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Adenosine Deaminase Level as an Indicator for Differentiating Between Active Pulmonary Tuberculosis Infection and Other Pulmonary Infections

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ABSTRACT

Background: In spite of recent advents, and novel improvements in the diagnosis and treatment of pulmonary tuberculosis (TB), definitive diagnosis of pulmonary TB in children is problematic. Therefore, measurement of the serum level of adenosine deaminase (ADA) was later introduced as a helpful marker for the diagnosis of TB.

Objectives: The purpose of this study was to determine the usefulness of the ADA test in the diagnosis of pulmonary TB, and compare enzyme activity between patients with pulmonary TB and those with other pulmonary infections. The sampling strategy was randomized, and the design of study was case-control diagnostic descriptive, we used IBM SPSS V-16.0.2 software for analyzing our data.

Patients and Methods: This study was performed at the National Research Institute of Tuberculosis and Lung Diseases (NRITLD) in Tehran, IR Iran. In all, 49 children, divided into 3 groups, were examined. Of these, 22 had pulmonary TB, 17 had other pulmonary infections, and the remaining 10 children were normal and were assigned to the control group.

Results: Serum ADA levels were higher in the pulmonary TB patients than in the control group ($P < 0.05$), however, these levels did not differ significantly between TB patients and patients with other pulmonary infections ($P = 0.391$).

Our evaluation revealed that ADA level in TB patients with a positive smear of gastric washing were higher than those in patients with a negative smear ($P = 0.006$).

Conclusions: Similar to the other studies, this study showed higher serum ADA level in pulmonary TB patients than in normal individuals. However, ADA was not found to be a suitable marker for differentiating between pulmonary TB and other pulmonary infections.

▸ *Implication for health policy/practice/research/medical education:*

ADA elevation in serum is seen in pulmonary tuberculosis infection, but ADA measurement is not a reliable indicator for differentiation between tuberculosis and other pulmonary infection. Reading of this manuscript is beneficial for general practitioners, internist, pulmonologist and infectious specialist.

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1. Background

According to a report by the World Health Organization (WHO), 1.3 million children are annually infected with tuberculosis (TB) worldwide, and approximately 450,000 children die from this infection every year (1, 2).

The diagnosis of a pulmonary infection in children is based on 5 major criteria:

1) A history of close contact with a TB patient
2) Presence of clinical symptoms
3) Positive smear
4) Positive results of the purified protein derivative (PPD) test
5) Chest X-ray (CXR) findings (3)

Despite the advent of novel improvements in the diagnosis and treatment of pulmonary TB, a definite diagnosis of TB in a large number of patients is problematic. Adenosine deaminase (ADA) is one of the major enzymes in purine metabolism. There are2 isoforms of ADA: ADA1 and ADA2. The principal action of this enzyme is in immune system cells, the level of ADA in T-cell is 5-20 fold more than B-cell (4).

Measurement of the level of (ADA) enzyme in body fluids is a helpful diagnostic tool. The level of ADA elevates as the lymphocyte (T-cell) activity increase. Elevated ADA levels are observed in patients with tuberculosis pleurisy (5). Mishra and coworkers, in 1995, found that serum ADA levels were elevated in TB patients (6). The study by Throra in 1994 showed an increase in the levels of ADA after Bacillus Calmette-Guerin vaccination (7).

2. Objectives

The goal of this study was to evaluate the usefulness of estimating ADA levels for the diagnosis of pediatric tuberculosis and compare ADA activity in pulmonary TB patients with other pulmonary infections patients.

3. Patients and Methods

This study was prospective study that performed between 2003 and 2005 in the pediatric ward of the National Research Institute of Tuberculosis and Lung Diseases (NRITLD), in Tehran, IR Iran. The type of study was case-control and diagnostic descriptive. The sampling strategy was randomized. The age of the children was between 0 and 15 years. After getting permission from children's parents, we evaluated them in three separate groups:

1) 22 children with pulmonary TB
2) 17 children with other pulmonary infections, including pneumonia (bacterial, viral, and fungal) and abscess
3) 10 children as the control group

Among the patients in groups 1 and 2, those with normal CXR or if they had rheumatologic and malignant disease were excluded from the study.

Blood samples from all the participants were collected and sent to the reference laboratory where the activity of ADA was estimated by spectrophotometer device (Eppendorf Ecomm 6122) using Guist method.

ADA level > 42 IU/L was considered positive.

Information about age, sex, results of lab data, PPD and the measure of serum ADA level were collected and registered in specific forms.

The findings were analyzed using IBM SPSS (Version 16.0.2) software. The relationship between variables was evaluated using the Tukey test and the *t* test, and the significance was set at $P < 0.05$.

The performance of ethnical foundation in this study was approved by ethnical committee in the course of our study.

4. Results

The mean age of the children was 10.4 ± 3.6 years. The age and sex of the patients did not significantly differ among the 3 groups. Evaluation of variables showed no significant correlation between age, sex and serum level of ADA enzyme. Serum ADA levels in TB patients were higher than those in normal individuals significantly ($P < 0.05$), but these levels did not significantly differ between pulmonary TB patients and patients with other pulmonary infections ($P = 0.319$). ADA levels in patients with a positive smear of gastric washing were significantly higher than those in patients with a negative smear ($P = 0.006$) (*Table*). The ADA test results were positive in the case of 6 patients with pulmonary TB (27.3%) and in the 3 patients with other pulmonary infections (17.6%). The ADA test results were negative in the case of all the individuals in the control group, and there was no significant difference between 3 groups.

Table. The Mean Serum Level of ADA in All 3 Groups

	No.	Mean ± SD
Pulmonary tuberculosis	22	39.70 ± 11.5
Other pulmonary infection	17	34.82 ± 11.2
Normal	10	26.60 ± 3.94
All	49	53.33 ± 11.28

5. Discussions

Nowadays measurement of ADA levels is the gold standard for the diagnosis of tuberculosis pleural effusion in developing countries (8). Multiple studies have shown a logical relation between serum ADA level and active pulmonary infection, but in other pulmonary diseases that are specific mimicker for tuberculosis such as lung cancer; chronic lung disease and bronchiectasis do not increase the serum ADA level (9, 10).

Some studies in all around the world have shown similar results between serum ADA and active tuberculosis, for example Ishii and coworkers in a study in Japan in 1997, performed study of serum ADA levels in tuberculosis patients and found that serum ADA levels were higher in TB patients as compare to normal individuals signifi-

cantly ($P < 0.001$). Similarly, in our study, serum ADA levels in TB patients were significantly elevated ($P < 0.05$) (11).

In the study in Indian on 120 patient with different pulmonary diseases, the serum ADA level more than 17 IU/L had a specific sensitivity about 97% for pulmonary TB ($P < 0.001$) (12).

In the another study by Kelbel in 1995 that performed on 44 pulmonary tuberculosis patients with respect to 70 patient with lung cancer, the increase of ADA level was detected in 64% of tuberculosis patients and in 95% of patients with pulmonary TB with positive smear and only in 2.8% lung cancer patients (13).

Mishra studied serum ADA levels in 51 TB patients (with pulmonary and non-pulmonary disease) and compared the findings of these patients with those of 20 normal individuals (control group) (6).

Their study showed that serum ADA levels were higher in non-pulmonary TB patients than in normal individuals. In the unpublished data of the study that performed by Aminiafshar and coworkers in 2004, they measured serum ADA levels in pulmonary TB patients and in other infectious diseases and found that serum ADA levels is higher in those group than normal population, but there is no significant difference in ADA levels between tuberculosis and other system infections.

Our study showed that serum ADA levels in pulmonary TB patients with a positive smear were higher than those in patients with a negative smear.

This difference in these two groups in our study may be due to including bias, for approving this finding another study with larger sample and focusing to this point should be design and perform in future. Two studies, one by Gakis in 1998 and the other by Klockars in 1991, have shown that serum ADA levels increased in pneumonia patients (14, 15). Fernandez and coworkers in 2003 compared serum ADA levels between TB patients and patients with other pulmonary infections and found no significant difference between the 2 groups, similar to the findings of our study (16). In against of other published reports in multiple different studies Yashuhara and coworkers also conducted a similar study and showed that serum ADA levels were higher in TB patients than in patients with pneumonia (17). Although we didn't find significant difference in ADA level between tuberculosis and other pulmonary infections.

In the study that performed by Atalas in 2003, their results suggest that ADA level in pulmonary TB patients is higher than normal population, additionally the ADA levels in patients with tuberculosis pleurisy was higher than patients with other tuberculosis manifestations (15, 18).

In our study, positive ADA test results were obtained in 27.3% of the pulmonary TB patients and in 17.6% of the patients with other pulmonary infections; however the difference between these groups was not significant and this result is compatible with other reports in literature in this field.

In the study of Rokayan in 2003 revealed that measurement of only ADA level is not a diagnostic indicator for differentiating TB from other pulmonary infections (19).

This study, similar to other studies, showed elevated serum ADA levels in pulmonary TB patients compared to those in normal individuals (7, 11, 15-23); however, ADA level was not found to be a reliable indicator for differentiating between pulmonary TB and other pulmonary infections.

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Author's Contribution

None declared.

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