



## Role of Adenosine Deaminase and Lymphocyte/Neutrophil Ratio in the Diagnosis of Tuberculous Pleural Effusion in Patients with Exudative Pleural Effusion

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### Abstract

**Background:** Pulmonary tuberculosis is the most common cause of death by an infectious agent worldwide. Failure to diagnose and treat pleural TB can result in progressive disease with the involvement of other organs in as many as 65% of patients.

**Objectives:** To evaluate the role of ADA and L/N ratio in the diagnosis of tuberculous pleural effusion in patients with exudative pleural effusion.

**Materials & Methods:** Statistical analysis carried out in hospitalized 60 consecutive patients with exudative effusion admitted in medical wards are taken in this study of age >12 years were included. Patients with immunodeficient states and on chemotherapy excluded.

**Results:** Out of 60 exudative effusions, males are more effected thanf emales (69.1%, females-30.9%). Out of these 49 were diagnosed to have tuberculousetiology. Most common age group was 21-40yrs with mean 26.6 years. Pleuritic chest pain is most common symptom. Mean ESR as 57mm/hr. Total ADA was >40u/l in tuberculous effusion with mean 153.6u/l.

**Conclusion:** Increased ADA activity in pleural effusionis classically associated with tuberculosis. When the L/N ratio's was considered together with ADA activity, the results improved considerably for the diagnosis of tuberculosis pleuritis.

### Introduction

Pulmonary tuberculosis is the most common cause of death by an infectious agent worldwide. Among the extra pulmonary presentations after tuberculous lymphadenitis, pleural TB is the second most common. Failure to diagnose and treat pleural TB can result in progressive disease with the involvement of other organs in as many as 65% of patients. Conventional methods have proven to be insufficient for diagnosis of pleural TB.

Direct examination of pleural fluid is inefficient because sensitivity is about 1% Pleural fluid

culture is more sensitive than direct examination But Mycobacterium tuberculosis requires 4 to 6 weeks to grow. Many studies have demonstrated the diagnostic significance of increased adenosine deaminase (ADA) in tuberculous pleurisy, other studies have shown that ADA is of limited value [3].

Raised levels are also associated with a number of other diseases-

1. Malignancies (especially those of hematologic origin)
2. Bacterial infections (Q-fever, brucellosis)
3. Empyema

4. Collagen vascular diseases (including SLE and Rheumatoid arthritis).

Pleural effusions may arise secondary to pulmonary or systemic disease, and their development is classically associated with an influx of inflammatory cells into the pleural space. Lymphocytes predominate in malignant and tuberculous pleural effusions<sup>[4]</sup>.

Pleural effusion is the abnormal collection of fluid in the pleural space. It is classified into exudate and transudate based on Light's criteria.

Light's criteria the most commonly used method.

The criteria are one or more of the following for diagnosing exudates.

- 1) Pleural fluid protein /serum protein >0.5
- 2) Pleural fluid LDH/serum LDH >0.6
- 3) Pleural fluid LDH more than 2/3rd of the upper limit of serum.

A Cochrane meta-analysis review of forty articles on ADA in pleural fluid shows that-

The test results for ADA with cutoff value > 40 U/L derived from the summary receiver operator curve(SROC) was 92.2% for both sensitivity and specificity.

ADA value > 40 U/L with a lymphocytic effusion Lymphocyte/Neutrophil (L/N)ratio>0.75 is considered diagnostic of TB pleural effusion.

### Aims & Objectives

- 1) To evaluate the role of ADA and L/N ratio in the diagnosis of tuberculous pleural effusion in patients with exudative pleural effusion.
- 2) To analyze the cause of nontuberculous exudative pleural effusion.

### Materials & Methods

60 consecutive patients with exudative effusion admitted in medical wards are taken in this study.

### Inclusion Criteria

1. Cases of Exudative pleural effusion.
2. Age >12 yrs

### Exclusion Criteria

1. Cases of Transudative pleural effusion.
2. Age <12yrs.

3. Haemodynamically unstable patients.
4. Patients with malignant pleural effusion.
5. Patients with immunodeficient states like HIV, those on chemotherapy were excluded.

The following data were noted:

- 1) Age, sex, occupation.
- 2) Clinical features-  
Fever, cough, sputum, pleuritic chest pain, breathlessness, haemoptysis, weight loss, anorexia. Any other specific history is also noted like joint pain alopecia, seizures and jaundice .
- 3) Previous history of tuberculosis, contact with tuberculosis, diabetes mellitus, smoking and alcoholism were also noted.
- 4) Investigations –  
Heamogram  
ESR  
blood urea  
serum creatinine  
liver function tests  
Mantoux test  
chest X ray(PA view and Decubitus)  
sputum AFB and culture & sensitivity was done in all cases.  
HIV ELISA was done in suspected cases and willing patients after counseling.  
Diagnostic thoracocentesis was done and fluid sent for analysis of glucose, protein, cytology and cell count, LDH, AFB& gram stain, culture & sensitivity and ADA.

### Results

Out of 60 exudative effusions, males are more effected than females (69.1%,females-30.9%)

Out of these 49 were diagnosed to have tuberculous etiology .

Most common age group was 21-40yrs with mean 26.6 years.

Pleuritic chest pain is most common symptom.

Mean ESR as 57mm/hr.

Total ADA was >40u/l in tuberculous effusion with mean 153.6u/l

Total ADA was done and found to be > 40 U/L in

all the cases with Tuberculous pleural effusion.  
 The mean ADA was 153.6 U/L.  
 The highest value noted in our study was 239 U/L, and the lowest was 42.19 U/L.  
 ADA value > 100U/L was noted in 18 cases.  
 It was found that the ADA value ranged between a lowest of 5 U/L to a highest of 76.5 U/L.  
 The mean ADA value was 25.6 U/L.

**ADA in Exudative Effusion**

ADA(U/L)	Tuberculous effusion	Nontuberculous effusion
Range	42.19 – 239	5 – 76.5
Mean	153.6	25.6

The range of ADA was between 5 to 239 U/L with a mean ADA value of 89.58 U/L  
 ADA was > 40 U/L in 50Cases .  
 L/N ratio was done in all cases.  
 L/N ratio was >0.75 in 49cases.

Based on ADA and L/N ratio 49 cases were classified to have Tuberculous pleural effusion. Other causes of exudative effusion noted are 4cases of lupus pleurisy, 3 parapneumonic effusion, 1 malignant effusion, 1rheumatoid pleurisy, 1 hypothyroidism and 1case of liver abscess with exudative effusion.

**ADA**

	ADA < 40 U/L	ADA > 40 U/L
ADA	10	50

**L/N Ratio**

	L/N ratio > 0.75	L/N ratio< 0.75
No of cases	49	11
L/N Ratio	Tuberculous effusion	Nontuberculous e ffusion
>0.75	49	0
<0.75	0	11

All cases of tuberculous pleural effusion were lymphocyte predominant with a (L/N) Lymphocyte/Neutrophil ratio of >0.75.  
 In cases of exudative pleural effusion due to nontuberculous etiology L/N ratio was < 0.75 cases.

13 cases with nontuberculous pleural effusion, ADA was < 40 U/L in 10 cases and L/N ratio was < 0.75 in all 13 cases.

**Distribution of Etiology of Pleural Effusion**

Etiology	NUMBER
Tuberculous effusion	49
Parapneumonic effusion	3
Malignant effusion	1
Rheumatoid pleurisy	1
Lupus pleurisy	4
Emphyema	0
Hypothyroidism	1
Liver abscess	1
TOTAL	60

**Discussion**

Increased ADA activity in pleural effusion<sup>[9]</sup> is classically associated with tuberculosis. It is due to number of causes and this negatively affect diagnostic utility of ADA measurements and decrease its specificity in the diagnosis of TB<sup>[2]</sup>.

Our results show that, at a cut off level are 50U/L, ADA has a sensitivity, specificity, PPV, NPV and efficiency of 61%, 71%, 83%, 45%, and 64% respectively<sup>[3]</sup>.

When the L/N ratio’s was considered together with ADA activity, the results improved considerably for the diagnosis of tuberculosis pleuritis<sup>[4]</sup>.

Pleural fluid lymphocytosis also found in malignant conditions, collagen vascular disease, heumaticpleuritis, sarcodosis and up to one third of all transudates.

Parapneumonic and empyematous effusions are characterised by neutrophil-predominant, exudative effusions.

In tuberculosis pleurisy, a predominant lymphocyte count was usually found, resulting in L/N ratio of 0.75 or greater, whereas in other conditions of exudative pleural effusion, L/N ratio was found to be less than 0.75.

TB pleurisy is diagnosed by either identification of M tuberculosis in pleural fluid or biopsy specimen cultures or from the presence granulomas in the pleural biopsy tissue<sup>[11]</sup>.

Pleural fluid cultures have sensitivity of 20- 30%.

Pleural biopsy have sensitivity of 50-80%.

Polymerase chain reaction, having a sensitivity of 78% for active disease, has not been found to be an efficient alternative.

60 cases of exudative pleural effusion were analysed based on Total ADA and L/N ratio.

49cases were due to tuberculosis.

4 cases were due to lupus pleurisy.

3 cases were due to parapneumonic effusion

1cases were due to malignant effusion.

1 cases were due to rheumatoid pleurisy,.

1 case were due to myxoedematous pleural effusion.

1 case were due to exudative effusion in liver abscess.

ADA level was > 40 U/L in 50 cases.

From 50 cases 47 were due to tuberculosis, 1 rheumatoid pleurisy, 1 malignant effusion and 1 case of effusion in myxedema.

ADA value of >100 U/L was observed only in tuberculous effusion.

L/N ratio was >0.75 in 47 cases of TB effusion and in none of the nontuberculous effusion.

Combined use of ADA and L/N ratio is more useful in the evaluation of exudative pleural effusion.

### Conclusion

60 cases of exudative pleural effusion were analysed based on Total ADA and L/N ratio. 49cases were due to tuberculosis, 4 lupus pleurisy, 3 parapneumonic effusion, 1 malignant effusion, 1rheumatoid pleurisy, 1myxoedematous pleural effusion and 1 exudative effusion in liver abscess.

ADA level was > 40 U/L in 50cases

ADA value of >100 U/L was observed only in tuberculous effusion.

L/N ratio was >0.75 in 49 cases of TB effusion and in none of the nontuberculous effusion.

Combined use of ADA and L/N ratio is more useful in the evaluation of exudative pleural effusion.

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