

Tuberculosis score chart signs and symptoms in children with positive tuberculin skin tests

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Abstract

Background The Indonesian Pediatrics Respiriology Working Group (IPRWG) developed the tuberculosis (TB) score chart to assist in diagnosing TB in community health centers (Puskesmas).

Objectives To document signs and symptoms of the IPRWG TB score chart, to analyze various combinations of these signs and symptoms, and to compare these combinations in children with TB to those without TB, based on a TB score chart.

Methods We performed a cross-sectional study from July to October 2008, in Padang, Bukittinggi and Pasaman. We recruited children with known positive tuberculin skin tests (TST) from a 2006 tuberculin survey. Questionnaires on signs and symptoms (IPRWG TB score chart) were completed and chest radiographs were obtained for all children. Subjects fulfilling a total score of six or more were considered to have a diagnosis of TB.

Results We diagnosed TB in 78/285 (27.3%) subjects. A score value of 3 for the category of household contact (HHC) positive smears was added in 21/78 subjects. However, the highest risk for TB disease was found in those diagnosed with no clear history of HHC (58.9%; OR 192, 95% CI 22 to 1679). The highest risk factors for TB were suggestive chest X-ray (34.6%; OR 9.2, 95% CI 3.6 to 23.4) and fever lasting > 2 weeks (17.9%; OR 8, 95% CI 2.2 to 29.1), respectively. Of 46 children with TB diagnosis but without HHC, the combination of undernourishment, lymph node enlargement and suggestive chest X-ray was highest (28.2%). Individual or dual combination signs and symptoms were also found in children without TB diagnosis.

Conclusion Various combinations of signs and symptoms could lead to fulfillment of scoring for TB diagnosis. [Paediatr Indones. 2012;52:78-85].

Keywords: tuberculosis score chart, children, signs, symptoms

Childhood TB remains a major challenge in the twentieth century. Children comprise a significant proportion of the disease population and experience considerable morbidity and mortality due to this ailment. In the year 2000, children made up as many as 884,000 out of 8.3 million new TB cases (10.7%),¹ with higher estimates in endemic areas.² As disease transmission continues, there are increasing numbers of new childhood TB cases. Indonesia, one of the 22 most highly burdened countries with TB, has little data on TB prevalence in children ≤ 15 years of age. However, the WHO estimated it to be 2.7%, with a case rate of 23 per 100,000.¹ A previous study in Padang, West Sumatera, on children 6-7 years of age, reported a prevalence of 9.9%.³

TB diagnosis in children is challenging, as there are limited specific signs and symptoms, making it difficult to differentiate from other diseases.⁴⁻⁶ Chest radiograph is regarded as a valuable diagnostic tool, but it is often difficult to interpret.^{7,8} Bacteriological confirmation is rarely achieved, and often not even

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attempted.⁹ Tuberculin skin test results frequently show false positives and negatives. In addition, the distinction between latent TB infection and active disease is highly problematic.^{10,11}

Diagnostic algorithms and TB score charts were developed especially for endemic areas. Most are partly based on signs and symptoms, poorly validated and lack standardized symptom definitions.¹²⁻¹⁵ The IPRWG developed a TB score chart for primary health care services.¹⁶ Traditional symptoms associated with TB, such as prolonged fever, and recurrent cough, and signs, such as nutritional status and lymph node enlargement, have been used for the score chart. But, there has been little data on the prevalence of TB or the various combinations of signs and symptoms using the TB score chart.

Methods

A cross-sectional study was carried out from July to October 2008, as part of a larger study to determine risk factors and prevalence of TB, two years after a

tuberculin survey. From the tuberculin survey, 368 children aged 6-7 years had positive TSTs. This region (Padang, Bukittinggi and Pasaman) is a highly endemic adult TB in West Sumatera. (The average case notification rate of new, positive AFB sputum-confirmed cases was reported to be 34/100,000 per year).¹⁷ This study was approved by the Ethics Committee of the Faculty of Medicine, Andalas University.

We attempted to recruit all children with positive TST, based on the results of the 2006 tuberculin survey in this area. Trained field workers collected the baseline data. Written informed consent was obtained from parents. We administered questionnaires, physical examinations and chest radiographs (CXR) to all subjects. Data was completed according to eight indicators in the IPRWG TB score chart (Table 1).

Questionnaires were completed by parents under supervision of trained field workers and were used to record symptoms commonly associated with TB, including history of household contact with positive smears, fever lasting ≥ 2 weeks, and cough lasting ≥ 3 weeks. We assessed for nutritional status

Table 1. IPRWG TB score chart, 2008¹⁶

Feature	0	1	2	3	Score
TB contact	not clear	-	By family report; smear neg/ not known/not clear	smear pos	
Tuberculin skin test (Mantoux test)	negative	-	-	positive (> 10mm or > 5mm if immunosuppressed)	
Nutritional status	-	BW/H <90% or BW/A < 80%	Severe malnutrition (BW/A <60%)	-	
Fever of unknown origin (FUO)	-	≥ 2 weeks	-	-	
Chronic cough	-	≥ 3 weeks	-	-	
Lymphadenopathy (cervical, axillary, inguinal)	-	≥ 1 cm, amount >1, pain (-)	-	-	
Joint swelling (hip, knee, vertebral, phalangeal)	-	Swelling	-	-	
CXR	Normal/ not clear	Suggestive TB		-	
Total Score					

- **ATTENTION:** Hospital referral should be made in presence of critical signs, such as seizure, decreased level of consciousness, neck stiffness, spinal masses, limping, chessboard phenomenon.
- **Notes:** Positive TB diagnosis if total score ≥ 6 (by doctor); BW based on present BW; fever and cough relevant if no response to standard therapy; CXR is not considered to be a main diagnostic tool; evaluated for accelerated BCG reaction (< 7 days); hospital referral to be made for children <5 y.o. if score > 5 or strong suspicion for TB; INH prophylaxis to be prescribed for score < 6 if (+) household contact

(WHO standard), lymph node enlargement > 1 cm, and joint-specific symptoms (spondylitis, coxitis) by physical examination.

Standard anteroposterior and lateral view CXRs were taken. Three independent experts (2 pediatric respirologists and 1 radiologist), blinded to all clinical information, evaluated the CXRs and documented their findings on a standard report form. Radiologic criteria scoring depended on the presence of a suggestive CXR according to IPRWG guidelines, and agreed upon by two of three independent experts.

Subjects were considered to have TB if they had a score total of ≥ 6 using IPRWG TB score chart guidelines. Because all subjects had positive TSTs, a minimum score total of 3 for the remaining categories resulted in a TB diagnosis.

Data analyses were carried out with a statistical analysis program. Frequencies of signs and symptoms were compared among subjects' age groups, nutritional status, as well as between positive TST subjects with and without a TB diagnosis. We performed binary logistic regression analysis with backward LR

method to assess significant signs and symptoms in TB diagnosis.

Results

Of the 368 children with positive TST in the 2006 study, 285 were included in our study. Demographic data of 207 children without TB and 78 children with TB, as diagnosed by TB score chart, is shown in **Table 2**. There were no significant differences in gender and age distribution between the two groups. There was a higher proportion of negative BCG scars in children with TB diagnoses (25.7%) compared to those without TB. Binary logistic regression analysis with backward LR method revealed that subjects with TB diagnoses had greater history of household contact by family report/negative smears than those with positive smears (OR 138, 95% CI 10.5 to 1807). Interestingly, subjects with TB diagnoses but without clear HHC had the highest risk for TB disease (OR 192, 95% CI 22 to 1679).

Table 2. Characteristics of subjects diagnosed with TB and without TB

	No TB (%) (n=207)	TB (%) (n=78)	OR (95% CI)	P value
Gender				
Male	116 (56.0)	45 (57.7)	1.1 (0.5 to 2.4)	0.80
Age distribution in years				
8-<10	77 (37.2)	33 (42.3)	1.2 (0.6 to 2.8)	0.59
10-12	130 (62.8)	45 (57.7)		
BCG scar				
positive	169(81.6)	58(74.3)	0.8 (0.3 to 2)	0.67
negative	38(18.4)	20(25.7)		
TB contact (HHC)				
Unclear	198 (95.7)	46(58.9)	192.5 (22 to 1679)	0.00
Family reported, but smear neg unknown/unclear	9 (4.3)	11(14.1)	138 (10.5 to 1807)	0.00
Smear positive	0	21(27.1)		

Table 3. Comparison of signs and symptoms reported in children with and without TB

	No TB (%) (n=207)	TB (%) (n=78)	OR (95% CI)	P value
Individual symptoms				
FUO > 2 weeks	6(2.9)	14(17.9)	8 (2.2 to 29.1)	0.00
Chronic cough > 3 weeks	18(8.7)	18(23.1)	2.97 (1 to 9.13)	0.56
Nutritional status				
Well-nourished	160(77.3)	44(56.4)		
Undernourished*	47(22.7)	34(43.6)	6 (2.6 to 14.1)	0.00
Lymph node enlargement	43(20.8)	35(44.9)	3.26 (1.4 to 7.5)	0.006
Joint swelling	0(0.0)	0(0.0)		
Suggestive CXR	22(10.6)	27(34.6)	9.2 (3.6 to 23.4)	0.00

*One subject with TB was severely malnourished

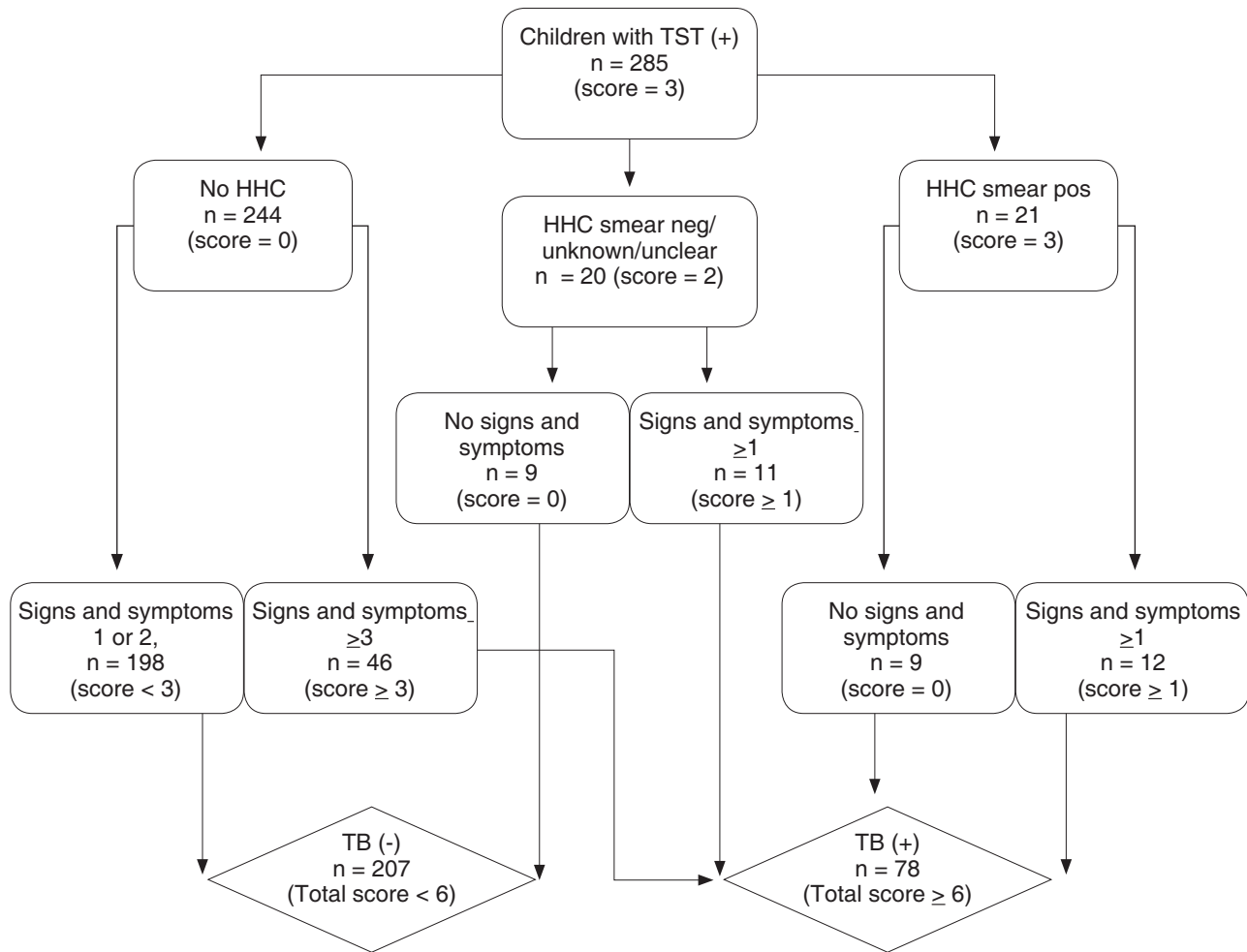


Figure 1. Flowchart of subjects to diagnose TB using the TB score chart

Table 3 compares the signs and symptoms reported in children diagnosed to have and not have TB. All signs and symptoms were significantly more frequent in children with TB, with $P < 0.05$ and $OR > 1$, except for well-nourished nutritional status. Using logistic regression, the presence of suggestive CXR showed the greatest odds for TB (34.6% of patient diagnosed with TB; $OR\ 9.2$, 95% $CI\ 3.6\ to\ 23.4$), followed by fever of unknown origin (FUO) lasting ≥ 2 weeks (17.9% of patients diagnosed with TB; $OR\ 8$, 95% $CI\ 2.2\ to\ 29.1$). Only one subject was severely malnourished. Significantly, more children with TB had lymph node enlargement than those without TB (44.9% vs 20.8%, respectively). In addition, chronic cough ≥ 3 weeks showed the lowest odds for disease ($OR\ 2.97$, 95% $CI\ 1\ to\ 9.1$). None of our subjects

exhibited bone or joint swelling.

According to the IPRWG TB score chart, a minimum total score of 3 for non-TST criteria was needed to diagnose TB in our subjects since all had positive TST (score value 3). In order to further evaluate the contribution of other signs and symptoms to the fulfillment of score value 6 in subjects with TB, we separated subjects with HHC according to the IPRWG TB score chart, into a positive smear group (additional score value of 3), and a negative smear group (additional score value of 2) (**Figure 1**).

Table 4 shows the frequency of five clinical signs and symptoms in the TB score chart in various combinations (fever, cough, nutritional status, lymph node enlargement and suggestive CXR) in 46 children with TB but without clear HHC. There were 6

Table 4. Combinations of signs and symptoms in children diagnosed with TB but with no clear HHC (n = 46)

Combinations of signs and symptoms	TB (%)
Add score value of 3	
Lymph node enlargement, severe malnourishment	1 (2.2)
Fever, cough, lymph node enlargement	4 (8.7)
Fever, cough, suggestive CXR	5 (10.9)
Fever, lymph node enlargement, suggestive CXR	6 (13.1)
Cough, lymph node enlargement, suggestive CXR	7 (15.2)
Lymph node enlargement, suggestive CXR, undernourishment	13 (28.2)
Add score value of > 4	
Fever, cough, lymph node enlargement, suggestive CXR	4 (8.7)
Fever, cough, lymph node enlargement, undernourishment	3 (6.5)
Fever, lymph node enlargement, suggestive CXR and undernourishment	3 (6.5)

Table 5. Comparison of signs and symptoms prevalence reported in children without TB (n=216) and with TB (n=32) based on HH contact

Indicator	No TB (%)		TB (%)	
	No HHC (n=207)	HHC smear (-) (n=9)	HHC smear (-) (n=11)	HHC smear (+) (n=21)
1 signs/symptom (add 1 score value)				
Undernourishment	30 (14.5)	0	1 (9.09)	4 (19)
Lymph node enlargement	24 (11.6)	0	1 (9.09)	3 (14)
Suggestive CXR	15 (7.2)	0	1 (9.09)	0
>2 signs/symptoms (add >2 score values)				
Cough + lymph node enlargement	4 (1.9)	0	1 (9.09)	0
Fever + undernourishment	2 (1)	0	1 (9.09)	0
Fever + lymph node enlargement	2 (1)	0	1 (9.09)	0
Cough +undernourishment	2 (1)	0	1 (9.09)	0
Lymph node enlargement + suggestive CXR	3 (1.4)	0	1 (9.09)	1 (5)
Cough + suggestive CXR	1 (0.5)	0	1 (9.09)	1 (5)
Lymph node enlargement + undernourishment	10 (4.8)	0	1 (9.09)	2 (9.5)
Cough + lymphnode enlargement + undernourishment	0	0	1 (9.09)	1 (5)
No other signs/symptoms	114 (55)	9 (4.3)	0	9 (42.5)

combinations (score value of 3) to obtain total score of 6, and 3 combinations (score value > 3) to obtain total score of > 6. We found the highest prevalence in the combination of 3 indicators: lymph node enlargement, suggestive CXR and undernourishment (28.2%). The lowest prevalence was the combination of severe malnourishment and lymph node enlargement (2.2%). The presence of lymph node enlargement and FUO lasting ≥ 2 weeks were found in almost all combinations (6 out of the 9 combinations), followed by cough lasting ≥ 3 weeks (5 out of the 9 combinations).

Table 5 shows the comparison of signs and symptoms prevalence reported in children without TB (n=216) and with TB (n=32) based on HH contact. In the single sign/ symptom category, undernourishment and lymph node enlargement were more frequent in children with TB diagnosis compared

to those without TB, but suggestive CXR was more frequent in children without TB diagnosis. More patients with TB diagnosis had ≥ 2 sign/ symptom combinations than those without TB. Interestingly, there were 9 (4.3%) children without TB diagnosis reported to have HHC, but with negative/unclear smears (score value of 2). Furthermore, there were 9 (42.5%) children with TB diagnosis who had positive HHC smears (score value of 3) but no other signs/ symptoms.

Discussion

We have documented TB signs and symptoms based on the IPRWG TB score chart in children with positive TST. There were eight signs and symptoms

in the TB score chart, including TST and HHC. All subjects in our study had positive TST, but only 7.3% had HHC with positive smears. There was a statistically significant difference for HHC positive smears in children with TB compared to those without TB. All subjects without TB diagnosis had no history of HHC positive smears. The majority of subjects with TB diagnosis were without clear history of HHC. Household contact was a major determinant for TB diagnosis, but is difficult to identify HHC due to the social stigma of TB. Therefore, having no history of HHC does not exclude a TB diagnosis. However, in a setting of high TB prevalence, most infections, particularly in children older than 2 years, are contracted from outside the household but within the community. Additional caregivers outside the household are also important sources of infection, especially grandparents or extended family members who care for children during the day.¹⁸ In addition, there has been poor recording of positive sputum smears at community health centers (Puskesmas), making HHCs difficult to confirm.

Cough lasting ≥ 3 weeks, fever lasting ≥ 2 weeks and/or undernourishment often leads to the investigation of TB in children. Indeed, we found these conditions to be more frequent in children with TB. Individual symptoms in the IPRWG TB score chart contributed an additional score value of 1, increasing when combined with other symptoms. The combination of lymph node enlargement, suggestive CXR and undernourishment was the most frequently observed combination. Contribution of these three signs and symptoms should be further defined for more objective use.¹⁵ Although significant differences were found, they are of limited diagnostic value and only relevant for an epidemiological perspective. A study at Cape Town randomly selected children from a high burden community and reported specific definitions of cough and weight loss in the preceding 3 months as symptoms associated with TB. Well-defined symptoms such as acute cough with delayed recovery, recurrent acute cough, and persistent non-remitting cough were important for increased diagnostic value.¹³ Improved case definitions and symptom characterization are required when assessing the diagnostic value of symptoms.^{12,15} Therefore, if a symptom could not be defined more specifically, it could potentially increase the score value, leading to overdiagnosis of TB.

We found that children with positive TSTs and undernourishment had a 6 times higher likelihood for TB than those in a study in India (3.9 times).¹⁹ In children without TB diagnosis, we observed that undernourishment was the most frequent sign, both individually and in combination with other signs and symptoms. Nutritional status in the IPRWG TB score chart was based on the WHO standard. However, we did not distinguish between subjective and objective weight loss. Subjective weight loss showed poor correlation with TB, differing from that of objective weight loss. Marais *et al.* found objective weight loss to be more sensitive and significant when used for TB contact tracing.¹² In endemic TB settings, the diagnostic value of weight loss may be enhanced by first eliminating other common causes of poor weight gain, such as worm infestation and food security. Therefore, a more specific definition of undernourishment in the TB score chart may prevent TB overdiagnosis.

We found about one-third of subjects with TB had abnormal CXRs, based on three reports from independent experts (2 pediatric respirologists and a radiologist) blinded to all clinical information. In daily practice, a CXR is evaluated by only one radiologist who has the summarized clinical data, potentially leading to overdiagnosis, too. It is important for pediatricians to competently evaluate CXRs, in order to confirm the radiologist's findings.

Since all subjects in our study had positive TST, an initial score value of 3, a TB diagnosis could be made if subjects had score values of ≥ 3 from other signs and symptoms, for a total score value of ≥ 6 . The additional signs and symptoms in the TB score chart included reports of HHC with (i) positive smear (score value of 3), or (ii) negative/unclear smear (score value of 2). Other signs and symptoms contribute a score value of 1, except for severe malnutrition which contributes 2 score values. In 9 children, TB was diagnosed by adding the score from HHC positive smears (score value of 3) to the positive TST (score value of 3). These 9 subjects had no other contributing signs and symptoms. In fact, the internationally accepted definition of TB infection is positive TST, without other signs and symptoms.¹⁰ Based on the looser definition, it is possible that those 9 subjects were diagnosed with TB when they actually had no disease. By this standard,

oral antituberculosis treatment should be given, as prophylaxis or therapy.

We found 3 signs and symptoms presenting individually and 8 combinations of two signs and symptoms in both children with and without diagnosed TB. Interestingly, the majority of the 2 sign and symptom combinations had lymph node enlargement, followed by cough lasting ≥ 3 weeks and undernourishment. This observation suggests that these three signs and symptoms should be evaluated by physicians prior to making a TB diagnosis. If these three signs and symptoms are poorly validated by the physician at the community health center (Puskesmas), additional score values may be included, leading to overdiagnosis of TB.

This study had several limitations. The questionnaire was subject to recall bias and reporter subjectivity. We attempted to limit recall bias by focusing on current signs and symptoms to reduce reporter subjectivity by standard characterization of symptoms. Investigator bias was limited, as symptom characterization was done before CXR results were known.

We describe the potential for overdiagnosis of TB in children when using the IPRWG TB score chart. All our subjects were TST positive, and therefore, at a higher risk to be diagnosed with TB. It is essential to know the prevalence of signs and symptoms within the general community being studied in order to assign appropriate score values to particular symptoms. Most importantly, our study emphasizes the need for improved symptom characterization and accurate outcome definitions to adequately diagnose active TB disease. A large prospective, community-based study is required to validate the diagnostic value of this symptom-based approach.

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