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# Serum Adenosine Deaminase Level as an Indicator of Pulmonary Tuberculosis Activity versus Other Infectious Diseases

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## ABSTRACT

***Background:*** *We evaluated the association of active pulmonary tuberculosis with level of serum adenosine deaminase in order to have an acceptable rapid test to help the clinicians in the diagnosis of active pulmonary tuberculosis.*

***Materials and Methods:*** *We measured serum total adenosine deaminase level in three groups:*

*1- Cases of active pulmonary tuberculosis that were confirmed by positive sputum smears for acid-fast bacilli in association with compatible clinical and radiological findings.*

*2- Cases of other infectious diseases including brucellosis, endocarditis, salmonellosis, and meningitis confirmed by clinical findings and related laboratory tests.*

*3- Healthy controls.*

*Serum adenosine deaminase levels were measured before starting the treatment. Data analysis was performed by Chi-Square; ANOVA and LSD tests. The significant level was evaluated for p- value of less than 0.05.*

***Result:*** *We evaluated 51 cases (21 females and 30 males aged 47.7±19 years) of active pulmonary tuberculosis, 11 cases (6 females and 5 males aged 44.7±21 years) of other infectious diseases and 50 cases (14 females and 36 males aged 48.4±11 years) of healthy individuals. Mean serum adenosine deaminase level in pulmonary tuberculosis (42.4±21.5 IU/ml) and other infectious diseases (38.3±23.4 IU/ml) was significantly more than controls (26.6± 8.2 IU/ml), (P<0.0001 and p<0.03 respectively), but the difference between the pulmonary tuberculosis and other infectious diseases was not statistically significant. There was no significant difference in age and gender between the above mentioned groups.*

***Conclusion:*** *We conclude that serum adenosine deaminase level increases in infectious diseases but it cannot differentiate pulmonary tuberculosis from other infectious diseases.* ***(Tanaffos2004; 3(12): 19-23)***

***Key words:*** *Active pulmonary tuberculosis, Serum adenosine deaminase, Indicator*

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## INTRODUCTION

Tuberculosis continues to be a major cause of morbidity and mortality worldwide. The diagnosis is usually based on clinical presentation, radiologic findings and positive tuberculin and/or BCG tests. However, clinicoradiological features are variable and the latter tests may be falsely negative. Under such circumstances, anti-tuberculous therapy is started empirically. It therefore becomes imperative to find some rapid and useful tests for the diagnosis of tuberculosis (1).

Adenosine deaminase is involved in the propagation and differentiation of various lymphocytes, particularly T-lymphocytes, so that estimation of its level of activity in various body fluids has been used in the diagnosis of tuberculous effusions especially pleural forms (2). Conversely its decrease has been noticed by Collazos et al. in treated cases (3).

S.Thora showed the raised activity of adenosine deaminase in the new born sera, six weeks after B.C.G. vaccination (4). Mishra et al. noticed raised serum adenosine deaminase activity in a group of 51 tuberculous cases compared to 20 healthy individuals (1). The same results were obtained by Ishii et al. in Japan (5).

Therefore, previous studies are merely concentrated on ADA values for tuberculosis with little or no comparison to other systemic infections.

Our study is mainly focused on active pulmonary tuberculosis and other systemic infections to find out the usefulness of serum adenosine deaminase values for differentiation of these two conditions.

## MATERIALS AND METHODS

In this cohort analytic study, we measured total ADA activity in the sera of three groups in Labbafinejad, Boo-Ali, and Loghman Hakim Hospitals from November 2002 to May 2003.

Inclusion criteria:

1. To have at least one positive sputum smear for acid fact bacilli
2. Lack of any infectious diseases (malignancy, rheumatologic disorder etc.) according to physician's judgement and patient's medical documents.
3. To have abnormal chest x-ray that is reported by radiologist
4. To have respiratory symptoms

Exclusion criteria:

1. No respiratory symptoms
2. No previous contact with known tuberculosis according to patient's history
3. Normal chest x- ray

Groups included:

- Fifty-one cases of active pulmonary tuberculosis confirmed by positive sputum smears for acid - fast bacilli in association with relevant clinical and radiological findings, and were negative for other kinds of infectious, malignant, and autoimmune disorders.
- Eleven cases of other infectious diseases, including brucellosis, salmonellosis, endocarditis and pneumococcal meningitis which were found to be negative for malignancies and autoimmune disorders.
- Healthy controls lacking any infectious, malignant or autoimmune disorders.

All three groups were matched according to the age and sex and all cases were informed ethically.

Three milliliters of blood was obtained before commencing any medication and was sent to the reference lab. The enzyme activity level was measured by Giusti method.

Data analysis was performed by Chi-Square, ANOVA and LSD tests. The significant level was evaluated for P value of less than 0.05.

## RESULTS

We evaluated 51 (21 females and 30 males aged 47.7 ±19 years) cases of active pulmonary tuberculosis, 11 (6 females and 5 males aged 44.7± 21 years) cases of other infectious diseases and 50 (14 females and 36 males aged 48.4±11 years) cases of healthy individuals. There was no significant difference in sex and age of all groups.

Mean serum ADA level in pulmonary tuberculosis (42.4± 21.5 IU/ml) and other infectious diseases (38.3± 23.4IU/ml) was significantly more than controls (26.6±8.2IU/ml), ($p<0.0001$ and $p<0.03$ respectively), but the difference between pulmonary tuberculosis and other infectious diseases was not statistically significant (Table1 ).

**Table 1.** Distribution of serum adenosine deaminase level variables in active pulmonary tuberculosis, non-tuberculous infections, and healthy controls in Labbafinejad, Boo-Ali, and Loghman Hakim Hospitals 2002-2003.

| Variables / Groups | Number | Mean (X) | SD |
|---|---|---|---|
| Active Pulmonary TB | 51 | 42.4 | 21.5 |
| Non Tuberculous Diseases | 11 | 38.3 | 23.4 |
| Healthy Controls | 50 | 26.6 | 8.2 |
| Total | 112 | 35.7 | 17.7 |

## DISCUSSION

ADA is an enzyme in the purine metabolic pathway, and is shown to consist of two iso-enzymes (ADA1 and ADA2). The enzyme is scattered through out the human body and its main physiological function is found in T-lymphocyte propagation and differentiation. The enzyme is higher in T-cells compared with B-cells with the ratio of 5-20 folds more (2).

Adenosine deaminase catalyzes the deamination of adenosine and deoxyadenosine to inosine and deoxyinosine, respectively .Two isoenzymes of ADA coded by different gene loci exist, namely ADA1 and ADA2, each with unique biochemical properties. The ADA1 isoenzyme is found as a monomer (ADA1m) and as a dimer (ADA1c), where two ADA1m molecules are combined with a combining protein. The ADA1 isoenzymes are found in all cells, with the highest activity in lymphocytes and monocytes, whereas ADA2 isoenzymes gene products appear to be found only in monocytes (2).

Although mycobacterial culture is sensitive and standard for diagnosing tuberculosis, the time for diagnosis requires a minimum of 2-3 weeks. Acid-fast bacilli smear, the rapid screening method for the diagnosis of pulmonary tuberculosis, is insensitive for detecting mycobacteria among tuberculosis patients (6) .

The assay of ADA activity in pleural and other infections is very useful in differential diagnosis, especially in the case of tuberculosis, which is characterized by an increase in activity (2). However, the increased serum level of ADA has been reported for viral and bacterial pneumonia, HIV infection, and extra pulmonary tuberculosis (7, 8).In fact diseases caused by intracellular micro-organisms are characterized by an elevated level of ADA in serum (7).

Ungerer et al. studied serum levels of ADA isoenzymes in 51 cases of confirmed tuberculosis (41 pleural effusions, and 10 ascitic fluids), and 6 cases of bacterial pleural effusions (empyema), and noticed increased level of ADA2 in tuberculosis effusion (ADA2 / ADA total=88%), and ADA1 in non tuberculosis effusion (ADA1 / ADA total=70%), concluding that isoenzyme study is a helpful measure in differentiating these two kinds of effusions (2).

Thora et al. studied ADA levels of 100 newborn sera who were vaccinated with BCG showing a significant increase, indicating human cell-mediated immune response against mycobacterium antigens (4).

Mishra et al. evaluated serum ADA levels of 51 children with confirmed tuberculosis (pulmonary, peritoneal, meningeal, and bone), and 20 healthy controls showing significant increase in the first group with a p-value of <0.001 (1).

Collazos et al. performed a prospective follow up study of 25 cases of pulmonary and/or pleural tuberculosis with a normal immune response for a period of 6- months after initiation of treatment. There was a significant decline in the serum ADA values during the first two months in the patients as a whole (P=0.04), followed by stabilization of the serum ADA activity .This decline was due to a marked decrease in the serum ADA activity in 13

patients (52%) who had initial high levels of enzyme (p=0.03), whereas there were no changes in those patients with normal initial levels (p=0.27) (3). Similar results were obtained by Ishii et al. in Japan together with a direct association between serum ADA level and erythrocyte sedimentation rate (5).

Conde et al. evaluated serum ADA in active pulmonary tuberculosis and other pulmonary infections and showed no significant difference between them (9).Their results were in disagreement with the report by Yasuhara et al. (10) in which serum ADA activity of children with active pulmonary tuberculosis was found to be significantly greater than those with bacterial or viral pneumonia.

We found a significant rise in the serum ADA level of patients suffering from active pulmonary tuberculosis compared to the healthy controls with a P value of <0.0001, consistent with the results of other studies. However, a similar rise in serum ADA was noticed in other infections with a P<0.03 .These infections included brucellosis, salmonellosis, pneumococcal meningitis, and enterococcal endocarditis in our series. Moreover it should be emphasized that there was no statistical significance between the serum level values of active pulmonary tuberculosis and other infections. The isoenzyme study may provide more information for differentiation of these conditions.

Our study is unique in comparing serum values of pulmonary tuberculosis with the non pulmonary acute or chronic infections, showing that although raised serum ADA level can denote active pulmonary disease, but cannot differentiate it from other infections. Appreciating that the number of non-tuberculosis cases of our study (11 cases) may be a confounding variable in our results; we recommend other studies with a greater number of cases in other infectious groups to be performed.

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