ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 11 | November - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SIGNIFICANCE OF ADENOSINE DEAMINASE IN MONITORING OF TUBERCULOUS PLEURAL EFFUSION

Respiratory Medicine

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ABSTRACT

Background: In India, tuberculosis is a frequent cause of pleural effusion. The enzyme ADA (adenosine deaminase) catalyses the conversion of adenosine to ionosine. Patients with tuberculous pleural effusion typically have an ADA (Adenosine Deaminase) level upwards of 40 U/L. **Methods:** From December 2020 to June 2022, a prospective observational study was done at the Department of Respiratory Medicine, Saraswathi Institute of Medical Sciences, a tertiary care centre. 70 individuals with pleural fluid ADA levels exceeding 40 U/L and a tuberculous pleural effusion diagnosis were selected. In addition to cytological, biochemical, and microbiological characteristics, pleural fluid was analysed for ADA. After 15 days of antitubercular therapy (ATT), pleural fluid ADA levels were measured again. **Results:** Pleural fluid ADA levels before the start of ATT intake and after 15 days of ATT intake were statistically analysed. Among 70 patients, 40 were male and 30 females. Mean age of the patients was 34.93±12.98 years. Mean pleural fluid ADA level before starting ATT was 63.01±13.03 for male and 68.08±22.77 for female. After 15 days of ATT intake mean Pleural fluid ADA level was 33.80±7.03 for male and 33.70±6.32 for female. P value was calculated and was statistically significant ($p<0.05$). **Conclusions:** After 15 days of anti-tubercular medication, the ADA level in pleural fluid reduced considerably. In situations of tuberculous pleural effusion, pleural fluid ADA can be utilized as a biomarker for follow-up.

KEYWORDS

INTRODUCTION

Pleural effusion is the accumulation of extra pleural fluid in the pleural cavity, the fluid-filled region surrounding the lungs. All this pleural fluid might hinder breathing by restricting lung expansion. Pleural fluid is an ultrafiltrate of plasma, and each pleural cavity typically contains less than 10ml of fluid. Particularly in India, tuberculosis is a frequent cause of pleural effusion. It is believed that the tuberculous pleural effusion results from the rupture of a subpleural caseous focus into the pleural space. 1

The development of tuberculous pleural effusion appears to be significantly influenced by delayed hypersensitivities.

Approximately one-third of patients with tuberculous pleural effusion experience symptoms for less than one week, and two-thirds for less than one month. 2 Non-productive cough and pleuritic chest discomfort are the most typical presenting symptoms. Other symptoms include different degrees of fever, night sweats, weight loss, malaise, and dyspnoea, depending on the amount of the effusion. Utilizing biochemical indicators such as ADA, interferon-gamma, and lysozyme has significantly enhanced the accuracy of the early diagnosis of pleural tuberculosis.3,4 The assessment of the ADA concentration in the suspected pleural fluid appears to be the most promising marker due to its simplicity, speed, and cost-effectiveness.

An early study conducted by Ocana and colleagues analysed the amounts of ADA found in the pleural fluid of 221 patients who had pleural or peritoneal effusions. 5 No patient had tuberculous pleuritis if the ADA level in their pleural fluid was below 40 U/L, however all patients who had an ADA level in their pleural fluid that was above 70 U/L had tuberculosis. The existence of an ADA level that is higher than 40 U/L in patients who have lymphocytic pleural effusion is highly suggestive of tuberculous pleurisy. The study by Liang et al. completed a meta-analysis of 63 publications that looked at the diagnostic value of ADA. The patients who were included in the study were 2,796 people who had tuberculous pleuritis and 5,297 people who had other illnesses. 6 They found a positive likelihood ratio of 9.03 and a negative likelihood ratio of 0.10, with a mean sensitivity of 0.92 and a mean specificity of 0.90.

In this aspect, this research study was designed to investigate the value of pleural fluid ADA as a follow-up biomarker in tuberculous pleural effusion and to assess its level prior to and 15 days after the initiation of ATT (Anti Tubercular Therapy).

METHODS

From December 2020 to June 2022, a prospective observational study was done at the Department of Respiratory Medicine, Saraswathi Institute of Medical Sciences, a tertiary care center. 70 individuals with pleural fluid ADA levels exceeding 40 U/L and a tuberculous pleural effusion diagnosis were selected. In addition to cytological, biochemical, and microbiological characteristics, pleural fluid was analysed for ADA. After 15 days of antitubercular Therapy (ATT), pleural fluid ADA levels were measured again.

Inclusion criteria

1. Age more than18 years irrespective of gender
2. Patients who have given informed consent
3. Chest X-ray showing evidence of pleural effusion

Exclusion criteria

1.Patients with bleeding disorders
2. Patients who do not give their consent
3. Pregnant women
4. Patient who have undergone repeated pleurocentesis

RESULTS

Pleural fluid ADA levels before the start of ATT intake and after 15 days of ATT intake were statistically analysed. Among 70 patients, 40 were male and 30 females. Mean age of the patients was 34.93±12.98 years (Table 1 and Figure 1).

Table 1: Demography of Patients Age in both gender

Gender	N	Mean Age (Years)	Std. Deviation
Female	30	32.63	12.538
Male	40	36.65	13.209
Total	70	34.93	12.989

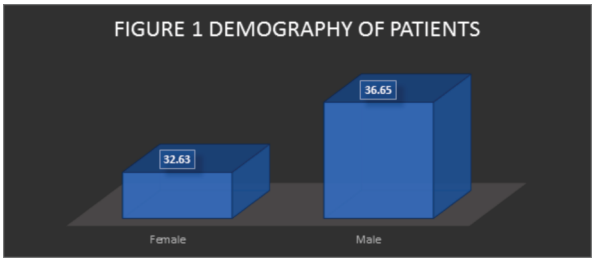
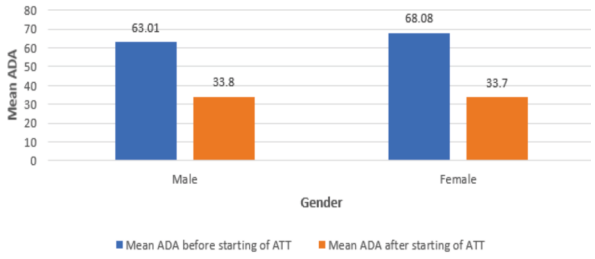


Table 2: Mean ADA level before and after ATT intake

Gender	Mean ADA before starting ATT	Mean ADA after starting ATT	P- Value
Male			0.002
Female			0.0006

Mean pleural fluid ADA level before starting ATT was 63.01±13.03 for male and 68.08±22.77 for female. After 15 days of ATT intake mean Pleural fluid ADA level was 33.08±7.03 for male and 33.70±6.32 for female. (Table 2 and Figure 2). P value was statistically significant ($p<0.05$).

FIGURE 2: Comparison of mean ADA before and after taking ATT of both gender



DISCUSSION

40 men and 30 women participated in our study of 70 individuals with lymphocytic, exudative pleural effusion. The patients' average age was 34.93±12.98 years. Males had a mean pleural fluid ADA level of 63.01±13.03 and females of 68.08±22.77 before beginning ATT. Male and female pleural fluid ADA levels were 33.80±7.03, 33.70±6.32 respectively, after 15 days of ATT administration. After 15 days of starting ATT, the level of pleural fluid starts to decrease. 58% of the 303 patients in a population with a high TB prevalence and exudative effusions had TB with a lymphocytic predominant effusion and an ADA level greater than 50 U/L. This information comes from a study that was conducted by Valdés et al.,7 which included 254 patients with tuberculous pleural effusions. Of these 254 patients, 99.6% had an ADA level that was greater than 47 U/L. 9,10.

The incidence of tuberculosis in the region, as well as the test's level of sensitivity and specificity, all have an impact on the diagnostic usefulness of ADA. In populations with a high tuberculosis prevalence and a clinical suspicion of TB effusion, elevated ADA levels may be regarded as a confirmatory test supporting the start of therapy. This is because elevated ADA levels provide additional evidence that TB effusion is present. Serum ADA has previously been used in research to track individuals with tuberculosis' responses to treatment.

One month after the start of the treatment, Malempati UD et al., 8 estimated the blood ADA activity to determine the effective treatment response to ATT. In pulmonary tuberculosis patients with pleural effusion, both the serum and pleural fluid ADA activities were raised before to the start of ATT, with the pleural fluid ADA activity being higher than the serum level. In patients with pulmonary tuberculosis receiving antitubercular therapy for a month, the serum ADA activity was lowered.

Rao et al., 9 assessed the serum adenosine deaminase activity over the duration of pulmonary tuberculosis treatment in a different investigation. 12 Serum adenosine deaminase levels in the study group were substantially higher than in the control group. When compared to the original reading, the serum ADA values did not significantly alter after the first month of treatment for pulmonary tuberculosis, but they did significantly decline after the second and sixth months of treatment. Similar findings were made in a research by Kartaloglu et al., 10 which revealed a modest increase in serum ADA in the first month, but that it dropped after therapy along with its efficacy.

CONCLUSION

The discovery of M. tuberculosis in pleural fluid or pleural biopsy specimens, either by microscopy and/or culture, or the histological proof of caseating granulomas in the pleura associated with AFB, continues to be the gold standard for the diagnosis of tuberculous pleuritis. However, in high burden environments, the diagnosis is frequently assumed in cases when the patient has a lymphocytic-predominant exudate and a high ADA level, which is a useful adjunct in the diagnostic assessment. When combined with lymphocyte predominance and ADA, which is typically easy to get, treatment can be started in patients with a high pre-test probability. Other biomarkers' functions are not as well understood. After 15 days of ATT use, pleural fluid ADA dramatically decreased in our study. As a follow-up biomarker in cases of tubercular pleural effusion, pleural fluid ADA may be helpful. In order to validate and determine whether there is any direct correlation between the level of adenosine deaminase (ADA), before and after initiating anti-tubercular medication in patients with tubercular pleural effusion, more such larger prospective studies must be undertaken.

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