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Assessment of a clinical score for screening suspected pulmonary tuberculosis cases

ABSTRACT

OBJECTIVE: To assess the accuracy (sensitivity) of a clinical score for presumptive pulmonary tuberculosis cases during screening.

METHODS: Descriptive cross-sectional study comprising 1,365 patients attending the department of lung diseases at a secondary care outpatient clinic in the city of Rio de Janeiro, Southeastern Brazil, during 2006 and 2007. All respondents answered a standardized questionnaire administered by the clinic's nursing staff. Information on age, weight and clinical symptoms were collected. The presumptive diagnosis of pulmonary tuberculosis was made by summing up the scores of the data collected. The diagnosis of active tuberculosis was based on bacteriological findings and medical criteria. There were estimated sensitivity, specificity, positive predictive value and negative predictive value for a set prevalence, and 95% confidence intervals for different score cutoffs. The score performance was assessed using the receiver operating characteristic (ROC) curve.

RESULTS: For the diagnosis of tuberculosis, cough for more than one week and cough for more than three weeks showed a sensitivity of 88.2% (86.2, 90.2) and 61.1% (57.93, 64.3), specificity 19.2% (16.6, 21.8) and 51.3% (48.1, 54.5), respectively. The clinical score of 8 had a sensitivity of 83.13% (77.8, 87.6), specificity of 51.8% (48.5, 55.1), positive predictive value of 91.6% (90.0, 83.2) and negative predictive value of 32.9% (30.1, 35.7).

CONCLUSIONS: Cough for more than three weeks showed low sensitivity and specificity. A highly sensitive clinical score can be an alternative tool for screening pulmonary tuberculosis as it allows early care of suspected cases and standard nursing care approach.

DESCRIPTORS: Tuberculosis, Pulmonary, diagnosis. Clinical Diagnosis. Diagnostic Techniques and Procedures. Triage. Sensitivity and Specificity.

INTRODUCTION

The World Health Organization (WHO) Stop TB Program was launched in 2006 as part of the Global Plan designed to scale up tuberculosis (TB) control. It intends to develop and assess new tools and strategies for TB control, diagnosis and treatment that would effectively allow to eliminating TB.[15]

It has become a priority to find and treat early active (bacilliferous) cases so that infection control measures can be implemented, thus preventing the contact of these patients with children, elderly and immunosuppressed individuals in waiting and examination rooms.[a]

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The WHO and other international organizations have suggested the implementation of TB control measures in so-called "risk environments." They defined high-risk environments for *Mycobacterium tuberculosis* transmission among patients, healthy individuals for the patient or the patient for health professionals.[6,16]

In recent years infection control measures in Brazil have been mostly recommended for and implemented in hospital or inpatient settings that require longer and more intensive care.[6,b] However, it was only in 2010 that the risk of TB infection in primary care units became a matter of concern among health policy makers[10,11] as a result of increased rates of TB infection reported among community health workers that provide care to TB patients in the Family Health Program in the municipality of Cachoeiro do Itapemirim, state of Espírito Santo, southeastern Brazil.

The actions implemented at primary care units (PCU) are part of a major TB control strategy as they have an impact on two main aspects of the disease: early detection and adequate flow of care for patients with pulmonary TB. They reduce the risk of *Mycobacterium tuberculosis* infection among providers and other patients or family members who attend the health unit.[15]

However, a major challenge remains the early detection of patients with pulmonary symptoms and potentially suspected cases among users of PCUs. Thus, preventive measures can be more quickly and effectively implemented, especially in priority municipalities with high rates of TB, as is the case of the city of Rio de Janeiro, Southeastern Brazil. [9]

This study aimed to assess the sensitivity, specificity and accuracy of a clinical score for presumptive diagnosis of pulmonary TB.

METHODS

A descriptive cross-sectional study was conducted. The study population consisted of patients cared at the pulmonology department of a secondary care outpatient clinic of a hospital in the city of Rio de Janeiro, from September 4, 2006 to July 3, 2007. The hospital is located in an area with approximately 1.1 million inhabitants and provides outpatient care to the districts of Guadalupe, Deodoro, Costa Barros, Pavuna, Acari, Anchieta, and Ricardo de Albuquerque (about 330,000 inhabitants). In 2000, the incidence rate of pulmonary TB reported in this area was approximately 100 cases per 100,000 inhabitants per year.

The questionnaire developed for this study was based on Santos et al[13] recommendations. Factors associated with pulmonary TB in patients treated at a university hospital identified by multiple regression analysis were assessed. A panel of experts consisting of two pulmonologists and a nurse selected the easiest questions to be included in the questionnaire so that no embarrassment would be caused to patients during the screening interview. It was set a zero-to-six score where six was the highest clinical evidence score for these variables, generating a scoring system for use in patients with suspected pulmonary TB (Table 1).

All interviews were conducted on alternate days by two nurses who were trained on questionnaire administration and standard operating procedure. Data collected were analyzed using SPSS 13.0.

In addition to their clinical evaluation, all symptomatic patients had their diagnosis of pulmonary TB confirmed by bacteriological examination, bacilloscopy with Ziehl-Neelsen staining and mycobacterial culture. Culture isolation of mycobacteria was done using the Löwenstein-Jensen medium in the Mycobacteriology Laboratory at the Clementino Fraga Filho University Hospital of Universidade Federal do Rio de Janeiro and Fundação Oswaldo Cruz Evandro Chagas Institute of Clinical Research.[a] HIV testing was offered only to those patients diagnosed with pulmonary TB following the Brazilian Ministry of Health guidelines.

Other study variables included: chest pain (pain, pressure or discomfort in the chest); cough (involuntary, spasmodic and particularly audible expulsion of breathed air caused by foreign bodies in the larynx or irritation of the mucosa in the trachea and bronchi); sputum expectoration (coughing up discharge from the lungs); hemoptysis (expectoration of bright red blood);

Table 1. Mean score of questions.

Questions	Scores	
	Yes	No
Age: younger than 59 years	1	0
Chest pain	2	0
Cough for 2 weeks	1	0
Cough > 2 weeks	2	0
Sputum expectoration for 2 weeks	1	0
Sputum expectoration >2 weeks	2	0
Hemoptysis	6	0
Night sweats	2	0
Fever	2	0
Shortness of breath	1	0
Weight loss: ≥3 kg in those ≤70 kg	2	0
Weight loss: ≥5 kg in those > 70 kg	2	0

[b] Ministério da Saúde. Fundação Nacional de Saúde. Centro de Referência Prof. Helio Fraga. Sociedade Brasileira de Pneumologia e Tisiologia. Controle da tuberculose: uma proposta de integração ensino-serviço. 6. ed. Rio de Janeiro; 2008.

fever (body temperature above 37.2ºC or feeling hot without checking the temperature); shortness of breath (difficult breathing with the sensation of an incomplete breath); night sweats (excessive sweating during the night soaking bedclothes and/or bedding); weight loss (loss of 3 kg in individuals weighing up to 70 kg and loss of 5 kg in those over 70 kg); and alcohol abuse (identified using the Cut down, annoyed, guilty, eye-opener – CAGE tool).[2]

The incidence rate of pulmonary TB was estimated by dividing the number of patients diagnosed with TB by the total number of people living in the area (about 330,000 inhabitants).

For the univariate analysis, there were assessed the frequency distribution, measures of central tendency and association between variables using the chi-square test for categorical variables and Student's t-test for continuous variables. The probability of statistical significance was estimated by dividing patients into two groups: pulmonary TB and non-pulmonary TB patients. For hypothesis testing a 5% level of significance was used.

Sensitivity was defined as the percentage of patients identified by the score as having pulmonary TB among those with positive bacteriological examination or meeting clinical criteria for pulmonary TB. Specificity was defined as the percentage of patients identified by the score as non-pulmonary TB among those with negative bacteriological examination and no clinical evidence of TB. There were excluded those patients who were initially not considered as having TB but were diagnosed with pulmonary TB within two years from the date of their enrollment in the study according to the *Sistema de Informação de Agravos de Notificação* (SINAN – Notifiable Diseases Surveillance Database). Positive predictive value (PPV) and negative predictive value (NPV) were defined as the probability of a patient with suspected pulmonary TB have or do not have active pulmonary TB, respectively, by the proposed score. Accuracy was defined as the proportion of correct predictions (sum of true positives and true negatives) and expresses the degree of certainty to make decisions on patient selection based on the score. Accuracy ranges from 0% to 100% and the higher the accuracy the greater the likelihood of identifying patients with pulmonary TB using the proposed score. The related 95% confidence intervals were also estimated.

Duration of cough was used to define symptomatic patients. Its accuracy was assessed based on the bacteriological examination. Then a scenario different pulmonary TB prevalences was used to assess the predictive power (PPV and NPV) of the clinical score at a cutoff ≥8.

The score performance was assessed using the receiver operating characteristic (ROC) curve. The ROC curve provides the cutoff values with more optimal sensitivity (vertical axis) against the complement of specificity (horizontal axis) which corresponds to a point on the ROC curve nearest to the upper left corner of the ROC graph as true-positive rate is 1 and false-positive rate is 0. The area under the curve was used to test its discriminative capacity: an area under the curve (AUC) lower than 0.6 indicates poor fit; 0.7, reasonable; 0.8, good; and higher than 0.9, excellent.[1]

To validate the cut-off score for the diagnosis of pulmonary TB the bootstrap method was used. This method generates samples with the same size n of the study sample by drawing and replacement of all elements and comparison of the samples generated.[c] The normal distribution of samples generated was assessed using the Shapiro-Wilk test. This test calculates a W-statistic that tests whether a random sample of size n comes from a normal distribution.[5]

The study project was approved by the Research Ethics Committee of the Clementino Fraga Filho University Hospital, Universidade Federal do Rio de Janeiro (protocol no. 067/06).

RESULTS

During the study period 1,365 symptomatic patients sought care at the health unit, of which 1,148 were screened with the study questionnaire. Of these, 243 (20.9%) were diagnosed with pulmonary TB, 905 (77.7%) did not have pulmonary TB and 16 (1.4%) were first diagnosed as non-TB and then reported as TB cases in the SINAN within two years of their enrollment in the study. The incidence rate of TB in the sample studied was 73.6 per 100,000 inhabitants per year. Among 1,148 symptomatic patients, 134 (16.7%) were alcohol dependent, 673 (58.6%) were smokers and 272 (23.6%) had history of prior TB treatment. Among those diagnosed with pulmonary TB, 160 (65.8%) were HIV tested, of which 18 (11.2%) tested positive for HIV.

The comparison between screened and non-screened patients showed that 50.3% of screened and 48.8% of non-screened individuals were males (p=0.734). The prevalence of pulmonary TB was 20.9% and 25.4% (p=0.215) in the screened and non-screened patients without any statistically significant differences between these variables.

Table 2 shows the variables included in the clinical score according to TB and non-TB patients. All variables showed a statistically significant association, except for shortness of breath.

[c] Figueiredo AT. Mensuração e análise da evolução da produtividade total dos fatores agregada no Brasil: aplicação da abordagem de bootstrap ao índice de Malquist [Master's dissertation]. Porto Alegre: Universidade Federal do Rio Grande do Sul; 2007

Table 2. Distribution of the clinical score variables between pulmonary tuberculosis and non-pulmonary tuberculosis patients. Rio de Janeiro, Southeastern Brazil, 2006–2007. (n = 1.148)

Variable	PTB (n=243)		Non-PTB (n=905)		p-value
	n	%	n	%	
Age <59					
Yes	211	86.8	662	73.1	<0.001
No	32	13.2	243	26.9	
Chest pain					
Yes	167	68.7	581	64.2	0.018
No	76	731.3	384	35.8	
Cough					
Yes	230	94.7	746	82.4	<0.001
No	13	15.3	159	17.6	
Sputum expectoration					
Yes	203	83.5	626	69.2	<0.001
No	40	16.5	279	30.8	
Hemoptysis					
Yes	58	23.9	99	10.9	<0.001
No	185	76.1	806	89.1	
Night sweats					
Yes	134	55.1	280	30.9	<0.001
No	109	44.9	625	69.1	
Fever					
Yes	165	67.9	336	37.1	<0.001
No	78	32.1	569	62.9	
Shortness of breath					
Yes	148 95	60.9	603	66.6	0.112
No		39.1	302	33.4	
Weight loss					
Yes	167	68.7	278	30.7	<0.001
No	76	31.3	627	69.3	

PTB: pulmonary tuberculosis

Table 3 shows the association of the symptom cough with the diagnosis of pulmonary TB due to its clinical importance. The prevalence of cough in the study sample was 85% (976/1.148). The highest sensitivities were found when there was cough for more than one week.

The clinical score for pulmonary TB showed sensitivity of 3.3% to 100%, specificity of 1.0% to 99.6%, and accuracy of 21.9% to 79.1%. The cut-off ≥8 showed the highest sensitivity and accuracy (Table 4).

The AUC for the pulmonary TB score was 0.734. The choice of a cutoff of 8 ("reasonable" fit in this model) favored a higher sensitivity compared to a cutoff of 9.

The internal validation score ≥8 assessed using the bootstrap method with 40 samples showed that in 39 (97.5%) the mean was within the mean range estimated for the sample studied (0.5263 to 0.5793).

Table 3. Distribution of the variable duration of cough in patients diagnosed with pulmonary tuberculosis. Rio de Janeiro, Southeastern Brazil, 2006–2007. (n =972)

Length of cough[a]	Sensitivity (95%CI)	Specificity (95%CI)	Accuracy (95%CI)
Current cough	94.7% (93.3;96.1)	17.6% (15.4;19.8)	33.9% (31.1;36.7)
Cough ≤1 week	11.8% (9.8;13.8)	80.8% (77.6;84.0)	64.5% (61.5;67.5)
Cough >1week	88.2% (86.2;90.2)	19.2% (16.6;21.8)	46.4% (43.2;49.6)
Cough >2 weeks	72.9% (70.1;75.7)	39.7% (36.5;42.9)	47.5% (44.3;50.7)
Cough >3 weeks	61.1% (57.9;64.3)	51.3% (48.1;54.5)	53.6% (50.4;56.8)
Cough >4 weeks	42.4% (39.2;45.6)	70.0% (67.0;73.0)	63.5% (60.5;66.5)

[a] Four patients with missing information on length of cough

Table 4. Distribution of the clinical cutoff scores for pulmonary tuberculosis. Rio de Janeiro, Southeastern Brazil, 2006–2007. (n = 1.148)

Score	Sensitivity (%) n=243	Specificity (%) n=905	Accuracy (%) n=1148
≥ 6	90.5	33.4	45.4
≥ 7	88.1	42.2	51.9
≥ 8	**83.1**	**51.8**	**58.6**
≥ 9	76.5	63.1	65.9
≥ 10	65.0	70.3	68.9
≥ 11	55.1	78.9	73.8
≥ 12	47.7	83.3	75.7

Bold: higher sensitivity and accuracy

The test of normality of 40 samples using the Shapiro-Wilk test showed a p-value = 0.17, which confirms the null hypothesis of a normal distribution and validation of the clinical score.

Table 5 shows the expected results of PPV and NPV with the use of the clinical score in scenarios of different pulmonary TB prevalence, at a cutoff ≥8 as the best performance, with high NPV for pulmonary TB prevalences usually seen at primary care units (5% to 10%).

DISCUSSION

The incidence of reported pulmonary TB cases in the state of Rio de Janeiro in 2006 was 79.1 per 100,000 inhabitants/year,[a] slightly higher than that found in the current study.

Table 5. Positive predictive value and negative predictive value according to different pulmonary tuberculosis prevalences for a clinical cutoff score ≥8. Rio de Janeiro, Southeastern Brazil, 2006–2007.

Disease prevalence	PPV (95%CI)	NPV (95%CI)
5%	8.4% (6.8;10.0)	98.4% (97.6; 99.2)
10%	16.2% (14.0;18.4)	96.5% (95.5; 97.5)
15%	23.5% (20.9;26.1)	94.6% (93.2; 96.0)
21%[a]	32.9% (30.1;35.7)	91.6% (90.0; 93.2)

PPV: positive predictive value
NPV: negative predictive value
Prevalence seen at the study care unit.

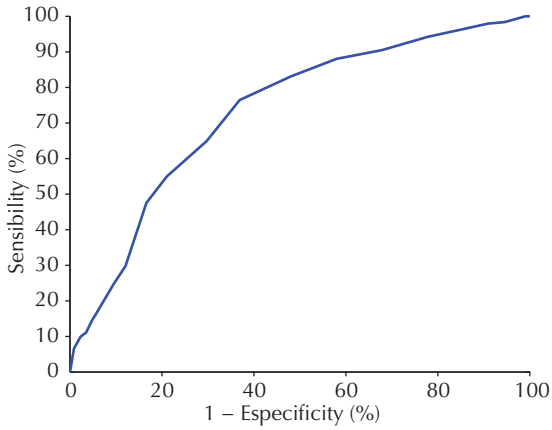

Figure. Receiver operating characteristic (ROC) curve of the clinical score for pulmonary tuberculosis. Rio de Janeiro, Southeastern Brazil, 2006–2007.

There was no statistically significant difference of gender and pulmonary TB between screened and non-screened patients, suggesting potentially homogeneous groups.

There was found a proportionally larger number of individuals younger than 59 than among patients diagnosed with pulmonary TB than among non-TB patients, similar to that reported in the literature.[6,b] This finding confirms that pulmonary TB affects a greater number of people during their most productive years of life, although some studies have indicated that in Brazil there is a shift in the incidence of pulmonary TB to the elderly.[3,11,12]

The association between chest pain and pulmonary TB was also found in other studies that described chest pain as a clinical sign of pulmonary TB[13,14] while others considered it only a typical acute manifestation of extrapulmonary (pleural) tuberculosis.[16]

Similar to other studies,[4,7] cough was reported in 94.7% of patients with pulmonary TB. According to the WHO recommendations, the Brazilian Ministry of Health guidelines and several authors, active search for new TB cases should be made among people with cough and/or sputum expectoration for more than two or three weeks (symptomatic individuals), hence the importance of cough as a symptom.[9,d] However, the study population was drawn from a referral secondary care outpatient clinic and it is a convenience sample from a department specialized in pulmonary diseases with low prevalence of HIV-TB co-infection (11%). As described in previous studies with populations with similar characteristics, cough for more than one week is a suggestive symptom leading to a presumptive diagnosis of pulmonary TB.[1]

Sputum expectoration and hemoptysis showed an association with pulmonary TB in the patients studied, which corroborates the literature.[6,d] However, the proportion of hemoptysis was higher than that reported in Macedo studies.[7]

The proportion of fever, night sweats, shortness of breath and weight loss was similar to that reported in other studies.[7,8]

Our results suggest that the clinical score can be a useful tool for screening of pulmonary TB cases in primary care settings in areas with low prevalence of HIV infection. In addition, it can be applied by nursing staff. Because it is a simple, effective and efficient tool, no costly complex equipment is required. When used by trained providers, the questionnaire can provide better quality information because screening will not be based exclusively on the criterion cough, as recommended by WHO and the Brazilian Ministry of Health.[9,15,16]

Nursing staff are the first providers to see suspected TB cases. They often identify pulmonary symptoms (cough for more than 2 or 3 weeks), and make decisions about exams and referral, taking a subjective approach, which makes it difficult to assess quality of care and compare their performance.

The clinical score can also be used for selecting patients for more costly and complex diagnostic examinations such as mycobacterial culture, chest X-rays and/or other molecular tests. Thus, it is recommended that further research be undertaken in different scenarios of TB prevalence with different cultural backgrounds to better assess the score's applicability and its impact on morbidity/mortality of patients receiving care in the health system.

[d] Melo FCQ. Modelos preditivos para tuberculose pulmonar paucibacilar [doctoral thesis]. Rio de Janeiro: Faculdade de Medicina da Universidade Federal do Rio de Janeiro, Brazil; 2001.

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