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Research Article

ADA LEVELS IN BRONCHOALVEOLAR LAVAGE FLUID AS DIAGNOSTIC INDICATORS FOR PULMONARY TUBERCULOSIS: A COMPREHENSIVE STUDY

Dr. V. Naga Basava Raju*

*Assistant Professor in Pulmonary Medicine, Sri Lakshmi Narayana Institute of Medical Sciences & Hospital, Kudapakkam Post, Villianur, Puducherry 605502, India.

ABSTRACT

Currently, tuberculosis (TB) diagnostic tests take a long time. In this study, ADA in bronchoalveolar lavage fluid was evaluated for its diagnostic utility in treating pulmonary TB. AFB was not found in sputum smears of patients with suspected pulmonary TB. A comparison was made between study groups regarding ADA levels in BAL fluids. We included 126 patients, 30 of whom had pulmonary tuberculosis, 66 of whom had other pulmonary diseases, and 30 healthy subjects as a control. According to BAL fluid samples, there was mean levels of ADA of 3.13 ± 1.55, 1.42 ± 1.05, and 1.82 ± 0.79, respectively. As compared to the other two groups, pulmonary TB had a significantly higher infection rate (P 0.001). In ROC curves, 3.5 IU/L was selected as a cut off value were most sensitive (57%) and specific (84%) for diagnosing TB. However, a negative result from the BAL fluid from TB patients shows higher ADA activity than BAL fluid from other diseases, but that test cannot exclude TB.

Keywords:- Pulmonary tuberculosis, ADA, BAL Bronchoalveolar lavage.

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INTRODUCTION

There are more than 600,000 deaths caused by tuberculosis (TB) every year [1]. Developing countries, face this problem. A number of drugs are being used to treat tuberculosis, which has become more important due to its multi-drug resistance and possible correlation with acquired immunodeficiency syndrome (AIDS). Usually, tuberculin and/or skin tests are positive, along with clinical presentation and radiologic findings. There are, however, some cases in which false negatives are detected due to clinic radiological features that are variable. TB is diagnosed through cultures of specimens, but According to the quality of cultures, positive rates range from 43% to 83% of the sample and the methods used. We must find methods that are faster and more sensitive in emergency situations since delay is unacceptable. It has been shown in some studies [3] that polymerase chain reactions (PCRs) are highly sensitive and specific, but they are not cost-effective and are seldom used in cancer centers. As an alternative non-invasive method for determining tuberculous etiology, several biomarkers have been proposed, including This enzyme deaminates adenosine, interferon beta (IFN-), and cytokines. As a cellular immunity marker, ADA Inosine is formed by the conversion of adenosine to inosine through this enzyme during purine catabolism. In Inflammatory TB can occur in the pleura, cerebrospinal fluid, peritoneum, and synovium cases, ADA activity was assessed in a variety of fluids.

Corresponding Author: - **Dr. V. Naga Basava Raju** Email: raju.vnb@gmail.com

BALF ADA activity has been evaluated in only a few studies [8–11], and the results are inconsistent. It was performed in order to determine the minimum TB patients' BALF ADA activity level.

METHODS AND MATERIALS

We adhered to the Helsinki Declaration of the Association of World Physicians (2000) while conducting this study. Afterwards, the forms for collecting demographic data were completed and an ethical committee at the university has approved this application.

Table 1: Sputum smears and BAL cultures indicate the frequency of pulmonary TB

	Negative Smear	**Positive Smear**	**Negative Culture**	**Positive Culture**
N (%) in sputum	32 (25.39%)	2 (1.58%)	22 (17.46%)	12 (9.52%)
N (%) in BAL fluid	12 (9.52%)	14 (11.11%)	6 (4.76%)	20 (15.87%)

Table:2 Three study groups averaged ADA levels in BAL

	Mean ± SD	Maximum	Minimum
TB in the lungs	3.13 ± 1.55	22	4
Lung diseases other than TB	1.42 ± 1.05	12	4
The control	1.82 ± 0.79	10	7

According to Kayacan et al. [8] study, For the BAL ADA levels to differ between patients with TB and those in the control group, at least 14 patients were needed in each group. AFB or other indications for bronchoscopy implied pulmonary TB in 126 patients with positive sputum smears. We excluded the following individuals: (1) hypoxia of the arterial blood supply, (2) patients that would not cooperate for bronchoscopy, (3) patients with Hypoxia refractory to treatment, (4) hemodynamic disorders, (5) patients Cardiovascular emergency arrhythmias, and (6) suspected case of TB (possessing a positive sputum test). A TB culture was performed on all sputum samples. The patients were given written consent prior to undergoing a fiberoptic bronchoscopy, which was performed using an Olympus bronchoscope type 1T20, Japan, after fasting for four hours and administering lidocaine 2% spray locally. When patients had in this lobe of the lung, BAL fluid was found because of diffuse involvement or normal chest X-rays. BAL fluid was obtained by injecting 150 cc of normal saline, then collecting it via suction and sending it to the laboratory for AFB smears and cultures. We centrifuged and stored the samples at 21°C to determine ADA activity. Based on Giusti's colorimetric method, ADA activity was measured comparing ADA levels among BAL fluids. As part of Giusti's process, adenosine is deaminated and ammonia is released. A glutamate dehydrogenase-accompanied allosteric activator catalyzes the second reaction. A direct correlation exists between ADA activity and low light absorption at 340 nm. A measurement of ADA activity of up to 100 IU/L can be achieved by using this method. In the pulmonary TB group, we included patients with positive sputum cultures for AFB and those with other forms of respiratory disease who were negative for TB. The control group consisted of individuals who were ruled out for TB and other pulmonary diseases. BAL fluids were measured and ADA levels in all three groups were compared using questionnaires. SPSS software version 11.5, along with independent t-tests and ANOVA, was used to analyse the data.

RESULTS

126 patients participated in this study. The average age of the pulmonary tuberculosis patients was 63.26 years, while the average age of the skin tuberculosis patients was 63.19 years. A total of 30 patients (20 males and 10 females; mean age: 41.25 years) and 30 control subjects were included in this study. 2 patients with Wegener's disease, 2 with sarcoidosis, 2 with silicosis, and 4 with usual interstitial pneumonia had interstitial pulmonary disease without TB lung disease. 8 of the 20 patients with lung cancer had chronic obstructive pulmonary disease (COPD), the other 8 had adenocarcinomas (12 adenocarcinomas, 8 squamous cell carcinomas, and 2 small cell carcinoma), and 8 patients with pneumonia. No pathologic findings were found in control subjects who underwent bronchoscopy for various reasons. In the pulmonary TB group, 10, 16, and 22 patients had positive sputum, BAL smears, and BAL cultures. There were positive sputum or BAL cultures in all TB patients (Table 1). BAL culture and sputum smear were negative for TB in the two other groups. According to results of BAL fluid tests of pulmonary TB patients, non-TB lung disease patients, and control patients, ADA level was 3.13 ± 1.55, 1.42 ± 1.05, and 1.82 ± 0.79 IU/L, respectively. The mean ADA level differed significantly

among the three groups according to one-way ANOVA (P = 0.000).

According to Tukey's test, TB patients differed significantly from non-TB lung disease patients (P = 0.02) as well as from TB patients differing from the control group (P = 0.01), but non-TB lung disease patients did not differ significantly (P = 0.55). A t-test showed no significant difference between the two groups in terms of ADA levels (P = 0.11, t = 1.58). Women's ADA levels were 1.32 IU/L and men were 2.10 IU/L. Based on ROC curves, ADA levels were not significantly different from baseline in diagnosing pulmonary TB (P = 0.10). For TB diagnosis, the 3.5 IU/L cut-off level proved to have the highest specificity and sensitivity (specificity = 84%, sensitivity = 57%). We calculated the sensitivity, specificity, positive predictive value, and negative predictive value of ADA according to the cut-off point of 2.2 IU/L in the control group. Seventy-three percent, six-seven percent, forty-one percent, and eighty-nine percent, respectively, were calculated using the cut-off point.

DISCUSSION

The ADA levels of the three groups were significantly different, with TB patients having a significantly higher level than the other two groups. As a result of mycobacterial antigens stimulating T-cell lymphocytes, ADA is an enzyme that increases in TB. Tuberculosis has been diagnosed with ADA since 1978, when it was discovered that ADA activity was high in tuberculous exudates [13, 14]. A relatively simple and inexpensive method is available for measuring ADA in the laboratory. Laboratories with limited resources, such as those in Iran, will especially benefit from it. Patients with pulmonary tuberculosis with smear-negative smears and those without smear-negative smears were compared in Orphanidou et al. [11], where the level and activity of ADA were investigated. In the BAL fluids of pulmonary TB patients and non-TB patients, Lysozyme was not significantly different, but ADA levels were. A study conducted by Kubota et al. [10] measured low levels of ADA in BAL fluids of patients with military TB, sarcoidosis, idiopathic interstitial pneumonia, and control men, respectively. As compared with the highest levels, the lowest levels were 0.21 - 0.43 IU/L, the highest levels were 1.04 - 0.99 IU/L. Military TB patients' BAL fluids contained higher levels of ADA than other groups (P =0.01), respectively. Kayacan et al. [8] found that ADA levels were highest in BAL fluids of patients suffering from TB, non-TB lung diseases (such as asthma, lung cancer, pneumonia, and COPD), and controls (P = 0.001). The ADA levels in BAL fluid from patients with pulmonary TB, lung cancer, and other forms of pulmonary disease, however, were not significantly different between these three groups (P = 0.56), according to Reechaipichitkul et al. [9].

In BAL fluid of patients with pulmonary TB, Orphanidou et al. [15] found a significant difference between BAL fluid levels of ADA and those of other pulmonary diseases. Boonsarngsuk et al. [16] demonstrated that pulmonary TB could only be differentiated from some other lung disorders using BALF ADA. The discrepancies between different studies usually result from differences in reported ADA levels and sensitivities and specificities. The discrepancies may be caused by difference in methods of measuring ADAs, diseases present, or differing techniques for bronchoalveolar lavage. There may also be differences between humans in regards to the activity of ADA in BAL fluid [17]. Therefore, studies in similar populations using similar methods should be used in determining the cut-off value. Additionally, it is important to understand TB epidemiology. A diagnostic test's value has been determined by its ability to predict disease. When a population has a low prevalence of a disease, we suspect a low positive predictive value (PPV) in diagnostic studies. Aside from its sensitivity and specificity, ADA's predictive value depends on the local prevalence as well as its sensitivity and specificity. The PPV increased with increasing prevalence [18]. NPV (negative predictive value) refers to the opposite relationship. In addition, most studies are focused on the total ADA level. However, it may be more accurate to measure ADA isoenzymes. ADA isoenzymes could not be determined. The results of this study indicated that ADA > 3.5 IU/L can confidently exclude non-TB pulmonary diseases at the designated cut-off level of 3.5 IU/L.

CONCLUSION

We concluded that despite the high ADA levels in BAL fluids of patients with pulmonary TB and the fact that ADA is a rapid and cost-effective technique, it cannot rule out pulmonary TB due to its limited sensitivity. The sample size of studies should be increased therefore.

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