

ORIGINAL RESEARCH ARTICLE

PLEURAL FLUID ADENOSINE DEAMINASE (ADA) LEVEL IN TUBERCULOUS PLEURISY

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ABSTRACT

Adenosine Deaminase (ADA) is used as a well established biological marker for diagnosis of tuberculous pleuritis. The aim of this study was to assess the sensitivity and specificity of ADA in patients with pleural effusion admitted in the medical ward. This was an cross sectional study. The information was gathered only from those patients whose pleural fluid sample was sent for ADA in clinical biochemistry laboratory of KIST Medical College and Teaching hospital. The data was acquired from the medical records of patients attending medical ward. The patients were considered as TB positive if they were clinically diagnosed so and taken as negative otherwise. Fifty six pleuritis patients were evaluated. Using the cut off value of 30 U/L, the overall sensitivity and specificity was 93.3% and 57.1% respectively. The association between ADA findings and the clinical findings were statistically significant ( $p < 0.001$ ). The positive predictive value (PVP) and the negative predictive value (PVN) were 82.3% and 80% respectively. ADA is an inexpensive, rapid and simple test for analysis of tuberculous pleuritis. Though, it is a sensitive test for tuberculosis, due to its low specificity, sometimes negative cases can be considered as positive.

**Key Words:** Pleural Effusion, Predictive Value, ADA, Sensitivity and Specificity.

INTRODUCTION

Adenosine deaminase (ADA) is an endogenous tissue enzyme which is released into the serum in patients with many different types of malignancies and infections, including viral hepatitis, infectious mononucleosis, typhoid fever, and tuberculosis. In pleural fluid, elevated ADA levels are very commonly associated with tuberculosis. In CSF, ADA is elevated in cases of tuberculous meningitis. <sup>1,2</sup> It is reported that it is a pleural fluid marker for tuberculosis. <sup>3</sup> It is found that Pleural fluid ADA levels in TB effusions were significantly higher than the non-TB effusions. <sup>4</sup>

MATERIALS AND METHODS

The study design was cross sectional. The information was gathered only from those patients whose pleural fluid sample was sent for ADA in clinical biochemistry laboratory of KIST Medical College and Teaching hospital. The data was acquired from the medical records of patients attending medical ward from 2010 to 2011. The patients were considered as TB positive if they were clinically diagnosed so and taken as negative otherwise. Descriptive statistics, Kappa test and independent t-test were used in proper context.

RESULTS

Among fifty six pleuritis patients, 37 (66.1%) were male and 19 (33.9%) were female. The patients were between the ages of 17- 82 years and mean age was 45.83 years. The ADA level in pleural effusion ranged from 10-219 U/L and the mean level was 80.23 U/L. The level in Tubercular effusion was between 26 U/L to 219 U/L and the mean was 99.387 U/L while in non tubercular ranged from 10 U/L to 103.3 U/L and the mean was 45.7 U/L ( $p < 0.001$ ). Using the cut off value of 30 U/L, the overall sensitivity and specificity of ADA was 93.3% and 57.1% respectively. The agreement between ADA findings and the clinical findings was fair and statistically significant (Kappa=0.55,  $p < 0.001$ ). The positive predictive value (PVP) and the negative predictive value (PVN) were 82.3% and 80% respectively.

Table 1: Agreement between ADA and Clinical findings in diagnosis of TB

ADA Finding	Clinical Finding		Total
	TB positive	TB negative	
TB negative	2 (20.0%)	8 (80%)	10 (100%)

Suspect	0 (0%)	2 (100%)	2 (100%)
Strong suspect	6 (60%)	4 (40%)	10 (100%)
TB positive	28 (82.4%)	6 (17.6%)	34 (100%)
Total	36 (64.3%)	20 (35.7%)	56 (100%)

## DISCUSSION

The study was carried out in fifty six pleuritis patients, 66.1% were male and 33.9% were female. The patients were between the ages of 17- 82 years and mean age was 45.83 years. The ADA level in pleural effusion was between 10 U/L to 219 U/L and the mean level was 80.23 U/L. The mean of tubercular effusion was 99.387 U/L while in non tubercular the mean was 45.7 U/L ( $p < 0.001$ ). The sensitivity and specificity was 93.3% and 57.1% respectively with positive and negative predictive values of 82.3% and 80% respectively (Table 1). The result shows the low specificity of ADA in the diagnosis of Tuberculous pleuritis.

The measurement of ADA levels is a useful test with good sensitivity and specificity.<sup>5,7</sup>; however, diagnosis in some patients has been reported to be impossible if only their ADA levels alone.<sup>8,9</sup>

In some reports, the diagnosis of tuberculous pleurisy is made with an ADA level in the pleural fluid of more than 37–50 IU/L.<sup>10,12</sup> The cut-off value of 30 U/L for tuberculous pleuritis as used in this study is expected to offer a specificity of 98%.<sup>13</sup>

Strankinga<sup>14</sup> investigated 10 patients with tuberculosis pleurisy and 76 patients with pleural effusions of other etiology. The ADA activity in the tuberculous patients was significantly higher than in the other groups while the exception of those with empyema. Specificity 87% and sensitivity 100% of this test for tuberculosis are high when a reference limit of more than 53 U/L is taken.

Burgess<sup>15</sup> showed ADA activity in tuberculous effusion was higher than in any other diagnostic group. At a level of 50 U/L the sensitivity and specificity for the identification of tuberculosis was 90% and 89% respectively.

Mohammadtaheri<sup>16</sup> showed that the total ADA activities in all the tuberculous effusions had above 46U/L (sensitivity of 100%). This level was also present in 11 of nontuberculous effusions mostly para-infective exudates (8 cases).

## CONCLUSION

The method of ADA estimation is easy, simple and doesn't require expensive equipment or elaborate laboratory arrangement except a simple colorimeter. Though, it is a sensitive test for tuberculosis, due to its low specificity, sometimes negative cases can be considered as positive.

## REFERENCES

- Gopi A, Madhavan SM, Sharma SK, Sahn SA. Diagnosis and treatment of tuberculous pleural effusion in 2006. *Chest* 2007;131(3):880-9.
- Dinnes J, Deeks J, Kunst H, Gibson A, Cummins E, Waugh N, Drobniewski F, Lalvani A. A systematic review of rapid

diagnostic tests for the detection of tuberculosis infection. *Health Technol Assess* 2007;11(3):1-196.

- Lima, DM, Colares, KJB, Fonseca, BAL. Combined use of the polymerase chain reaction and detection of adenosine deaminase activity on pleural fluid improves the rate of diagnosis of pleural tuberculosis. *Chest* 2003 September;124(3):909-914.
- Poyraz B, Kaya A, Oktem A. Diagnostic significance of gamma-interferon in tuberculous pleurisy. *Tuberk Toraks* 2004;52(3):211-7.
- Chen ML, Yu WC, Lam CW, Au KM, Kong FY, et al. Diagnostic value of pleural fluid adenosine deaminase activity in tuberculous pleurisy. *Clin Chim Acta* 2004;341:101-7.
- Titarenko OT, D'iakova ME, Perova TL, D'iakova AI, Popov MIu. Informative value of adenosine deaminase and 2-deoxyadenosine deaminase in the diagnosis of tuberculous pleurisy. *Klin Lab Diagn* 2002; 5:11-4. (in Russian)
- Sharma SK, Suresh V, Mohan A, Kaur P, Saha P, et al. A prospective study of sensitivity and specificity of adenosine deaminase estimation in the diagnosis of tuberculosis pleural effusion. *Indian J Chest Dis Allied Sci* 2001; 43:149-55.
- Bueso FJ, Hernando VH, Garcia-Buela JP, Juncal DL, Egana MMT, et al. Diagnostic value of simultaneous determination of pleural adenosine deaminase and pleural lysozyme/serum lysozyme ratio in pleural effusions. *Chest* 1988;93:303-7.
- Ocana I, Martinez-Vazquez JM, Segura RM, Fernandez-De-Sevilla T, Capdevila JA. Adenosine deaminase in pleural fluids. Test for diagnosis of tuberculous pleural effusion. *Chest* 1983;84:51-3.
- Safianowska A, Krenke R, Dmowska-Sobstyl B, Bogacka-Zatorska E, Domagała-Kulawik J, et al. Adenosine deaminase activity in tuberculous and malignant pleural effusions. *Pneumonol Alergol Pol* 2006;74:5-9.
- Smach MA, Garouch A, Charfeddine B, Ben Abdelaziz A, Dridi H, et al. Diagnostic value of serum and pleural fluid adenosine deaminase activity in tuberculous pleurisy. *Ann Biol Clin (Paris)* 2006;64:265-70.
- Valdes L, San Jose E, Alvarez D, Valle JM. Adenosine deaminase (ADA) isoenzyme analysis in pleural effusions: diagnostic role, and relevance to the origin of increased ADA in tuberculous pleurisy. *Eur Respir J* 1996;9:747-51.
- Blake J, Berman P. The use of adenosine deaminase assays in the diagnosis of tuberculosis. *S Afr Med J* 1982;62:19-21.
- Strankinga W.F. Adenosine deaminase activity in tuberculous pleural effusions: a diagnostic test. *Tubercle* 1987 (June);68(2):137-140.
- Burgess L.J. Use of adenosine deaminase as a diagnostic tool for tuberculous pleurisy. *Thorax* 1995 June;50(6):672-674.
- Zohreh Mohammadtaheri et al. Diagnostic Value of Adenosine Deaminase Isoenzyme (ADA2) and Total ADA in Tuberculous Pleural Effusion, *Tanaffos* 2005;4(15):37-42.