Is tuberculosis difficult to diagnose in childhood and adolescence?*,**

A tuberculose na infância e na adolescência é difícil de diagnosticar?

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Abstract

Objective: To determine the sensitivity of the scoring system proposed by the Brazilian National Ministry of Health in 2002 for the diagnosis of tuberculosis in children and adolescents suspected of having the disease. **Methods:** This was a retrospective study of 316 children and adolescents (0-14 years of age) diagnosed with pulmonary tuberculosis between 1997 and 2007 at the Brazilian Institute for Tuberculosis Research, located in the city of Salvador, Brazil. After reviewing the medical charts and chest X-rays of the patients, we calculated the tuberculosis scores. **Results:** The majority of the subjects (80.4%) had a history of close household contact with an AFB-positive adult within the last two years. The tuberculin test was negative in 11 subjects (3.5%). According to the scoring system, 251 (79.4%) were very likely to have tuberculosis (score, ≥ 40), 63 (19.9%) were moderately likely to have tuberculosis (score, 30-35), and 2 (0.7%) were unlikely to have tuberculosis (score, ≤ 25). When a cut-off score of 30 was used, the sensitivity of this scoring system was 99.3%. **Conclusions:** In our sample, the sensitivity of this scoring system was high when the selected cut-off score was employed. If a cut-off score of 40 had been used, 20% of the subjects would not have been treated. Therefore, scores between 30 and 35 are critical for diagnostic confirmation. Judicious clinical evaluation should prevail in the decision of treating these patients. When the cut-off score of 30 is used, 30% of individuals with other pathologies will be treated for tuberculosis. This highlights the need for improved diagnostic methods for tuberculosis.

Keywords: Tuberculosis/diagnosis; Epidemiology; Diagnostic techniques and procedures.

Resumo

Objetivo: Determinar a sensibilidade do sistema de escore proposto pelo Ministério da Saúde do Brasil em 2002 para o diagnóstico de crianças e adolescentes com suspeita de tuberculose. **Métodos:** Entre 1997 e 2007, 316 crianças e adolescentes (0-14 anos de idade) com diagnóstico de tuberculose pulmonar no Instituto Brasileiro de Investigação da Tuberculose, em Salvador (BA), foram incluídos no presente estudo retrospectivo. Foram revisados os prontuários médicos e as radiografias de tórax dos pacientes, e os escores foram calculados. **Resultados:** A maioria dos sujeitos (80,4%) tinha história de contato domiciliar com adultos com BAAR positivo nos últimos dois anos. O teste tuberculínico foi negativo em 11 sujeitos (3,5%). Conforme o sistema de escore, 251 (79,4%) muito provavelmente tinham tuberculose (escores ≥ 40), 63 (19,9%) possivelmente tinham tuberculose (escores entre 30 e 35) e 2 (0,7%) pouco provavelmente tinham tuberculose (escores ≤ 25). A sensibilidade desse sistema de escore foi de 99,3%, com um ponto de corte de 30. **Conclusões:** Em nossa amostra, a sensibilidade do sistema de escore foi alta para o ponto de corte selecionado. Com um ponto de corte de 40, 20% dos sujeitos não teriam sido tratados. Portanto, escores entre 30 e 35 são críticos para a definição diagnóstica. Uma avaliação clínica judiciosa deve prevalecer para a decisão de tratar esses pacientes. Com um ponto de corte de 30, 30% dos indivíduos com outras patologias seriam tratados para tuberculose. Isto enfatiza a necessidade de melhores métodos diagnósticos para a tuberculose.

Descritores: Tuberculose/diagnóstico; Epidemiologia; Técnicas e procedimentos diagnósticos.

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Introduction

Tuberculosis is a significant health problem in Brazil, which was ranked as one of the twenty countries in the world with the highest incidence rates of the disease. In 2009, the Brazilian Tuberculosis Control Program reported 85,000 cases of tuberculosis (approximately 45 cases per 100,000 inhabitants) to the World Health Organization (WHO).[1] Between 2005 and 2009, the incidence decreased by 2.9% per year.[1] In Brazil, 7% of reported cases affected children or adolescents (0-14 years of age); in the state of Bahia,[2] this is estimated to be even greater, with 15-20% of the cases affecting children or adolescents.[3] This is thought to be an underestimate of the true prevalence of tuberculosis due to the difficulty of diagnosis. The diagnosis is complex, because quite often the results for AFB are negative.[4] Although there have been technological advances and new, promising tuberculosis diagnostic tests have been developed, which have improved sensitivity and are easy to use, none are readily available in Brazil.[5-13] In 2002, in response to the difficulty in diagnosing tuberculosis, the Brazilian National Ministry of Health (NMH) approved the use of a scoring system to facilitate the identification and treatment of potential cases.[14,15] In 2006, the WHO published a handbook comparing various scoring systems for the diagnosis and treatment of tuberculosis in children and adolescents.[16] In a study published in 2007, Sant'Anna & Hijjar[17] hailed this as a great improvement, because these new guidelines presented a careful review on the diagnosis and treatment in pediatric patients. According to the WHO scoring system, individuals 0-14 years of age are considered "very likely to have tuberculosis" if presenting with at least three of the following: chronic symptoms suggestive of tuberculosis; physical examination revealing symptoms suggestive of tuberculosis; a positive tuberculin test; and chest X-ray findings suggestive of tuberculosis. However, on the basis of a detailed analysis of the systems proposed by Edwards et al.,[18] Sant'Anna & Hijjar[17] did not recommend the use of the WHO scoring system in Brazil. The scoring system proposed by the NMH showed a better balance between sensitivity and specificity (89% and 87%, respectively) than did the WHO scoring system. In addition, Sant'Anna & Hijjar[17] found that the Brazilian scoring system was easier to implement in a health care setting in Brazil, where the tuberculosis/HIV co-infection is less frequent than that reported for African countries.[17] Indeed, another group of authors found that the NMH scoring system was also valuable in HIV-infected children and adolescents.[19]

The objective of the present study was to determine the sensitivity of the NMH scoring system for the diagnosis of tuberculosis in individuals 0-14 years of age.

Methods

This was a retrospective study. Between 1997 and 2007, 4,297 cases of tuberculosis were treated at the *Instituto Brasileiro para Investigação da Tuberculose* (IBIT, Brazilian Institute for the Tuberculosis Research), located in the city of Salvador, Brazil. The IBIT has an overall cure rate 85% above the cut-off value for good care of tuberculosis patients. Of the 4,297 patients, 381 (9%) were 0-14 years of age. Of those, 56 (14%) were excluded because they were diagnosed with extrapulmonary tuberculosis. Therefore, the initial sample comprised 325 children and adolescents suspected of having pulmonary tuberculosis. All medical records, as well as chest X-rays, were reviewed by a physician and a nurse, both with more than 20 years of experience, in order to score the patients in accordance with the NMH scoring system.[15,17] Of those 325 patients, 9 were excluded for having unconfirmed diagnoses. Therefore, the final study sample consisted of 316 children and adolescents diagnosed with the pulmonary form of tuberculosis. Data regarding clinical and radiological patient status, evidence of household contacts, chest X-ray findings, tuberculin test results, and nutritional status were collected. This protocol was approved by the Research Ethics Committee of the Federal University of Bahia *Climério de Oliveira* Maternity Hospital.

Results

Of the 316 patients included in the study, 249 were in the 0-9 age bracket and 67 were in the 10-14 age bracket. The mean age was 6.0 years. There were 176 males (55.7%) and 140 females (44.3%). Table 1 shows the distribution of patients between 1997 and 2007. We found that 205 patients (64%) presented symptoms:

Table 1 - Tuberculosis cases in all patients and in patients 0-14 years of age (all presentations and only pulmonary tuberculosis) by year. *Instituto Brasileiro para Investigação da Tuberculose*, 1997-2007.

Year	All tuberculosis cases	Tuberculosis in patients 0-14 years of age			
		All presentations		Pulmonary form	
	n	n	%	n	%
1997	292	32	11.0	26	81.3
1998	344	37	10.8	31	83.8
1999	339	27	8.0	23	85.2
2000	348	26	7.5	20	76.9
2001	453	37	8.2	22	59.5
2002	582	65	11.2	54	83.1
2003	475	34	7.2	25	73.5
2004	410	35	8.5	30	85.7
2005	404	39	9.7	36	92.3
2006	353	32	9.1	30	93.8
2007	279	16	5.7	15	93.8
Total	4,279	380	8.9	312	82.1

fever, cough, adynamia, sputum production, weight loss, or sweating for more than two weeks. The remaining 111 patients (36%) were asymptomatic (Table 2). On chest X-rays, hilar lymph node enlargement or miliary pattern were present in 187 cases (59.2%), and condensation or infiltration for more than two weeks were present in 110 (34.8%). One patient (0.3%) presented with bronchial tuberculosis, normal radiological pattern, and positive culture in BAL fluid.

Of the 316 patients, 254 (80.4%) had a history of close household contact with an AFB-positive adult within the last two years, and 267 (82.2%) presented with adequate nutritional status (weight above the 10th percentile).

The tuberculin test was negative in 11 patients (3.5%). The characteristics of these cases were disseminated tuberculosis, in 2; HIV infection with probable immunosuppression, in 1; a positive culture for *Mycobacterium tuberculosis*, in 2 (1 of whom was diagnosed with bronchial tuberculosis); corticosteroid treatment for severe bronchial asthma, in 1; presence of fever when the test was performed, in 1; sickle cell anemia, in 1; positive tuberculin test upon retest in the second month of treatment, in 1; and history of household contact as well as clinical and radiological symptoms, which improved after two months of treatment, suggestive of tuberculosis, in 2. Of those 11 patients, 9 were considered cured at the final evaluation. One died due to uncontrolled lymphoma, and 1 abandoned treatment four months later, showing partial improvement in signs and symptoms.

According to the NMH scoring system (Table 3), 251 (79.4%) of the patients in our sample were very likely to have tuberculosis (score, ≥ 40), 63 (19.9%) were moderately likely to have tuberculosis (score, 30-35), and 2 (0.7%) were unlikely to have tuberculosis (score, ≤ 25). When a cut-off score of 30 was used, the sensitivity of the scoring system proposed by the NMH was 99.3%.

One of the patients scoring ≤ 25 on the NMH scoring system was an asymptomatic 10-year-old girl with a history of severe bronchial asthma, who was closely followed by a pediatrician. A chest X-ray showed perihilar condensation, and the tuberculin test was negative (the test became positive—12 mm—upon retest three months after the beginning of treatment). This child had no history of contact with tuberculosis patients. The other was an asymptomatic 4-year-old girl with a history of contact with a tuberculosis patient within the past 2 years; she was finishing treatment for Hodgkin's lymphoma and had normal weight for her age when she presented with hilar lymph node enlargement on a chest X-ray. The tuberculin test was negative. Three months after the initiation of the tuberculosis treatment, the chest X-ray was normal. However, she died during the second round of treatment for uncontrolled lymphoma.

Table 2 - General characteristics of the patients 0-14 years of age diagnosed with pulmonary tuberculosis. *Instituto Brasileiro para Investigação da Tuberculose*, 1997-2007.

Characteristic	n	%
Gender		
Male	176	55.7
Female	140	44.3
Age, years		
< 1	11	3.5
1-4	132	41.8
5-9	106	33.5
≥ 10	67	21.2
Respiratory symptoms, weeks		
> 2	205	64.9
≤ 2	111	35.1
Chest X-ray pattern		
Hilar lymph node enlargement or disseminated pattern	187	59.2
Condensation or infiltration (with or without excavation) unaltered for > 2 weeks	110	34.8
Condensation or infiltration of any type < 2 weeks	18	5.7
Normal[a]	1	0.3
History of household contact within the last 2 years		
Yes	254	80.4
Unknown	62	19.6
Severe malnutrition[b]		
Yes	51	16.1
No	265	83.9
Tuberculin test, induration, mm		
History of vaccination for ≥2 years		
< 5	11	3.5
5-9	8	2.5
10-14	44	13.9
≥ 15	189	59.8
History of vaccination < 2 years		
< 10	5	1.6
10-14	14	4.4
≥ 15	37	11.7
No history of vaccination		
< 5	0	0
5-9	0	0
≥ 10	4	1.3
Not tested/no results[c]	4	1.3

[a]This child presented with normal X-ray findings and positive culture for *M. tuberculosis* in BAL fluid. [b]In accordance with the Food and Nutritional Surveillance System, Brazilian National Ministry of Health. [c]Not performed in 2, no reading in 1, and missing data in 1.

Discussion

The NMH tuberculosis scoring system is meant to be used in children and adolescents with negative AFB results in primary care settings.[15] When a cut-off score of 30 was used, the sensitivity of this scoring system at the IBIT was 99.3%, which is quite high. These results are similar to those found by Sant'Anna et al. in two retrospective studies,[20,21] as well as to those reported by Maciel et al.[22] in a nested control-case study. If only patients with scores ≥ 40 had been considered for treatment, 20% of the patients would not have been treated. In the present study, patients with scores ranging from 30 to 35 points (20.3% of the cohort) represented a critical population for the diagnostic confirmation. In our experience,

Table 3 - Distribution of the patients by their scores on the scoring system recommended by the Brazilian National Ministry of Health, 2002.

Score	Diagnosis of tuberculosis	n	%
≥ 40	Very likely	251	79.4
30-35	Moderately likely	63	19.9
≤ 25	Unlikely	2	0.7
Total		316	100.0

judicious clinic evaluation should prevail in the decision of whether to treat such patients. The negative predictive value of the proposed scoring system, with the low treatment cut-off score of 30 and with the acceptance of a sensitivity of 70% proposed by Maciel et al.,[22] is problematic. When this cut-off score is used, at least 30% of the patients without tuberculosis (with other pathologies) will receive tuberculosis treatment. This highlights the need for improved diagnostic methods for tuberculosis.

Another important aspect addressed in this study was the importance of the presence of an identifiable household contact with tuberculosis. In this cohort, 79.1% of the parents or guardians of the patients revealed the existence of a close household contact with active tuberculosis. In Brazil, the identification of household contacts of tuberculosis patients needs to be radically improved.[23] The Tuberculosis Control Program in the State of Bahia reported that only 8-25% of the household contacts of tuberculosis patients were investigated between 2004 and 2008. This is representative of the country as a whole, with similar findings in other states, such as Mato Grosso.[24] In addition, the decrease in the incidence rate of tuberculosis in Brazil, according to the WHO, is 2.9%, which is much lower than the ideal 11% reduction that has been achieved in other countries with better treatment control and more efficient contact outreach.[25]

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