

# Adenosine Deaminase as a Biomarker for the Diagnosis of Tubercular Pleural Effusion.

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## ABSTRACT

**Background:** The aim of our study was to study and compare the levels of Adenosine deaminase, total proteins and glucose levels in tubercular and non tubercular Pleural Effusion patients, and simultaneously to establish the diagnostic utility of Pleural fluid adenosine deaminase activity in tubercular pleural effusion. Study Design: A hospital based cross sectional study was conducted on patients attending the Out Patient Department or admitted in Medicine or Pulmonary Ward of SMIH, Dehradun (UK) for a period of 6 months from Aug2017 to Jan 2018. 56 cases of tubercular pleural effusion above 15years were selected randomly for the study. The control group consists of 54 subjects of non tubercular pleural effusion. Exclusion criteria was age below 14 years & those who were not willing to participate. Inclusion criteria was age above 14 years, Pleural fluid smear positive for AFB or fluid culture positive for mycobacteria tuberculosis, positive sputum culture, positive pleural biopsy. All the cases and controls were subjected to complete history, clinical examination and pleural fluid estimation for ADA, protein and glucose. **Material & Method:** Both the cases and controls were subjected to complete history taking, clinical examination and pleural fluid estimation for ADA, protein and glucose. The pleural fluid sample was processed on Vitros 250 for glucose & protein and on semi autoanalyzer (Erba chem) for ADA. **Results & Conclusion:** In the test group the Mean  $\pm$  SD of ADA activity was 103.29 $\pm$ 61.26 IU/l whereas in control group it was 25.0 $\pm$ 18.2 IU/l. Thus the activity of ADA in the test group was significantly higher than the control group ( $p < 0.0001$ ). In the test group, the Mean  $\pm$  SD of glucose level was 65.80 $\pm$ 29.27 mg/dl and in the control group was 123.1 $\pm$ 79.9 mg/dl. Thus the level of glucose in the control group was higher than the test group ( $p < 0.0001$ ). Similarly the mean values of protein were found to be much higher in test group (4.69 $\pm$ 0.97 gm/dl) as compared to the control group (3.2 $\pm$ 1.0 gm/dl), which was found to be highly significant ( $p < 0.001$ ).

**Keywords:** Pleural effusion, Adenosine deaminase.

## INTRODUCTION

Pleural effusion is excess pleural fluid that accumulates in the pleural cavity, the fluid filled space that surrounds the lungs. This excess pleural fluid can impair breathing by limiting the expansion of the lungs.<sup>[1]</sup>

Pleural fluid is an ultrafiltrate of plasma, usually there is less than 10ml of fluid in each pleural cavity.<sup>[2]</sup> Tubercular pleural effusion occurs in upto 31% of TB cases.<sup>[3]</sup> It is considered as a form of extra pulmonary tuberculosis and constitutes a frequent clinical problem.<sup>[4]</sup> Pleural effusion occurs in approx 5% of patients with TB.<sup>[5]</sup> Tubercular pleural effusion is thought to result from a delayed hypersensitivity reaction in response to the presence of mycobacterial antigens in the pleural space.<sup>[6]</sup>

Delayed hypersensitivity reaction causes the stimulation and differentiation of lymphocytes that perform a variety of functions, including the release of certain lymphokines that activate macrophages for enhanced mycobactericidal effect.<sup>[7]</sup>

Tubercular pleural effusion manifests as an acute illness, with approx one third of patients being symptomatic for less than 1 week & two thirds for less than 1 month.<sup>[8]</sup> The most common presenting symptoms are nonproductive cough and pleuritic chest pain. Other symptoms include fever, night sweats, weight loss, malaise and dyspnoea varying in severity according to the size of effusion.

The reliability of the early diagnosis of pleural TB has been greatly improved by the use of biochemical markers such as ADA, interferon-gama and lysozyme.<sup>[9,10]</sup> The determination of the ADA level in the suspected pleural fluid appears to be the most promising marker because of the ease, rapidity and cost-effectiveness of the ADA assay.

ADA catalyzes conversion of Adenosine to Inosine. This enzyme is important in rapid proliferation of cells to prevent the accumulation of toxic metabolite. It is a significant indicator of active cellular immunity.

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The levels of ADA increase in Tuberculosis because of stimulation of T cells by mycobacterial antigens.<sup>[11]</sup> Two isoenzymes have been identified ADA-1 and ADA-2,<sup>[12]</sup> ADA-2 is the predominant enzyme in tubercular effusions, while elevated ADA-1 levels are found in non-tubercular effusions.<sup>[13,14]</sup>

### MATERIALS AND METHODS

A hospital based cross sectional study was conducted on patients attending the OPD or admitted in Medicine or Pulmonary ward of SMIH, Dehradun (UK) for a period of 6 months from August 2017 to January 2018. 56 cases of tubercular pleural effusion above 15 years of age were selected randomly for the study. The control group consists of 54 subjects of nontubercular pleural effusion.

Inclusion criteria was age above 14 year, pleural fluid smear positive for AFB or fluid culture positive for mycobacteria tuberculosis, positive sputum culture and positive pleural biopsy.

Exclusion criteria was age less than 14 years & those who were not willing to participate.

Both the cases and controls were subjected to complete history taking, clinical examination and pleural fluid estimation for ADA protein and glucose.<sup>[15-17]</sup> The pleural fluid sample was processed on Vitros 250 for glucose & protein and on Semi autoanalyzer (Erbachem) for ADA.

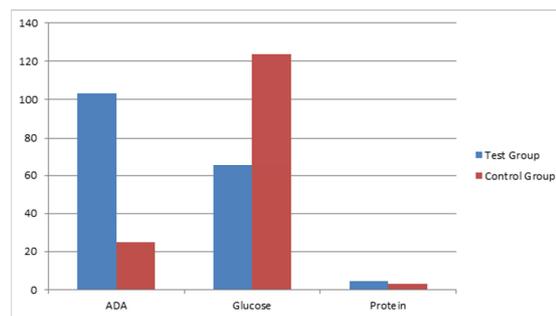
### RESULTS

In the test group the Mean±SD of ADA activity was 103.29±61.26 IU/l whereas in control group it was 25.0±18.2 IU/l. Thus the activity of ADA in the test group was significant higher than the control group (p<0.0001). In the test group, the Mean±SD of glucose level was 65.80±29.27 mg/dl and in the control group was 123.1±79.9 mg/dl. Thus the level of glucose in the control group was higher than the test group (p<0.0001).

Similarly the mean values of protein were found to be much higher in test group (4.69±0.97 gm/dl) as compared to the control group (3.2±1.0 gm/dl), which was found to be highly significant (p<0.001). The results are tabulated in Table 1 and depicted graphically in [Figure 1].

**Table 1: Comparison of Tubercular pleural effusion cases with controls.**

Parameter	Test Group N=56 Mean ±SD	Control Group n=54 Mean ±SD	t-value	p-value	Level of significance
ADA (IU/l)	103.29±61.26	25.0±18.2	9.0142	<0.0001	HS
Glucose (mg/dl)	65.80±29.27	123.7±79.9	5.0815	<0.0001	HS
Protein(gm/dl)	4.69±0.97	3.2±1.0	7.9326	<0.0001	HS



**Figure 1: Comparison of Tubercular pleural effusion cases with controls.**

### DISCUSSION

In the developing countries like India, the commonest cause of pleural effusion is tuberculosis. Untreated tubercular pleural effusion can develop into active TB, so it is important to make rapid and accurate diagnosis for tubercular Pleural effusion & initiation of treatment. Based on the mechanism of fluid formation pleural effusions are transudates or exudates. Transudates are ultrafiltrate of plasma, whereas exudates are the result of inflammation of pleura or decreased lymphatic drainage. TB is the major cause of pleural effusion & usually exudates.

In the present study we found high ADA and protein levels and low glucose levels in tuberculous pleural effusion as compared to non-tuberculosis pleural effusion in a study by Lusi Valdes et al the mean values for ADA was 118±40.6 IU/l in Tubercular Pleural Effusion and in Non-Tubercular Pleural Effusion 19.0±12.2IU/l (p<0.0001).<sup>[10]</sup> They also found the mean values for glucose as 70.0±12.1 mg/dl and in Non Tubercular Pleural Effusion as 87.7±5.0 mg/dl both the values are comparable to our study. In a study by Lee et al the mean levels of ADA in Tubercular Pleural Effusion were 90±29.6 IU/l and in Non Tubercular Pleural Effusion was 18.7±10.9 IU/l (p<0.0001).<sup>[18]</sup>

In a study by Priyadarshini K.S et al the mean levels of protein & glucose in Tubercular Pleural Effusion was 4.63±0.6 gm/dl and 67.3±14.2 mg/dl respectively.<sup>[19]</sup>

All these studies show similar results with the present study. Hence in developing countries like India, where incidence of Tuberculosis is very high, estimation of ADA is a convenient, rapid, inexpensive and a simple method & can be considered as a marker for early diagnosis of Tuberculosis Pleural Effusion.

### CONCLUSION

We conclude that the test performance of ADA in diagnosing tubercular pleural effusion is reasonably good & is a useful tool for diagnosing tubercular pleural effusion. It is rapid, easy, inexpensive & does not require elaborate laboratory arrangements. The present study showed that estimation of ADA

activity is a highly sensitive and specific method to routinely differentiate between tubercular and Non tubercular pleural effusion.

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