-	-	08	3.4	
15-34	23	59.0	100	42.6	
35-44	9	23.1	61	26.0	0.179
45-64	7	17.9	50	21.3	
≥ 65	-	-	16	6.8	
Total	39	100.0	236	100.0	
Response to the Tuberculin Test (PPD)					
non reagent	21	75.0	36	19.0	< 0.001
≥5mm	7	25.0	153	81.0	
Total	28	100.0	189	100.0	
Ziehl-Neelson acid-fast stain					
Positive	18	56.3	145	69.7	0.188
Negative	14	43.8	63	30.3	
Total	32	100.0	208	100.0	

Table 2 shows the radiological findings of the 275 pulmonary tuberculosis patients. *Focal infiltrate* was the most frequent radiographic pattern observed.

The chest radiographic findings were grouped into eight categories: normal, focal infiltrate, diffuse infiltrate,

pulmonary nodules, miliary disease, lymphadenopathy, pleural effusion and *absence of cavities* and the results presented according to the HIV status. It was found that *absence of cavities* was significantly associated with HIV infection ( $p < 0.001$ ) (Table 3).

Table 2 - Radiological patterns of 275 pulmonary tuberculosis patients HIV<sup>+</sup> and HIV<sup>-</sup>, Hospital das Clínicas - UFPE, January 1997 to March 1999.

Radiological pattern	N	%
Normal	17	3.6
Focal infiltrate	189	40.4
Diffuse infiltrate	26	5.6
Single cavity	57	12.2
Multiple cavities	67	14.3
Miliary	7	1.5
Nodules	6	1.3
Lymphadenopathy	12	2.6
Pleural effusion	25	5.3
Others	62	13.2
Total	468	100.0

Table 3 - Radiological patterns of pulmonary tuberculosis patients HIV<sup>+</sup> and HIV<sup>-</sup>, Hospital das Clínicas - UFPE, January 1997 to March 1999.

Radiological pattern	HIV <sup>+</sup>		HIV <sup>-</sup>		P-value
	n	%	n	%	
Normal	3	7.7	14	5.9	p=0.717*
Focal infiltrate	24	61.5	165	69.9	p=0.390**
Diffuse Infiltrate	2	5.1	24	10.2	p=0.552*
Nodules	-	-	7	2.9	p=0.598*
Miliary	3	7.7	4	1.7	p=0.061*
Lymphadenopathy	4	10.3	8	3.4	p=0.073*
Pleural effusion	6	15.4	19	8.1	p=0.141*
Absence of cavities	32	82.1	119	50.4	p=0.0005**

\*Fisher exact test

\*\*cc<sup>2</sup> Yates

## DISCUSSION

There seems to be a consensus regarding the modifications of the clinical-epidemiological pattern of pulmonary tuberculosis when associated with HIV infection. Traditional diagnostic methods to a certain extent lose their specificity<sup>15</sup>, thus necessitating the redefinition of their characteristics.

Regarding the age group, although a larger concentration of cases of co-infection among the individuals aged 20 to 39 years (74.4% of the cases) was observed, there was no statistically significant difference in the age distribution between the two groups HIV<sup>+</sup> and HIV<sup>-</sup>.

The difference in the frequency of patients with pulmonary tuberculosis associated with HIV<sup>+</sup> between sexes and age groups depends on the specific prevalence of both infections by sex and age in the population. Pozniak *et al*<sup>15</sup> found in Zimbabwe, Africa, that the distribution of co-infection by sex was similar, whilst Awil *et al*, in another area of Africa (Gulu, Uganda)

described a higher frequency of co-infection among women. In the present study there was a larger proportion of males among those infected by HIV ( $p=0.044$ ).

With respect to age distribution, there is an overlap of the population groups affected by both infections. The prevalence of tuberculosis is greater among young adults, and the individuals most frequently affected by HIV infection are aged 15 to 49 years<sup>2</sup>. A survey carried out in Rio de Janeiro showed that the highest frequency of HIV infection among tuberculosis patients, 7.4%, was found in the 15 to 39 age group<sup>7</sup>. In this study a larger number of individuals in the 15 to 34 age group was found among co-infected patients (59%), but a similar finding was observed in those with only pulmonary tuberculosis (Table 1).

The association found between a negative reaction to the tuberculin test (PPD=0mm) and a positive anti-HIV test ( $p < 0.001$ ) is in agreement with the literature<sup>15</sup>.

In HIV<sup>+</sup> patients, due to the absence of delayed-type hypersensitivity response, lung cavitation is not usual, so the dissemination of bacilli may occur and result in atypical findings. Absence of cavitation has been related to a higher frequency of negative acid-fast bacilli sputum smears in co-infected patients<sup>6 15</sup>. There was a similar proportion of positive sputum smears in the two groups in this study, which agrees with other reports in the literature<sup>4</sup>.

Some authors, analyzing the radiological pattern most frequently found among patients with pulmonary tuberculosis associated with HIV, describe the following features: hilar adenopathy, no cavitory infiltrates and miliary disease<sup>13 14 15 16</sup>. In Brazil, few studies have been carried out with the objective of studying the radiographic pattern of pulmonary tuberculosis associated with HIV infection<sup>3 5 9 17</sup>. Camera *et al*<sup>6</sup> found, in a retrospective study of 104 individuals with pulmonary tuberculosis /HIV<sup>+</sup>, that the most frequent findings were interstitial infiltrate (71.2%)

and alveolar lesion (63.5%). However, there was no comparison group i.e. HIV<sup>-</sup> individuals.

In the present study, the absence of cavities was the radiographic characteristic most strongly associated with co-infection. Miliary disease and lymphadenopathy were more frequent in the HIV<sup>+</sup> group, but the difference was not statistically significant, possibly due to the sample size. The small percentage of diffuse infiltrates among the HIV<sup>+</sup> patients may be due to the low sensibility of conventional radiology in detecting early interstitial disease.

It may therefore be concluded that *absence of cavities* may be considered a useful indicator for the need to investigate HIV infection in patients with a clinical or bacteriological diagnosis of pulmonary tuberculosis. This approach could contribute to increasing the effectiveness of local health services, which diagnose and treat tuberculosis cases, by providing appropriate treatment for co-infected patients, in addition to orientating them to prevent HIV transmission.

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