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## Diagnosis of pulmonary tuberculosis in children and adolescents: comparison of two versions of the Brazilian Ministry of Health scoring system

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### ABSTRACT

The aim of this study was to evaluate the concordance between two versions of the scoring system (2011 and 2019), recommended by the Brazilian Ministry of Health, for the diagnosis of pulmonary tuberculosis (PTB) in children and adolescents. A retrospective descriptive study was performed to assess the medical records of children and adolescents with PTB, in TB units from Brazilian cities located in Rio de Janeiro, Minas Gerais, and Parana States, from January 1<sup>st</sup>, 2004, to December 1<sup>st</sup>, 2018. Patients aged 0 to 18 years old with a diagnosis of PTB were included. The comparison between the two scoring systems showed a moderate concordance according to the  $\kappa$  coefficient value = 0.625. Fourteen patients showed a reduction in the TB score, going from 30 points in the 2011, to 25 points or less in the 2019 one. Seventy one percent of these 14 patients had radiological changes suggestive of PTB and 86% had tuberculin skin tests greater than 10 mm. The study concluded that a moderate agreement was observed between the 2011 and 2019 scoring systems, with an increase in the number of patients scoring 25 points or less in 2019, which can eventually hinder the diagnosis of PTB.

**KEYWORDS:** Pulmonary tuberculosis. Children. Diagnosis. Clinical protocols. Tuberculin skin test. Tuberculosis scoring system.

### INTRODUCTION

The World Health Organization (WHO) estimated 1.0 million new cases of tuberculosis (TB) in children younger than 14 years old in 2017<sup>1</sup>. Of these, 55% went undiagnosed and/or unreported. One possibility for this under-detection is the difficulty in TB diagnosis. In 2018, Brazil reported 75,709 new cases of TB, including 3.3% in children younger than 14 years old<sup>1</sup>.

Brazil is among the 30 countries with a high burden of TB and coinfections of *Mycobacterium tuberculosis* (*Mtb*) and the human immunodeficiency virus (HIV)

are considered a priority by the WHO for TB control in the world<sup>2</sup>.

The diagnosis of pulmonary TB (PTB) in children is challenging as childhood TB is paucibacillary, symptoms are nonspecific, and in the early stages of the disease up to 50% of children can be asymptomatic<sup>3-6</sup>.

Due to the difficulty of the bacteriological confirmation of TB in children, in 2002, the Ministry of Health, Brazil (MoH) recommended the use of a scoring system (score) for the diagnosis of PTB in childhood<sup>7,8</sup>. The score comprises clinical, epidemiological and radiological data of evidence of infection by *Mtb* (positive tuberculin skin test [TST]) and it does not involve the bacteriological confirmation<sup>2,9,10</sup>. The use of this score helps the early diagnosis and treatment, even in basic health units<sup>2,11</sup>. This score has already had several validation studies published with consistent values of sensitivity and specificity that legitimized its use in the routine of health services<sup>2,3,12-15</sup>.

In the MoH TB Manual of 2011, the TST response was interpreted in accordance with the BCG vaccination time<sup>16,17</sup> (Table 1). The MoH TB Manual was revised in 2019, and there was a change in the score because of the new interpretation of the TST cutoff point (Table 2)<sup>2</sup>. The TST is now interpreted as suggestive of infection by *Mtb* if a result of 5 mm or greater is present, regardless of the BCG vaccination time<sup>2</sup>. The scoring criteria in the MoH Manual

are the same as those in 2011 and 2019, except for TST, but the total points achieved by a TST positive response in the new version of the score is 5 points lower than in the previous version<sup>2,16</sup>.

The present study aims to contribute to the diagnosis of childhood PTB by assessing the impact of the 2019 version of the MoH score for the diagnosis of PTB in children and adolescents. Therefore, there was interest in assessing whether this reduction in the total points of the score would influence the 2019 final scoring system, as the MoH recommends this scoring system for the diagnosis of PTB children.

## METHODS

A retrospective descriptive study of medical records of children and adolescents from 0 to 18 years old was carried out, and the diagnosis of PTB was established based on clinical or laboratory criteria, in reference centers as well as in basic health units in Brazilian cities located in Rio de Janeiro State, such as Duque de Caxias, Niteroi, Itaboraí and São Gonçalo; Belo Horizonte in Minas Gerais State and Curitiba, in Paraná State, in the period from January 2004 to December 2018.

All patients underwent evaluation using the 2011 MoH scoring system in their original health services.

**Table 1** - Diagnosis of PTB in children and adolescents with negative smear<sup>16</sup>.

Clinical condition	Radiological pattern	Contact with adult with TB*	TST*	Nutritional status
Fever or symptoms such as cough, adynamia, expectoration, slimming, sweating > 2 weeks <b>15 points</b>	Hilar adenomegaly or miliary pattern and/or condensation or infiltrate (with or without cavitation) unchanged by ≥ 2 weeks and/or condensation or infiltrate (with or without excavation) for ≥ 2 weeks, progressing with worsening or without improvement with antibiotics for common germs <b>15 points</b>	Close contact in the last 2 years <b>10 points</b>	TST ≥ 5 mm in not vaccinated with Bacillus <i>Calmette-Guérin</i> (BCG), vaccinated for more than 2 years, immunosuppressed or ≥ 10mm in children vaccinated with BCG less than 2 years ago <b>15 points</b>	Serious malnutrition <b>5 points</b>
Asymptomatic or with symptoms < 2 weeks <b>0 points</b>	Condensation or infiltrate of any type for less than 2 weeks <b>5 points</b>	Occasional or negative <b>0 points</b>	TST between 0-4 mm <b>0 points</b>	<b>0 points</b>
Respiratory infection that improved after using antibiotics for common germs or without antibiotics <b>(-10 points)</b>	Normal radiography <b>(-5 points)</b>			

\*TB = tuberculosis; TST = tuberculin skin test. At least 40 points = very likely diagnosis; 30-35 points = possible diagnosis; Less than 25 points = diagnosis is unlikely.

**Table 2** - Diagnosis of pulmonary tuberculosis in children and adolescents with negative smear microscopy or undetected RMT<sup>2</sup>.

Clinical condition	Radiological patterns	Contact with adult with TB*	TST*	Nutritional status
Fever or symptoms such as cough, adynamia, expectoration, slimming, sweating > 2 weeks <b>15 points</b>	Hilar adenomegaly or miliary pattern and/or condensation or infiltrate (with or without cavitation) unchanged by ≥ 2 weeks and/or condensation or infiltrate (with or without excavation) for ≥ 2 weeks, progressing with worsening or without improvement with antibiotics for common germs <b>15 points</b>	Close contact in the last 2 years <b>10 points</b>	TST between 5 and 9 mm <b>5 points</b>  TST ≥ 10 mm <b>10 points</b>	Serious malnutrition <b>5 points</b>
Asymptomatic or with symptoms < 2 weeks <b>0 points</b>	Condensation or infiltrate of any type for less than 2 weeks <b>5 points</b>	Occasional or negative <b>0 points</b>	TST < 5 mm <b>0 points</b>	Weight ≥ 10 <sup>th</sup> percentile <b>0 points</b>
Respiratory infection that improved after using antibiotics for common germs or without antibiotics <b>(-10 points)</b>	Normal radiography <b>(-5 points)</b>			

RMT = rapid molecular test; TB = tuberculosis; TST = tuberculin skin test. At least 40 points (very likely diagnosis) = it is recommended to start TB treatment; 30- 35 points (possible diagnosis) = indicative of TB; it is advised to initiate treatment, at medical discretion; Less than 25 points (diagnosis is unlikely) = investigation of the child should be continued.

The 2011 score of patients diagnosed as having PTB was compared with those that would be obtained with the 2019 one. Diagnosis of PTB was confirmed by positivity of smear acid fast bacilli, *Mtb* culture or Xpert MTB/RIF in 48 (39.0%) of 123 patients undergoing diagnostic testing.

In the MoH TB Manual of 2011<sup>16</sup>, TST was considered positive if the skin induration was ≥ 5 mm in children not vaccinated with Bacillus Calmette–Guérin (BCG) vaccine, vaccinated for more than 2 years, or immunosuppressed, and ≥ 10 mm in children vaccinated with BCG in the previous 2 years, that scored 15 points. TST between 0 and 4 mm equals to zero points<sup>16,17</sup>.

In the MoH TB Manual of 2019<sup>2</sup>, regardless of BCG vaccination time, when the TST is ≥ 10 mm, equals to 10 points. TST between 5 and 9 mm, equals to 5 points. TST between 0 and 4 mm equals to zero points.

The studied variables were sex, age, TB symptoms, contact with an adult presenting with TB, chest X-ray, TST and the presence of malnutrition. The diagnostic criterion for malnutrition was weight below the 10<sup>th</sup> percentile, according to MoH<sup>2,16</sup>. The human immunodeficiency virus infection was also investigated.

A descriptive statistics was used, and the agreement analysis was performed using the kappa ( $\kappa$ ) index to

evaluate the two scores (2011 and 2019) and a dispersion graph was plotted.

This study was carried out in accordance with the Declaration of Helsinki and the Resolution 466/2012 of the Brazilian National Health Council of the Ministry of Health and was approved by the Research Ethics Committee of Oswaldo Cruz Institute -Fiocruz (coordinating center) on April 19<sup>th</sup>, 2017.

## RESULTS

The sample consisted of 235 patients with PTB diagnosed in their original health services using the 2011 score. One hundred and three patients (52.3%) had a bacteriological/molecular test done and 39% of them (48/123) had a positive result. If we consider the total population, only 20.4% had a laboratory-confirmed diagnosis of TB (48/235).

Of the 11 health establishments involved in the study, three were primary care units, and the others were TB referral centers.

Most patients were female (56%), and 64.7% were children (aged < 10 years). Human immunodeficiency virus testing was performed in 135 (57.4%) of the 235 patients, with 11 (8.1%) of positivity. History of contact with an

adult presenting with PTB, radiographic changes suggestive of PTB, and positive TST (> 5 mm) were recorded in most patients. The general characteristics of the patients, demographic and clinical aspects, and the diagnostic criteria for PTB are described in [Table 3](#).

In our study, only one 8-month-old infant who had a TST of 9 mm received zero points in 2011, and 5 points in 2019, reaching a final score varying from 40 to 45 points. Therefore, in 2019 this patient did not change the final

**Table 3** - General characteristics of patients aged 0 to 18 years old diagnosed with pulmonary tuberculosis, from January 2004 to December 2019 (the total number of patients was 235).

Characteristics	N	%
<b>Sex</b>		
Female	131	56.0
Male	104	44.0
<b>Age (years)</b>		
< 2	47	20.0
2-9	105	44.7
10-14	72	30.6
≥ 15	11	4.7
<b>Symptoms</b>		
Absent	74	31.4
< 2 weeks	9	3.8
> 2 weeks	150	63.8
Improvement after antibiotic use or without antibiotics	2	1.0
<b>Contact with TB</b>		
Negative	41	18.0
Positive	194	83.0
<b>Chest X-ray</b>		
Changes suggestive of PTB	202	86.0
Changes not suggestive of PTB	19	8.0
Normal	14	6.0
<b>TST (in mm)</b>		
0-4	41	17.0
5-9	14	6.0
≥ 10	180	77.0
<b>Malnutrition</b>		
Absent	205	87.0
Present	30	13.0
<b>HIV</b>		
Negative	124	92.0
Positive	11	8.0

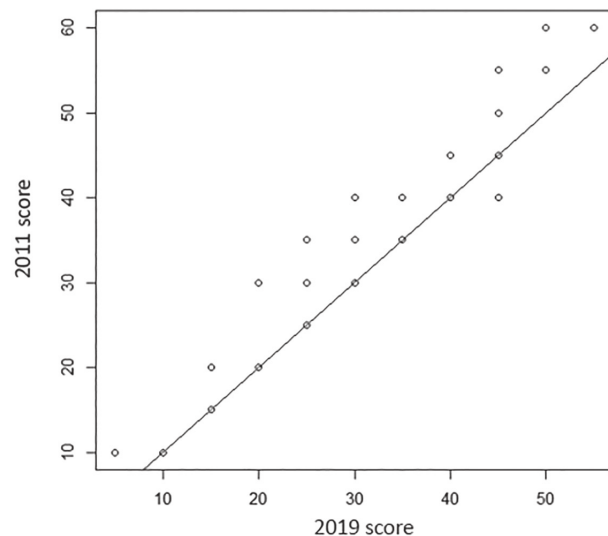
ST = tuberculin skin test.

classification, i.e., continued to be in the category “very likely TB”.

In the 2011 scoring system, 224 (95.3%) of 235 patients had a score of 30 points or greater, referring to a very likely ( $\geq 40$ ) or possible (30–35) PTB diagnosis. In 2019, there were 210 patients (89.3%) with 30 points or more.

In 2011, the median score was 40 (interquartile range [IQR], 40-55), with a mean of 43 (standard deviation  $\pm 11$ ). In 2019, the median score was 40 (IQR, 35–50), with a mean of 39 (standard deviation  $\pm 10$ ). The difference between the mean scores was 4.09 points.

The 2019 score was lower than the one obtained in 2011. The agreement between 2011 and 2019 score categories was 70.2%; being lower in the age range of 2 to 9 years-old (63.1%) with respect to patients < 2 years old (72.9%) and  $\geq 10$  years old (77.4%). The  $\kappa$  coefficient value was 0.625, referring to a moderate agreement ( $0.4 \leq \kappa < 0.8$ ). The scatter plot with the 2011 and 2019 scores is shown in [Figure 1](#).



**Figure 1** - Scatter plot with the comparison between the 2011 score and the 2019 one.

It was found that 14 patients had a score of 30 or more in 2011, while they would have a score of 25 or less (TB unlikely) using the 2019 scoring system. According to the 2011 score, 11 patients obtained 25 points or less.

The 11 patients with 25 or less by the 2011 score and the 14 patients who were evaluated with this score in 2019 were analyzed separately ([Table 4](#)).

The majority of these 14 patients who presented with a reduction in points, i.e., started to score 25 or less in 2019, had radiological changes suggestive of TB (71.4%) and a TST of 10 mm or greater (86%). On the other hand, 86% were asymptomatic and 71.5% had no contact with an adult with TB. Regarding the HIV test, 43% were negative;

**Table 4** - Analysis of patients who scored 25 points or less (unlikely TB) in 2011 (n = 11) and 2019 (n = 14).

Characteristics	2011 score	2019 score
	n = 11 n (%)	n = 14 n (%)
<b>Sex</b>		
Male	3 (27.0)	6 (43.0)
Female	8 (73.0)	8 (57.0)
<b>Age</b> (mean value in years)	7.1	5.1
<b>Contact with TB</b>		
Yes	7 (64.0)	4 (28.5)
No	4 (36.0)	10 (71.5)
<b>Symptoms</b>		
No symptoms	4 (36.0)	12 (86.0)
Symptoms < 2 weeks	1 (9.0)	2 (14.0)
Symptoms > 2 weeks	6 (55.0)	0
<b>Malnutrition</b>		
Yes	4 (36.0)	1 (7.0)
No	7 (64.0)	13(93.0)

none was positive, and 57% had no information about the HIV test.

In the 2019 score, there were approximately three times more asymptomatic patients and others presenting with symptoms for less than 2 weeks. On the contrary, there were less malnourished patients than with the 2011 score (Table 4).

The evaluation of these 14 patients has also shown that 5 of 11 (45%) patients underwent tests for the diagnostic investigation with smear, culture, or polymerase chain reaction that showed positive results, confirming the TB diagnosis. All these 5 patients (n = 2, < 2 years old; n = 3, ≥ 10 years old and adolescents) who had microbiological positive results also had chest radiography results suggestive of PTB; TST of 10 mm or greater; no history of contact with a TB patient; malnutrition; or PTB suggestive symptoms.

## DISCUSSION

The retrospective assessment of the 2011 and 2019 scores carried out in the present study showed a moderate agreement between both systems, as expressed by the  $\kappa$  coefficient of 0.625.

In the present study, 194 patients (82.5%) were reported as having PTB by different health services, having had contact with an adult with TB, thus reflecting the importance of researching these data for the diagnosis of childhood

PTB<sup>18</sup>. Tuberculosis in children is directly associated with the prevalence of the disease in adults. The risk of acquiring *Mtb* infection is higher in children living in regions in which there is a high prevalence of active TB, in houses with high population density and poor ventilation<sup>19</sup>.

The finding of 13.0% of cases with severe malnutrition may reflect the frequent consumptive nature of TB<sup>20</sup>. Malnutrition is associated with TB, both as a risk factor and a consequence of the illness. The consumptive nature of TB is related to both, anorexia and increased production of inflammatory cytokines, which lead to a catabolic state<sup>20</sup>.

Regular assessment of weight in childhood is essential. In the study of Marais *et al.*<sup>21</sup> the identification of persistent cough associated with documented failure to thrive contributed to the diagnosis of PTB, with a sensitivity of 68.3%, specificity of 80.0%, and a positive predictive value of 82.0%.

It is noteworthy that the 2011 scoring system has higher scores than the ones obtained in 2019. However, it is important to note that the increase in the number of cases that scored 40 or more to a score of 30-35 points did not affect the diagnosis of PTB, as 30 points or more would already be indicative of PTB, even allowing the beginning of TB treatment according to clinical criteria<sup>2</sup>.

The increase from 11 to 25 patients with a score of 25 or less, in the comparison between 2011 and 2019, resulted in a higher number of patients who would be considered to present with unlikely PTB in 2019. This apparent loss of diagnostic capacity of the 2019 scoring system would only result in expanding the indication to proceed with the investigation in these patients, as has been recommended since 2011<sup>16</sup>. However, it was evident, in the present study, that the group with 25 points or less had radiological patterns compatible with PTB and TST-positive in most cases, although with other characteristics less suggestive of PTB. Thus, the diagnosis of these patients would naturally be more difficult and would corroborate the indication of more detailed investigation<sup>2,16</sup>.

The study has some limitations. Firstly, we can mention the lack of information in some medical records regarding the HIV testing. Secondly, it is important to note that although the score is more applicable to health services with low technological density, such as outpatient clinics and basic health units, the patients included in the study were mostly from referral centers and they have a greater operational capacity for TB investigation, limiting the extrapolation of results found in other levels of care. Thirdly, the score is recommend for children who are generally unable to expectorate and are mostly sputum negative as well as adolescents with negative smear microscopy or undetected RMT. In the present study, all children had a

clinical diagnosis of PTB. The majority of adolescents were smear microscopy or RMT-negative, as well, or had no sputum tested. Finally, the study only included participants who had already been diagnosed with PTB according to the 2011 scoring system. Therefore, the results should not be subjected to generalization for the usual clinical scenario, which would include a large proportion of patients who do not actually have PTB.

## CONCLUSION

Despite the aforementioned limitations, the present study is a subsidy for the National TB Control Program regarding the diagnosis of Childhood PTB. We observed that the percentage of patients with 25 points or less in 2011 increased in 2019. The change in the 2019 score decreased the importance of TST as a diagnostic criterion for PTB, probably leading to a more specific and less sensitive score in comparison with 2011. However, a moderate agreement was observed when the two scores were analyzed. New studies are needed to evaluate the sensitivity, specificity and predictive values of the 2019 scoring system.

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## AUTHORS' CONTRIBUTIONS

RFC, MFBPS, CCS, CAAC had primary responsibility for protocol development, the final data analysis and writing the manuscript; RFC, MFBPS, CCS, CAAC, ALK, ACCC and AMOR participated in the enrollment of patients, analytical framework for the study and contributed to the writing of the manuscript; LGCV, RBA, SMAS, CMS, ASRM, PSM, LIG, TMM, APFB, APQS, RMCR, MGRO, LMOD, ALC, SCL, MLSC, MCS, TTT and COR were responsible for patient screening or contributed to the writing of the manuscript. All the authors agree in submitting the manuscript.

## CONFLICT OF INTERESTS

None were declared.

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