

Full Length Research Paper

Evaluation of tuberculosis diagnostic criteria in children

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Accepted 5 April, 2012

The research was performed to review the diagnostic criteria for tuberculosis (TB) in 198 children with confirmed TB. A cross-sectional descriptive study was conducted on a series of 525 children aged 1 to 15 years. Among 525 patients, 198 were diagnosed with TB. Data were collected from patient records, chest radiographs, and laboratory examinations. Demographic and diagnostic characteristics of patients were reviewed using the currently available criteria. In this study, 38.9% of patients were male and 61.1% were female. Among all patients, 34.8% were Iranian and 65.2% were Afghanis. In total, 82.8% of patients reported close contact with a TB case. Among all patients, 13.1% had extrapulmonary tuberculosis, 72.7% had pulmonary tuberculosis, and 14.1% had both pulmonary and extra pulmonary involvement. The frequency of Tuberculin Skin Test (TST), contact, clinical symptoms, radiograph findings, and bacteriology as diagnostic methods was 79.3, 83.8, 83.8, 85.9, and 58.1%, respectively. In our case, 90.4% of patients fulfilled the criteria. A high diagnostic value was determined for smear and culture of gastric aspirates in children. However, this could not be considered as a gold standard for diagnosis of tuberculosis in children. The results of our current diagnostic criteria showed a significant efficacy and accuracy of the mentioned criteria.

Key words: Child, tuberculosis, diagnosis.

INTRODUCTION

Childhood tuberculosis accounts for a major proportion of the tuberculosis (TB) disease burden in the world; however, its diagnosis still remains challenging. In children, diagnosis of tuberculosis is complicated due to its paucibacillary nature, which leads to atypical signs and symptoms and a lower probability of bacterial confirmation (Eamranond and Jaramillo, 2001; Mirza et al., 2003).

The lack of a practical gold standard has (Anane and Grangaud, 1992; Graham, 2011) led to the use of alternative approaches for TB diagnosis in children. Because bacterial confirmation in children is so difficult, many studies have suggested TB diagnosis based on clinical evaluation, radiography suggestive for TB, and evidence of TB disease or history of close contact with an adult case, in countries with low endemic TB rates

(Anane and Grangaud, 1992; Neu et al., 1999). In areas with high endemic rates, most people acquire *Mycobacterium tuberculosis* (MTB) infection during childhood and transmission of TB is not limited to household contacts. In these cases, the accuracy of Tuberculin skin test (TST) and close contact with household TB cases as diagnostic methods is undetermined.

Although, Iran is considered as an endemic country for TB, data on diagnostic characteristics for TB are limited. In this study, we reviewed the diagnostic criteria for tuberculosis in 198 children diagnosed with TB in the Pediatric Tuberculosis Ward of Masih Daneshvari Hospital during 2005-2010.

MATERIALS AND METHODS

A cross-sectional, descriptive study was conducted on a series of 525 children aged 1 to 15 years who were admitted to the Pediatric Tuberculosis Ward of Masih Daneshvari Hospital, a TB reference

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Table 1. Summary of the patients' characteristics.

Patients' characteristics	Number	Percent (%)
Age-year		
1-5	45	22.7
6-10	41	20.7
11-15	112	61.1
Gender		
Male	77	38.9
Female	121	56.6
Race		
Iranian	69	34.8
Afghani	129	65.2
Previous contact with TB		
Yes	164	82.8
No	34	17.2
BCG scar		
Yes	73	36.9
No	125	63.1

center, for TB rule out between March, 2005 and March, 2010. Data for the study were collected from patient medical records, reports of chest radiographs, and laboratory examinations. TST, chest x-ray, and three consecutive gastric aspirates were carried out in all patients and the results were recorded in their files. Chest CT scans were obtained for patients with suspicious findings. Among 525 patients, 198 were diagnosed with TB and tuberculosis treatment was initiated for these patients.

In our previous study on childhood TB (Velayati et al., 1999), the criteria for TB diagnosis included:

1. History of recent close contact.
2. A positive PPD (PPD \geq 10 mm in non contacts and PPD \geq 5 in contacts).
3. Radiographic findings compatible with TB.
4. Presence of clinical symptoms.
5. Positive pathology or bacteriology compatible with TB.

The presence of at least three of these criteria was needed to establish a diagnosis. Through this descriptive study, demographic and diagnostic characteristics of patients were reviewed using the available criteria. All statistical data were analyzed using SPSS 9 software.

Ethical clearance and permission to access medical records was obtained from the ethical committee of Masih Daneshari Hospital.

RESULTS

Patient ages ranged from 1 to 15 years, with mean of 10 \pm 4.5 years. A total of 38.9% of patients were male and 61.1% were female. Among all patients, 34.8% were Iranian and 65.2% were Afghani. In this study, 82.8% of patients reported having close contact with a TB case.

Table 2. The result of CXR and Chest CT Scan findings.

Findings	Number	Percent (%)
Hilar adenopathy	135	68.2
Parenchymal Infiltration	122	61.6
Consolidation	80	40.4
Collapse	49	24.7
Mediastinal mass	36	18.2
Pleural effusion	34	17.2
Bronchiectasis	31	15.7

Among these individuals, contact was more frequent in patients aged 6-10 years. Table 1 summarizes the patient characteristics.

All patients underwent a TST and 69.2% (137/198) showed a positive induration (\geq 10 mm), while 24 out of 198 (21%) showed indurations of 5 to 9 mm and 37 of 198 (18.7%) had no reaction ($<$ 5 mm).

In this study, 166 of 198 patients were symptomatic (83.8%), with the most frequent symptoms being fever (74.7%), cough (74.2%), weight loss (42.9%), sweating (40.4%), sputum (32.3%), and hemoptysis (15.2%).

Chest x-Rays for all cases and chest CT scans in suspicious cases were carried out in all patients and were normal in 14.1% cases. Among the abnormal Chest X-Rays and Chest Ct Scans, (85.9%), the most common findings were Hilar adenopathy, 68.2% (Table 2).

The AFB (Acid Fast Bacilli) smears prepared from gastric aspirates were positive in 47% of cases. Cultures were prepared for all children and were positive for *Mycobacterium tuberculosis* in 48% of patients. Histopathology examination was positive in 12.1% of extrapulmonary patients (Figure 1).

Among all patients, 13.1% had extrapulmonary tuberculosis, 72.7% had pulmonary tuberculosis, and 14.1% had both pulmonary and extra pulmonary involvement.

Diagnostic characteristics of patients were reviewed by means of the available criteria. The frequency of each diagnostic method and the diagnostic characteristics of patients are summarized in Figure 2 and Table 3, respectively.

DISCUSSION

Diagnosis of childhood TB, which accounts for a large proportion of TB disease burden, is an ongoing challenge. Considering Iran as an endemic country for TB, no updated diagnostic criteria exist for childhood TB. This study reviewed the currently available diagnostic criteria.

Our study showed that no single diagnostic test can be considered as a gold standard. Most of the patients were

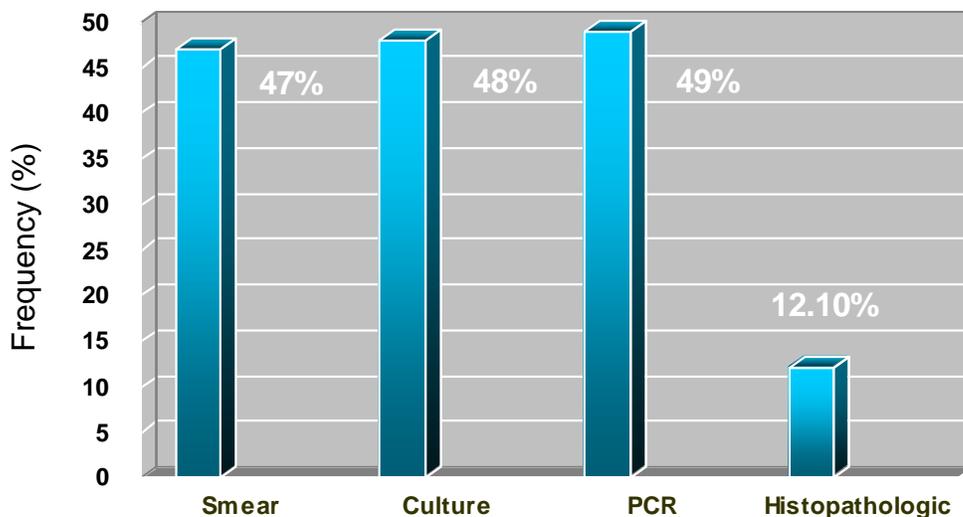


Figure 1. Frequency of smear, culture and PCR of gastric lavage in the study population.

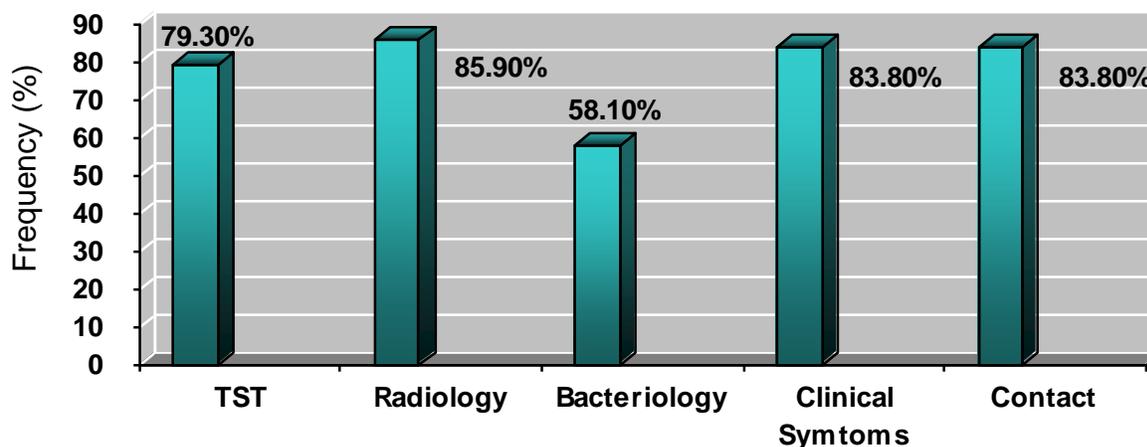


Figure 2. Frequency of diagnostic methods in the study population.

Table 3. Diagnostic characteristics.

Number of positive criteria	Number	Percent (%)
1 positive criteria (only positive bacteriology or pathology)	3	1.5
2 positive criteria simultaneously	14	7.1
3 positive criteria simultaneously	46	23.2
4 positive criteria simultaneously	69	34.9
5 positive criteria simultaneously	66	33.3

diagnosed based on positive findings for four or five criteria. The dominant positive diagnostic method in the study was radiological findings (85.9%). This is a high rate compared to that reported in other studies; however, the previous studies mostly evaluated the CXR findings

and chest CT scan findings separately. In addition, clinical suspicion and other positive diagnostic tests could have prompted the physician to interpret the radiological findings more positively. In a study in South Africa, chest radiographs were compatible with TB in 18.8% of patients

(Boloursaz et al., 2010).

The most common radiological finding was hilar adenopathy (68.2%). In another study carried out at this center (Leung et al., 1992), hilar adenopathy accounted for 85% of pulmonary tuberculosis radiological findings. In the present study, CXR and CT scan were used for both pulmonary and extrapulmonary TB; therefore, this probably reduced the frequency of hilar adenopathy.

In total, 83.8% of patients in our study were symptomatic and the most common signs and symptoms were fever and cough. Previous studies have shown that the sensitivity and specificity of clinical findings are extremely low (Glasziou et al., 2008; Rasmussen and Christensen, 1989) and they are not solely a reliable method for diagnosis, although the use of clinical findings with other diagnostic methods can lead to an accurate diagnosis (Schaaf et al., 1995).

In our study, 83.8% of patients had a history of contact with a TB case. This is a high rate; however, the rate could be even higher because transmission of TB is not limited to contact with household members in endemic areas. The active screening of TB among contacts at our center could also have contributed to the observed high rate.

A total of 79.3% of patients had a positive TST (PPD \geq 10 or PPD \geq 5 in contacts). A negative TST can rule out TB, but a positive test is useful as a diagnostic method in this diagnostic setting. The Quantiferon TB test, which measures the interferon gamma in whole blood, is another test for screening latent tuberculosis infections and tuberculosis patients and can be used instead of the TST (Kariminia et al., 2009; Legesse et al., 2011). Results of a previous study at this center showed a correlation between the TST and the whole blood IFN- γ assay in both the contact and TB groups, but no priority was defined for the use of QFT in children (Kariminia et al., 2009; Mardani et al., 2010).

The presence of AFB in sputum or other specimens is the gold standard for diagnosis of TB in adults. In pediatric TB, due to its paucibacillary nature, sputum microscopy is positive in less than 10-15% of cases and cultures become positive in less than 30-40% (Steingart et al., 2009; Steingart et al., 2007). In 2007, Brinza and colleagues studied 254 children with pulmonary TB in Romania and a positive bacteriology was detected in 24.8% of cases (Brinza and Mihăescu, 2007). In the present study, 47% of patients had a positive AFB smear and MTB culture was positive in 48%.

The high rate of positive bacteriology in this study is significant. We attributed this high rate of positive smear and culture to better sample collection and improved culture techniques in the referral lab of Masih Daneshvari Hospital. All children underwent three consecutive gastric aspirates, which was the alternative method to obtain sputum in children (Gómez et al., 2000; Oberhelman et al., 2010). In addition, our patients were mainly fulminated TB patients who are usually referred to this center.

Among 198 patients who were diagnosed with TB and who initiated treatment, 181 (90.4%) had three or more positive criteria. This result indicated the diagnostic accuracy of the available criteria.

In total, 17(8.6%) patients failed to fulfill the criteria; these were mostly those patients who had extrapulmonary TB and were mainly diagnosed by biopsy and pathological approval. In the present study, 13.1% had extra pulmonary TB and 12.11% of patients had a positive histopathology examination.

Conclusion

The results of this study indicated a high diagnostic value of smear and culture of gastric aspirates in children. However, this cannot be considered to be a gold standard for diagnosis of TB in children. The available criteria were determined to have significant accuracy and could be considered as an efficient diagnostic setting for the diagnosis of childhood TB. This setting needs to be modified by including newer diagnostic methods, such as the use of advanced methods in bacteriology and molecular-based diagnosis.

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