

## Level of Serum Adenosine Deaminase in Cases of Tuberculous Pleural Effusion

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### ABSTRACT

**Aim:** To assess the value of adenosine deaminase activity (ADA) for the diagnosis of tuberculous pleural effusion without performing needle pleural biopsy.

**Methods:** This prospective study was conducted at Nishtar Hospital, Multan from May 2013 to September 2013. A total of 60 patients with history and clinical examination suggestive of tuberculous pleural effusion were included in the study.

**Results:** The ADA activity in the pleural aspirate of all the subjects of group-I and group-II was estimated. The ADA activity was compared in both groups by setting a cut off value 40 U/L. the results were statistically analyzed by applying chi square test. The ADA activity of the group-I was  $4.2 \pm 10.82$  U/L while that of group-II was  $24 \pm 11$  U/L. thirty three in group-I and one of group-II had ADA activity above cut off value.

**Conclusion:** The results of this study favour the application of ADA activity in pleural fluid as the diagnostic tool for tuberculous pleural effusion without performing an invasive procedure like the pleural biopsy.

**Keywords:** Tuberculous pleural effusion, adenosine deaminase, pleural biopsy.

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### INTRODUCTION

Conventionally the diagnosis of tuberculous pleural effusion is made on the basis of clinical data, biochemical and microscopic examination of pleural fluid as exudates and containing high count of lymphocytes, which is non specific. Other methods are ZN staining and culture of pleural fluid which lack sensitivity. The sensitivity ZN staining and culture is 1040% and 8-49% respectively. Moreover culture identification takes long time i.e. about 4-6 weeks. So these clinical, biochemical and bacteriological tests for diagnosis of tuberculous pleural effusion are less sensitive and time consuming. Pleural biopsy is invasive procedure and its overall sensitivity is 50-80%<sup>1</sup>. It has not become routine medical procedure due to invasive nature. This causes the diagnostic problem as there are several other causes of pleural effusion. In most of these situations therapeutic trial of anti-tuberculous drugs is given. So there is a need of a sensitive test, which is reliable and rapid. Now-a-days the high sensitivity and specificity of ADA for early diagnosis of tuberculosis in cases of tuberculous pleural, pericardial, perineal effusion and tuberculous meningitis have been confirmed<sup>2</sup>.

Adenosine is widely distributed in animal and human tissues. The highest activity is found in intestinal mucosa and spleen, lower activity is found in liver, skeletal muscle, kidney and serum<sup>3</sup>. The ADA

increase has been attributed to cell mediated response to mycobacterial antigens.

High activity of ADA was reported in a study with specificity of 87% and sensitivity of 100% in cases of tuberculous pleural effusion<sup>4</sup>. In an other study it is found that pleural fluid ADA activity is very useful, low cost test with sensitivity of 100% for diagnosis of pleural effusion<sup>5</sup>. In patients with tuberculous and malignant effusion and higher levels of tumour necrosis factor (TNF) and ADA were found in tuberculous patients than in patients with benign disorder of cancer<sup>6</sup>. A study conducted to observe the clinical significance of serum ADA in patients of viral hepatitis, revealed that ADA activity was significantly higher in the sera of patients of acute fulminant hepatitis than in control group<sup>7</sup>.

### MATERIAL AND METHODS

This prospective study was conducted at Nishtar Hospital, Multan from May 2013 to September 2013. A total of 60 patients with history and clinical examination suggestive of tuberculous pleural effusion were included in the study and denoted as group-I. In addition as control of study, the pleural fluid was aspirated in 20 selected patients having transudative pleural effusion secondary to congestive cardiac failure and cirrhosis of liver, denoted as group-II. The P value was < 0.001.

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## RESULTS

Out of 60 patients of tuberculous pleural effusion, 26 (43%) were male and 34(57%) were female. Whereas in 20 control subjects 10(50%) were male and 10(50%) were female. Fifty three patients had unilateral effusion (31 patients on right side and 22 on left side). Seven patients had bilateral pleural effusion. The age of the patients of tuberculous pleural effusion range from 13-60 years, the mean age of all the patients was 28.7±9.73 years. The male patients were of older age as compared to female patients. The mean age of male and female patients was 30.88±8.33 and 27-14±12.20 years respectively as shown in table-1. ADA activity of pleural fluid of tuberculosis patients was 40.2±10.82 U/L while that of control subjects having transudative pleural effusion was 24.0±11.0 UI (Table-2).

Table 1: Clinical features

| Features                    | Male | Female |
|-----------------------------|------|--------|
| Fever                       | 2    | 3      |
| Dyspnea                     | 2    | 2      |
| Fever & chest pain          | 2    | 4      |
| Fever & dyspnea             | 6    | 10     |
| Chest pain & dyspnea        | 2    | 2      |
| Fever, chest pain & dyspnea | 11   | 14     |

Table 2: ADA activity

| Status       | Patients   | control |
|--------------|------------|---------|
| Mean + SD    | 40.2±10.82 | 24±11   |
| Above 40 U/L | 33         | 1       |
| < 40 U/L     | 27         | 19      |

## DISCUSSION

The diagnosis of pleural effusion demands a pleural aspiration and biopsy<sup>8</sup>. These both are invasive procedures. Further cytological and microbiological testing needs a large quantity of pleural fluid<sup>9</sup>. The diagnostic tap of 1020 ml of pleural fluid without a pleural biopsy is inadequate. In about 20% of all pleural effusion, these basic testing don not establish the diagnosis and even a thoracotomy or thoracoscopy may not reveal the cause of effusion<sup>10</sup>.

Tuberculous pleural effusion has been recognized as a feature of primary tuberculosis until the near past but as many as 50% now develop inconjunction with post primary tuberculosis. The fluid accumulates in pleural space as a result of a delayed hypersensitivity reaction to tuberculous proteins<sup>11</sup>. The number of mycobacterium tuberculosis present in pleural fluid are a few in number, so smear and culture yield a low diagnostic value; less than 25%<sup>12</sup>. The diagnosis of tuberculous pleurisy is important, although tuberculous pleural effusion often resolve

spontaneously, 43-65% patients will develop active tuberculosis in the coming 5 years<sup>13</sup>.

The tuberculous pleural fluid contains sensitive biochemical markers. These include ADA, interferon gamma, TNF and interleukin-1. ADA is enzyme of catabolism of purine bases. It catalyses the conversion of adenosine to inosine and is released by T-lymphocytes and macrophages during cellular immune response. The different studies have revealed high sensitivity and specificity of ADA for early diagnosis of tuberculous pleural and pericardial effusion, tuberculous ascites and tuberculous meningitis<sup>14</sup>. These pleural fluid levels of ADA have a higher positive predictive value in the region of high prevalence of tuberculous pleurisy among cases of pleural effusion<sup>15</sup>. This study revealed high level of ADA in pleural fluid of biopsy proven cases of tubercles pleural effusion as compared to non-tuberculous group.

The results were statistically significant between tuberculous and non-tuberculous group (P value <0.001). The cut off level was kept >40 U/L. The results of this study are comparable with many other national and international studies. However, a high ADA activity in pleural effusion in region with a low tuberculous incidence is neither sensitive not specific for diagnosis of tuberculous pleurisy<sup>16,17</sup>.

## CONCLUSION

The results of this study favour the application of ADA activity in pleural fluid as the diagnostic tool for tuberculous pleural effusion without performing an invasive procedure like the pleural biopsy.

## REFERENCES

1. Kataria YP, Imtiaz K. Adenosine deaminase in the diagnosis of tuberculous pleural effusion. *Chest*. 2001;2:298–300.
2. Adenosine Deaminase (ADA) Level in Tubercular Pleural Effusion Lung India: Official Organ of Indian Chest Society 2008; 25(3): 109.
3. Boonsarngsuk V, Suwannaphong S, Laohavich C. Combination of adenosine deaminase activity and polymerase chain reaction in bronchoalveolar lavage fluid in the diagnosis of smear-negative active pulmonary tuberculosis. 2012; 16(9):e663-8.
4. Dimakou K<sup>1</sup>, Hillas G, Bakakos P. Adenosine deaminase activity and its isoenzymes in the sputum of patients with pulmonary tuberculosis. *Int J Tuberc Lung Dis*. 2009 Jun;13(6):744-8.
5. Afrasiabian S, Mohsenpour B, Bagheri, KH, Sigari N. Diagnostic value of serum adenosine deaminase level in pulmonary tuberculosis. *J Res Med Sci* 2013; 18(3): 252–4.
6. Dimakou K, Hillas G, Bakakos P. Adenosine deaminase activity and its isoenzymes in the sputum

- of patients with pulmonary tuberculosis. *Int J Tuberc Lung Dis.* 2009 Jun; 13(6):744-8.
7. Boonsarngsuk V, Suwannaphong S, Laohavich C. Combination of adenosine deaminase activity and polymerase chain reaction in bronchoalveolar lavage fluid in the diagnosis of smear-negative active pulmonary tuberculosis. *Int J Infect Dis.* 2012; 16(9):e663-8.
  8. Jadhav AA, Jain A. Sputum adenosine deaminase and alkaline phosphatase activity in pulmonary tuberculosis. *Arch Physiol Biochem.* 2012; 118(1): 6-9.
  9. Dinnes J, Deeks, J, Kunst H. A systematic review of rapid diagnostic tests for the detection of tuberculosis infection. *Heal Technol Assess* 2007; 11(3): 1-196.
  10. Tuon FF, Litvoc MN, Lopes MI. Adenosine deaminase and tuberculous pericarditis. *Acta Trop* 2006; 99(1): 67-74.
  11. Shen YC, Wang T, Chen L. Diagnostic accuracy of adenosine deaminase for tuberculous peritonitis. *Arch Med Sci* 2013; 9(4): 601-7.
  12. Su SB, Qin SY, Guo XY, Luo W. Assessment by meta-analysis of interferon-gamma for the diagnosis of tuberculous peritonitis. *World J Gastroenterol* 2013; 19(10): 6145-51.
  13. Reuter H, Burgess LJ, Carstens ME, Doubell AF. Adenosine deaminase activity. *Cardiovasc J S Afr.* 2005; 16(3): 143-7.
  14. Tuon FF, Silva VI, Almeida GM. The usefulness of adenosine deaminase in the diagnosis of tuberculous pericarditis. *Rev Inst Med Trop Sao Paulo* 2007; 49(3): 165-70.
  15. Liang QL, Shi HZ, Wang K, Qin SM, Qin XJ. Diagnostic accuracy of adenosine deaminase in tuberculous pleurisy. *Respir Med* 2008; 102(5):744-54.
  16. Reuter H, Burgess L, van Vuuren W, Doubell A. Diagnosing tuberculous pericarditis. *QJM.* 2006; 99(12): 827-39.
  17. Pellerson T, Ojala K, Weber TH. Adenosine deaminase in the diagnosis of pleural effusion. *Acta Med Scand* 1984; 215:299-304.