

Intestinal nematodes and pulmonary tuberculosis

Nematóides intestinais e tuberculose pulmonar

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Abstract We report a significantly higher prevalence of intestinal nematodes in patients with pulmonary tuberculosis (TB) compared to a matched control group: 33/57 (57.8%) in patients with TB and 18/86 (20.9%) in the control group; OR=5.19; 95% CI= 2.33-11.69; p=0.000. When TB patients eosinophilia was also significantly higher among those with intestinal parasites (69.8%) compared to those without this condition (45.6%). We hypothesized that the immune modulation induced by nematodes is a factor that enhances TB infection/progression and that eosinophilia seen in TB patients is a consequence of helminth infection.

Key-words: Tuberculosis. Helminthiasis. Strongyloidiasis. Mycobacterium tuberculosis.

Resumo Nesta comunicação relatamos uma prevalência significativamente maior de nematóides intestinais em pacientes com tuberculose pulmonar (TB), comparada a um grupo controle pareado: 33/57 (57,8%) nos pacientes com TB e 18/86 (20,9%) no grupo controle; OR=5.19; IC a 95%= 2.33-11.69;p=0.000). Dentre os pacientes com TB, a eosinofilia foi significativamente maior nos pacientes com nematóides intestinais (69,8%) comparados àqueles sem parasitas (45,6%). Nossa hipótese é que a imunomodulação induzida por nematóides é fator facilitador da infecção/progressão da doença na TB e que a eosinofilia frequentemente vista em pacientes com TB é secundária à infecção helmíntica.

Palavras-chaves: Tuberculose. Helmintíases. Estrongiloidíase. Mycobacterium tuberculosis.

Immune modulation induced by worm infections can affect the outcome of other infectious diseases². Based on findings from studies related to immunological status of humans with intestinal worms³⁻¹⁰, Bentwich et al² hypothesized that the eradication of these worms could change the impact of some infectious disease, such as AIDS and tuberculosis. In agreement with this idea it has been reported that either the acute phase of *Schistosoma mansoni* infection or infections with intestinal nematodes or *Toxocara* are risk factors for pyogenic liver abscess, pyomyositis and other staphylococcal infections in children and adults^{11-13, 14, 15, 16, 17, 18}. However, despite evidence supporting the role of helminth infection in the enhancement of other infectious diseases, these arguments are not conclusive⁵.

To verify if there is a higher prevalence of helminth infection in patients with tuberculosis we studied the

frequency of intestinal nematodes in patients with and without pulmonary tuberculosis diagnosed at the *Hospital Universitário Cassiano Antônio de Moraes* (HUCAM), Vitória, ES, Brazil.

Data on stool examinations and eosinophil counts were retrieved from the records of 57 patients with pulmonary tuberculosis admitted to HUCAM between September 1997 and August 1999. For control we used a randomized sample of 86 stool examinations from hospitalized adult patients, with other diseases, performed in the routine laboratory of the same Hospital, during the same period. The control group was matched by age, gender and neighborhood. All stool examinations were performed in three samples by the Lutz-Hoffman method.

The most prevalent intestinal nematodes found among the adult in-patient control population were *Ascaris lumbricoides*, *Strongyloides stercoralis*,

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Trichuris trichiura, Ancylostomidae (*Necator americanus* or *Ancylostoma duodenale*), respectively. When considered separately, *S. stercoralis* was more prevalent than other nematode species among patients with pulmonary tuberculosis. *Schistosoma mansoni* occurred in two patients with pulmonary tuberculosis and in two controls.

The frequency of infections by at least one nematode was significantly higher in patients with pulmonary tuberculosis than among the control group. This difference persists if we considered the frequency of *Strongyloides stercoralis* or the frequency of the other intestinal nematodes grouped together as *other nematodes* (Table 1).

Eosinophil counts higher than 600 cells/mm³ were found in 26 out of 57 (45.6%) patients with tuberculosis and 69.8% of those who presented one or more intestinal parasites (Table 2).

Our results showed higher prevalence of nematode infection (especially *S. stercoralis*) in patients with tuberculosis than in controls. Although the two samples, cases and controls, were matched by age, gender and neighborhood, we cannot rule out several confounders that are frequent when using in-patients samples. Thus all the conclusions may consider the caveats resulting from the assumption that the two samples are comparable.

Table 1 - Frequency of intestinal nematodes in patients with pulmonary tuberculosis and in patients with diseases other than tuberculosis, admitted at the same hospital.

	Patients with tuberculosis positive/total (%)	Patients without tuberculosis positive/total (%)	OR (95% CI)	P*
Intestinal worms				
At least one worm	33/57 (57.8)	18/86 (20.9)	5.19 (2.33-11.69)	0.000
<i>Strongyloides stercoralis</i>	14/57 (24.5)	7/86 (8.1)	4.00 (1.38-11.80)	0.003
Other nematodes**	19/57 (33.3)	11/86 (12.3)	3.41(1.37-8.61)	0.003

* χ^2 test. Nematodes other than *S. stercoralis*.

Table 2 - Eosinophil counts in patients with pulmonary tuberculosis associated or not with intestinal nematode infection.

Group	Eosinophils/mm ³ Mean \pm SD (Median)	Patients with more than 600 eosinophils/mm ³
All patients (N=57)	585.3 \pm 548.8 (503)	28/57 (49.1 %)
Without intestinal worms (N=34)	437.2 \pm 545.6 (237)	8/34 (23.5 %)
With intestinal worms (N=23)	804.3 \pm 485.8 (686)	19/23 (82.6 %)*

* p=0.000; χ^2 test

The high frequency of intestinal nematodes in patients with pulmonary tuberculosis suggests that the immune modulation induced by worms may facilitate the infection with *Mycobacterium tuberculosis* and disease progression. This suggestion corroborates previous reports showing that lymphocyte activation, defects on signal transduction, and anergy can be associated with intestinal helminth infection in humans^{3,4,10}. Furthermore, our results support a recent observation showing that the frequency of intestinal nematodes was significantly higher among patients with multibacillary forms of leprosy when compared with patients with paucibacillary leprosy or controls without leprosy⁷. Also our results corroborate with the observation that the response to PPD, *in vivo* and *in vitro*, was diminished in children with intestinal parasites and improved after deworming⁸.

Eosinophilia has not been reported in patients with tuberculosis⁹ but high levels of IgE during pulmonary tuberculosis were recently reported, in South Africa where intestinal worms are endemic¹. Both eosinophilia and high levels of IgE are consequences of Th2 activation, a preferential response induced by intestinal worms^{6,12}. Thus, the results presented here indicate that a possible cause of eosinophilia (and possibly of the high levels of IgE) in patients with pulmonary tuberculosis could be intestinal helminth infections.

A case control study and the study of immune response in patients with pulmonary tuberculosis associated or not to helminth infection are in progress in our laboratory in an attempt to clarify the relationship between the two infections.

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