Efficacy of the scoring system, recommended by the Brazilian National Ministry of Health, for the diagnosis of pulmonary tuberculosis in children and adolescents, regardless of their HIV status*

Eficácia do sistema de pontuação, preconizado pelo Ministério da Saúde, para o diagnóstico de tuberculose pulmonar em crianças e adolescentes infectados ou não pelo HIV

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Abstract

Objective: To determine the efficacy of the scoring system, recommended by the Brazilian National Ministry of Health (NMH), for the diagnosis of pulmonary tuberculosis (TB) in children and adolescents, regardless of their HIV status. **Methods:** This was a cross-sectional analytical study carried out between January of 2002 and December of 2006, involving 239 individuals less than 15 years of age. The patients were divided into four groups: latent TB (LTB group; n = 81); no-TB (NTB group; n = 41); TB group (n = 104); and TB/HIV group (n = 13). We studied the clinical, radiological and laboratory findings according to the scoring system. **Results:** Reports of fever, cough, asthenia and weight loss for at least two weeks were significantly higher in the TB group ($p < 0.0001$). The proportion of cases with a history of any contact and household contact with a TB patient was, respectively, 95.0% and 86.1% in the TB group, versus 75.0% and 58.3% in the TB/HIV group. In the TB and TB/HIV groups, respectively, chest X-rays revealed parenchymal alterations in 75.0% and 53.9%, revealing combined parenchymal/lymph node alterations in 18.2% and 30.8%. There were no significant differences among the groups regarding the tuberculin skin test results. In the TB group, 16.3% of the patients were malnourished ($p < 0.005$ *vs.* the LTB group). The mean NMH system scores in the LTB, NTB, TB and TB/HIV groups were, respectively, 24.2, 18.5, 45.3 and 41.5. **Conclusions:** The NMH system scores were significantly higher in the TB and TB/HIV groups than in the other two groups. Therefore, this scoring system was valid for the diagnosis of pulmonary TB in this population, regardless of HIV status.

Keywords: Tuberculosis/diagnosis; HIV seropositivity; Diagnostic techniques and procedures.

Resumo

Objetivo: Verificar a eficácia do sistema de pontuação, preconizado pelo Ministério da Saúde (MS), para o diagnóstico de TB pulmonar em crianças e adolescentes, infectadas ou não pelo HIV. **Métodos:** Estudo analítico transversal realizado entre janeiro de 2002 e dezembro de 2006, no qual foram incluídos 239 indivíduos menores de 15 anos. Os pacientes foram divididos em quatro grupos: grupo TB latente (TBL; n = 81); grupo não TB (NTB; n = 41); grupo TB (n = 104); e grupo TB/HIV (n = 13). Foram estudadas as características clínicas, radiológicas e laboratoriais segundo o sistema de pontuação. **Resultados:** Os relatos de febre, tosse, astenia e emagrecimento há mais de duas semanas foram significativamente maiores no grupo TB ($p < 0,0001$). No grupo TB, 95,0% dos casos tinham história de contato com indivíduo com TB, sendo que em 86,1% esse contato era intradomiciliar. No grupo TB/HIV, 75,0% dos casos haviam entrado em contato com TB e, em 58,3%, esse contato era intradomiciliar. Nos grupos TB e TB/HIV, respectivamente, 75,0% e 53,9% dos casos apresentaram alterações radiológicas parenquimatosas, enquanto 18,2% e 30,8% apresentaram alterações ganglionares e parenquimatosas. Os resultados da prova tuberculínica não apresentaram diferenças significativas entre os grupos. No grupo TB, 16,3% dos pacientes estavam desnutridos ($p < 0,005$ *vs.* o grupo TBL). A pontuação média utilizando o sistema MS foi a seguinte: grupo TBL, 24,2; grupo NTB, 18,5; grupo TB, 45,3; e grupo TB/HIV, 41,5. **Conclusões:** Os pacientes dos grupos TB e TB/HIV apresentaram pontuação significativamente maior do que aqueles nos outros grupos. Portanto, esse sistema de pontuação foi válido para o diagnóstico de TB pulmonar nessa população, independentemente do status HIV.

Descritores: Tuberculose/diagnóstico; Soropositividade para HIV; Diagnóstico.

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Introduction

The diagnosis of tuberculosis (TB) is more difficult in children, especially in HIV-infected children, than in adults. The clinical and radiological profile is quite nonspecific, and bacteriological confirmation is difficult in most cases. Therefore, it is crucial to use diagnostic criteria that dispense with bacteriological data.[1,2]

Since the 1950s, scoring systems have been developed to diagnose pulmonary TB in children; however, there is no standardization among these systems, most systems have not been validated and no system is adapted for HIV-infected patients.[1,2] In Brazil, the comparison between three international systems in the 1990s showed that none of them were recommended for use in practice.[3] However, the Brazilian National Ministry of Health Manual of Epidemiological Surveillance for Tuberculosis, published in 2002,[4] recommended that the diagnosis of childhood TB be based on a scoring system, which is currently used and aimed at primary health care clinics (Chart 1). This system, which has been validated, has shown good sensitivity and specificity.[5-7] To date, few prospective studies have tested this scoring system.[8,9]

The objective of the present study was to determine the efficacy of the scoring system recommended by the Brazilian National Ministry of Health for the diagnosis of pulmonary TB in children, regardless of their HIV status. Our hypothesis was that this system does not allow the diagnosis of TB in HIV-infected children due to the limitations regarding the tuberculin skin test (TST), the radiological test and the nutritional status of immunocompromised patients.

Methods

This was a cross-sectional analytical study carried out at the pediatric pulmonology clinic of the Raphael de Paula e Souza Hospital—a referral hospital for the treatment of TB in the region of Jacarepaguá, in the city of Rio de Janeiro—between January of 2002 and December of 2006.

This study involved outpatients who were younger than 15 years of age, who were clinically suspected of having TB, as well as asymptomatic individuals with a history of contact with TB patients.

Considering the clinical findings, the complementary test results and the evolution of each case after a 30-day observation period, the following groups were formed:

- Latent TB (LTB) group: asymptomatic patients with a history of contact with an adult TB patient, normal chest X-ray and positive TST result (induration greater than 10 mm in size).
- No-TB (NTB) group: patients with other pulmonary diseases (diagnosed based on clinical and radiological findings) in whom the disease evolved satisfactorily without the use of antituberculosis drugs.
- TB group: patients diagnosed with TB (based on clinical and radiological findings) in whom the disease evolved satisfactorily after 30 days of antituberculosis treatment[4] and who might present positive smear microscopy for AFB or positive culture for *Mycobacterium tuberculosis*.
- TB/HIV group: patients diagnosed with the same criteria as those for the TB group who also presented positive HIV serology.

Individuals of the LTB group were submitted to TB chemoprophylaxis.[4]

The clinical, radiological, and laboratory characteristics included in the scoring system for the diagnosis of TB were investigated for all patients.[4] Nutritional status was assessed by means of Z scores for weight/age.[10]

The collected data were stored in the Epi Info statistical program, version 6.0. Statistical analysis was performed using the Statistical Analysis System, version 6.04 (SAS Institute, Cary, NC, USA).

In order to determine whether the variables of investigation for pulmonary TB were significantly different between the groups, the following methods were applied:

i) To compare numerical (quantitative) data between the three groups, non-parametric ANOVA was used. The multiple-comparison test, based on the Kruskal-Wallis test, was applied in order to identify differences among groups. For comparisons between groups, the nonparametric Mann-Whitney test was used.

ii) To compare proportions (qualitative data), we used the chi-square test or Fisher's exact test.

Chart 1 - Scoring system for the diagnosis of childhood pulmonary tuberculosis. Brazilian National Ministry of Health, Brazil, 2002.

Clinical and radiological profile	Points
• Fever or symptoms such as cough, adynamia, expectoration, weight loss and sweating for more than two weeks	+15
• Asymptomatic or symptomatic for less than two weeks	0
• Improvement in respiratory infection with the use of antibiotics for common germs or without the use of antibiotics	−10
• Hilar lymph node enlargement, miliary pattern, condensation or infiltrate (with or without cavitation) for more than two weeks, with worsening of symptoms or lack of improvement with the use of antibiotics for common germs	+15
• Condensation or infiltrate of any type for less than two weeks	+5
• Normal chest X-ray	−5
Contact with adult TB patient	
• Close contact within the last two years	+10
• Occasional or negative	0
Tuberculin skin test	
• > 10 mm in children who had been vaccinated with BCG more than two years prior or who had not been vaccinated with BCG	+15
• > 15 mm in children who had been vaccinated with BCG within the last two years	
• ≥ 5 and ≤ 9 mm	+5
• < 5 mm	0
Nutritional status[10]	
• Weight below the 10th percentile	+5
• Weight at or above the 10th percentile	0

Diagnostic interpretation of the chart: ≥ 40 points: highly likely; ≥ 30 and ≤ 39 points: possible; ≤ 29 points: unlikely.

Nonparametric methods were used because the variables did not present normal distribution. The level of significance was set at 5%.

The study design was approved by the Research Ethics Committee of the Municipal Health Department of Rio de Janeiro—CEP SMS-RJ 104/06.

Results

Initially, 245 children were studied. Of those, 6 were excluded because they interrupted outpatient follow-up treatment or were transferred to another health care facility. Therefore, our final sample comprised 239 patients, distributed as follows: 81 patients in the LTB group; 41 patients in the NTB group; 104 patients in the TB group; and 13 patients in the TB/HIV group.

Of those 239 patients, 131 (54.8%) were male. The mean age was 76.8 months.

Sputum smear microscopy for AFB was conducted in 23 cases, and 6 (26.1%) tested positive. In addition, sputum samples from 21 patients were submitted to culture for *M. tuberculosis*, and 7 (33.3%) of those cultures tested positive. It was not possible to perform a smear microscopy test for AFB in the gastric lavage samples from the TB group; however, positive cultures for *M. tuberculosis* were obtained in 8 (16.7%) of the 48 TB group cases tested. Of the 4 TB/HIV group patients in whom sputum smear microscopy for AFB and *M. tuberculosis* culture were performed, 1 (25%) presented positive smears and 2 (50%) presented positive cultures. The gastric lavage samples from this group yielded no positive results.

Of the 239 patients in the sample, 89 (38%) were submitted to HIV testing, and 13 tested positive.

Table 1 shows the clinical findings distributed by group.

The analysis of the chest X-rays showed that 100% of the X-rays from the LTB group were normal. In the NTB group, the alterations most frequently found were parenchymal alterations (75.5%) and combined pleural/parenchymal alterations (14.6%). In the TB and TB/HIV groups, respectively, chest X-rays revealed parenchymal alterations in 75% and 53.9% of the

Table 1 - Clinical findings distributed according to the study groups. Raphael de Paula Souza Hospital, Rio de Janeiro, 2002-2006.

Variable	Present	LTB group (n = 81)		NTB group (n = 41)		TB group (n = 104)		TB/HIV group (n = 13)		p*	Significant differences**
		n	%	n	%	n	%	n	%		
Fever (n = 239)	no	77	95.1	18	43.9	44	42.3	6	46.1	< 0.0001	LTB ≠ NTB
	yes	4	4.9	23	56.1	60	57.7	7	53.9		LTB ≠ TB
Fever > 2 weeks (n = 239)	no	81	100	33	80.5	55	52.9	7	53.9	< 0.0001	LTB ≠ NTB, TB
	yes	0	0.0	8	19.5	49	47.1	6	46.1		NTB ≠ TB
Cough (n = 239)	no	57	70.4	0	0.0	8	7.7	1	7.7	< 0.0001	LTB ≠ NTB
	yes	24	29.6	41	100	96	92.3	12	92.3		LTB ≠ TB
Cough > 2 weeks (n = 238)	no	76	93.8	14	34.1	17	16.5	2	15.4	< 0.0001	LTB ≠ NTB, TB
	yes	5	6.2	27	65.9	86	83.5	11	84.6		NTB ≠ TB
Asthenia (n = 239)	no	79	97.5	39	95.1	83	79.8	9	69.2	< 0.0001	LTB ≠ TB
	yes	2	2.5	2	4.9	21	20.2	4	30.8		NTB ≠ TB
Asthenia > 2 weeks (n = 239)	no	81	100	40	97.6	85	81.7	10	76.9	< 0.0001	LTB ≠ TB
	yes	0	0.0	1	2.4	19	18.3	3	23.1		NTB ≠ TB
Weight loss (n = 239)	no	79	97.5	33	80.5	56	53.9	4	30.8	< 0.0001	LTB ≠ NTB, TB
	yes	2	2.5	8	19.5	48	46.1	9	69.2		NTB ≠ TB
Weight loss > 2 weeks (n = 236)	no	81	100	35	85.4	61	60.4	4	30.8	< 0.0001	LTB ≠ NTB, TB
	yes	0	0.0	6	14.6	40	39.6	9	69.2		NTB ≠ TB
Malnourishment (n = 239)	no	79	97.5	35	85.4	86	82.7	8	61.5	0.006	LTB ≠ NTB
	yes	2	2.5	6	14.6	18	17.3	5	38.5		LTB ≠ TB

LTB group: children with latent tuberculosis (TB); NTB group: children with pulmonary diseases other than TB; TB group: children with TB; TB/HIV group: children diagnosed with TB/HIV co-infection. *Comparison between the LTB, NTB and TB groups. **According to Fisher's exact test. adjusted at a level of 1.7%.

cases, revealing combined parenchymal/lymph node alterations in 18.2% and 30.8%.

Reports of contact with a TB patient were more common in the LTB and TB groups, household contact being more frequently reported than was community contact. A history of contact with a TB patient was reported by all of the children in the LTB group, 95.1% reporting household contact. In the TB and TB/HIV groups, respectively, a history of contact with a TB patient was reported by 99 (95%) of the 104 children and 10 (75%) of the 13 children, 86.1% and 58.3% reporting household contact.

Revaccination with BCG had greater statistical validity in the LTB group than in the TB group. The proportion of children revaccinated in the LTB and TB groups was, respectively, 35.8% and 19.6%.

Table 2 describes the distribution by age, TST result and diagnostic score for each group.

The scoring system for the diagnosis of TB adopted in Brazil was applied to all patients, and the mean scores were as follows: 24.2 for the LTB group; 18.5 for the NTB group; 45.3 for the TB group; and 41.5 for the TB/HIV group. The scores were significantly higher in the TB group than in the LTB and NTB groups. In addition, the TB group scores were above the cut-off value of 30 points, which indicated the need to initiate antituberculosis treatment.[7] Despite the small number of cases, the mean scores for the TB/HIV group were also above 30 points, which also allowed the diagnosis of TB in these patients.

Discussion

The diagnosis of pulmonary TB in children continues to be challenging because the signs, symptoms and radiological patterns are less specific in children than in adults. In addition, bacteriological confirmation is difficult in children. The diagnosis in HIV-infected children is even more complex, since chronic pulmonary symptoms and radiological alterations related to HIV-associated diseases might be present. In addition, the sensibility of the TST might be affected by HIV-induced anergy.[11]

Table 2 - Distribution of the 239 children according to age, tuberculin skin test results, scoring system and group. Raphael de Paula Souza Hospital, Rio de Janeiro, 2002-2006.

Variable	Group	n	Mean	SD	Median	Minimum	Maximum	p*	Significant differences**
Age, months	LTB	81	90.0	44.1	95	13	180	0.002	LTB ≠ NTB
	NTB	41	61.5	44.4	48	9	168		
	TB	104	72.3	50.5	65	2	180		LTB ≠ TB
	TB/HIV	13	79.2	54.3	80	5	180		
Tuberculin skin test, mm	LTB	81	16.0	3.4	16	10	25	0.081***	
	NTB	7	8.3	3.8	7	5	16		
	TB	85	14.8	4.3	15	2	26		
	TB/HIV	6	15.2	2.8	15	12	20		
Scoring system	LTB	81	24.2	2.8	25	15	30	0.0005	LTB ≠ NTB
	NTB	41	18.5	6.7	20	5	35		LTB ≠ TB
	TB	104	45.3	8.1	45	25	60		
	TB/HIV	13	41.5	10.3	40	25	55		NTB ≠ TB

LTB group: children with latent tuberculosis (TB); NTB group: children with pulmonary diseases other than TB; TB group: children with TB; TB/HIV group: children diagnosed with TB/HIV co-infection. *ANOVA and Kruskal-Wallis test between the LTB, NTB and TB groups. **According to the multiple-comparison test at a level of 5%. ***Mann-Whitney test between the LTB and TB groups.

In the present study, we found low positivity in gastric lavage samples, and the values observed were much lower than those reported in the literature. This might be due to the small number of samples. Sputum samples yielded more significant results: of the TB group samples, 26.1% were smear-positive for AFB and 33.3% were positive for *M. tuberculosis* culture; of the TB/HIV group samples, 25% were smear-positive for AFB and 50% were positive for *M. tuberculosis* culture. Our findings for the TB group are similar to those reported in the literature.[12]

Although over 50% of the cases of pulmonary TB in children might be asymptomatic, the literature shows that the combination of persistent cough for at least two weeks and asthenia, adynamia and weight loss has diagnostic value for the disease.[13-15] In the present study, fever, cough, asthenia and weight loss had the greatest statistical relevance for the diagnosis of TB. Although the LTB group, by definition, was the group in which the patients presented with fewer symptoms, cough for less than two weeks was observed in 29.6% of the cases, probably due to acute infections of the upper airways. Cough was the most common symptom in the remaining three groups. However, the proportion of children who presented cough for at least two weeks was lower in the NTB group than in the TB and TB/HIV groups, which shows the importance of this finding for the diagnosis of childhood TB and is in accordance with the data found in the literature.[14,15] Asthenia and weight loss were more frequently reported in TB patients (regardless of HIV status). Weight loss for longer than two weeks was observed in 39.6% of the children in the TB group and in 69.2% of the children in the TB/HIV group, which suggests that general health in these groups of patients was more significantly affected.

Based on the fact that 41.2% of the children in the TB group and 76.9% of the children in the TB/HIV group had been treated with antibiotics for common germs for more than two weeks, we can suggest that this caused the TB symptoms to be persistent and uncharacteristic in nature, which can lead to a delay in the diagnosis of TB. In addition, we can suppose that HIV-infected children presented other infectious diseases that are frequently observed in immunocompromised patients.

Our radiological findings for the patients with TB or TB/HIV (parenchymal alterations or combined parenchymal/lymph node alterations) are in accordance with those reported in the literature. The disseminated forms of TB are observed in approximately 10% of the HIV-positive adults.[16] Miliary TB was identified in only one child in the TB/HIV group. However, due to the small number of cases, we were unable to determine differences regarding the number of patients not infected with *M. tuberculosis*.

Taking a history of contact with an adult TB patient is often the starting point for investigating TB in a child. In the present study, this variable was positive for almost all TB group patients and for 75% of TB/HIV group patients. Since the families that have been infected with HIV often feel discriminated against because of the disease, they might avoid reporting cases of TB in the household, which could explain the difference in the percentages between the two groups. Because TB itself is a stigmatizing disease, the lack of reporting of contact with a TB case does not rule out a diagnosis of TB in a child. In the present study, there was a predominance of household contact with TB, which is similar to the findings of a study involving children residing in Rio Grande do Sul, according to which 79% of the TB index cases were the father or the mother.[17] However, we must not forget that children living in areas of high TB prevalence might be infected through community contact.[18] In the present study, the lowest percentage of household contact was observed among HIV-infected patients. We can speculate that, due to immunosuppression, HIV-infected children are at greater risk of being contaminated with *M. tuberculosis* as a result of community contact than are immunocompetent individuals.[18]

The TST is an important tool for the diagnosis of TB in children. Approximately 10% of the children with confirmed *M. tuberculosis* infection present nonreactive TST; many of these children have positive TST results after treatment is initiated, which suggests that TB itself contributes to immunosuppression and leads to anergy.[19] The TST results should be interpreted, according to the scoring system, considering the BCG vaccination status of the child[4]; in the present study, this interpretation was affected by the possible interference of BCG revaccination. More than one third of the children in the LTB group had been revaccinated with BCG. Only 19.6% of the non-HIV-infected patients with TB had been revaccinated with BCG. The mean age was significantly different between patients in the LTB and TB groups, including patients in which BCG revaccination, a procedure that was widely performed in Rio de Janeiro and that was only discontinued in 2006, was indicated.[4] This prompts us to speculate as to whether BCG revaccination would have provided some degree of protection against pulmonary TB in our sample.

In the present study, the proportion of malnourished children was greater in the TB/HIV group than in the other groups. However, due to the small number of cases, it was not possible to perform statistical calculations. Nevertheless, the levels of malnourishment were statistically higher in the TB group than in the NTB group and in the LTB group, providing evidence of the consumptive nature of TB, which has been well-established in the literature.

The limitations of the present study were the lack of specific information on the clinical forms, especially regarding symptoms such as asthenia and sweating, and the lack of bacteriological confirmation in children with TB, which is frequently observed in studies such as ours.[13,19] Other limitations were the development of the study in a specialized clinic instead of in a primary health care clinic, and the small number of HIV-positive children. Testing for HIV was performed in a limited number of patients, partly because of the lack of material in the laboratory during certain periods. However, since the prevalence of TB/HIV co-infection in Latin America (2/100,000 population) is much lower than is that observed in other regions, such as Africa,[20] Testing for HIV is not indicated for all children diagnosed with TB, only for those who are at high risk for HIV infection.[19]

The scoring system adopted for the diagnosis of TB in Brazil[4] dispenses with bacteriological tests and, when the score is equal to or higher than 30 points, antituberculosis treatment is indicated.[21] Therefore, the present study confirmed that the scoring system for the diagnosis of pulmonary TB in children (regardless of HIV status) is effective and can be used by professionals working in the Brazilian primary health care system. Further studies carried out in different regions of Brazil could corroborate the conclusions drawn in the present study.

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