

Original Research Article


# Study of adenosine deaminase and lymphocyte/neutrophil ratio in combination as diagnostic tool for tubercular pleural effusion

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	International Archives of Integrated Medicine, Vol. 7, Issue 8, August, 2020.	
	Available online at <a href="http://iaimjournal.com/">http://iaimjournal.com/</a>	
	ISSN: 2394-0026 (P)	ISSN: 2394-0034 (O)
	Received on: 24-07-2020	Accepted on: 30-07-2020
	Source of support: Nil	Conflict of interest: None declared.
<b>How to cite this article:</b> Joseph Varghese, Hemamalini G. Study of adenosine deaminase and lymphocyte/neutrophil ratio in combination as diagnostic tool for tubercular pleural effusion. IAIM, 2020; 7(8): 26-30.		

## Abstract

**Background and Objectives:** PTB is a disease of mankind that still causes tremendous mortality and morbidity. The incidence is still higher in our country and an early detection and treatment is of utmost importance. Our study suggest a better diagnostic tool, in terms of technical simplicity and less time consuming manner in the diagnosis of pleural effusion of tubercular origin by estimating the activity of ADA along with L/N ratio in pleural effusion without escalating the cost for diagnosis of the same.

**Materials and methods:** All patients attending the medical services of SDM College of Medical Sciences & Hospital, Dharwad from November 2017 to October 2018 and diagnosed to have tubercular pleural effusion were included in the study, data were collected through Performa. Spearman's correlation test and Students paired t-test was employed to come to a conclusion and asses the statistical significance based on clinical examination, blood test, and other data

**Results:** When the individual parameters of ADA and L/N ratio (which had got a very good sensitivity and specificity), was combined together the sensitivity and specificity (66.7%) further raised (p value <0.001), that helps in the diagnostic accuracy.

**Conclusion:** Lymphocyte/neutrophil ratio, Adenosine Deaminase in combination provides a better diagnostic tool which is cost effective for the diagnosis of tubercular pleural effusion, obviating the need for other invasive diagnostic procedures like pleural biopsy and others.

## Key words

Lymphocyte/neutrophil ratio, Adenosine Deaminase, Pulmonary Tuberculosis, Tubercular pleural effusion, Sensitivity, Specificity.

## Introduction

Tuberculosis (TB), which is caused by bacteria of *Mycobacterium tuberculosis* complex, is one of the oldest diseases known to affect humans and a major cause of death worldwide. This disease most often affects the lungs, although other organs are involved in up to one-third of cases. If properly treated, TB caused by drug-susceptible strains is curable in the vast majority of cases. If untreated, the disease may be fatal within 5 years in 50- 65% of cases. Transmission usually takes place through the airborne spread of droplet nuclei produced by patients with infectious pulmonary TB.

Adenosine deaminase enzyme activity, gamma interferon, polymerase chain reaction, lysozyme measurement pleural fluid tuberculous protein antibodies and various tumor markers like CA15 [1], squamous cell carcinoma antigen, etc. have been used to differentiate TB from nonTB [2, 3, 5].

Despite the availability of all tests, it might be necessary to avail of more invasive diagnostic tools like pleural biopsy or thoracoscopy to establish a diagnosis.

Adenosine deaminase although shown to be promising in the West to differentiate tubercular from non-tubercular effusion, in Asian countries was not found to be of much diagnostic value and has shown mixed results [3, 4]. Leucocyte count and lymphocyte /Neutrophil ratio in pleural fluid (L/N ratio >0.75 and ADA Several studies has also suggested that ADA activity when combined with differential activity >50 IU/L) the results improved considerably for the diagnosis of the same in a more easy and less time consuming manner, which in turn was the aim of the study.

## Materials and methods

### Source of data

The present study was carried out in the patients admitted to Department of General Medicine and attached respiratory medicine wing, SDM College of Medical Sciences and Hospital, Sattur, Dharwad, Karnataka.

### Study design

A hospital based prospective observational study.

### Study period

One year period study from November 2017 to October 2018.

### Method of collection of data

All patients attending the medical services of SDM College of Medical Sciences and Hospital, Dharwad from November 2017 to October 2018 and diagnosed to have tubercular pleural effusion were included in the study, data were collected through Performa. The data was collected according to the proforma in terms of detailed history, clinical examination and the necessary investigations. The following investigations were carried out.

### Investigations done

1. Screening hemogram
2. Chest X-ray
3. Sputum for AFB
4. Mantoux test
5. Pleural fluid analysis (ADA, Protein, Sugar, Albumin, Cell type and count, LDH)

Finally statistical analysis was carried out using appropriate statistical methods.

### Inclusion criteria

- All patients admitted with tubercular exudative pleural effusion were included in the study.

### Exclusion criteria

- All cases of transudative pleural effusion (congestive cardiac failure, rheumatoid arthritis, etc.) were excluded.

- All cases of malignant pleural effusion were excluded.

**Statistical method**

Spearman’s correlation test

Students paired t-test

**Results**

**Demographic data**

Totally fifty consecutive patients with tubercular pleural effusions were studied from November 2017 to October 2018. There were 31 males and 20 females. The mean age was 40.94±18.99. The mean age among men was 43.82±18.50 and in

women was 35.43±18.97. Majority of the patients were in the age group of 50-70 years. The male to female ratio was 2:1.

**Lymphocyte/ Neutrophil ratio Individual sensitivity and specificity**

In our study, the cut-off for lymphocyte/ neutrophil ratio had been taken as >75%. The individual sensitivity of this test was found to be 93.3%, and the specificity to be 50%. The positive predictive value was 93.3%, and the accuracy rate was 88.2% (Table – 1).

**Table – 1:** L/N Ratio sensitivity and specificity.

L/N ratio		Sputum for AFB		Total
		Positive	Negative	
Positive	Count	42	3	45
	%	93.3%	50.0%	88.2%
Negative	Count	3	3	6
	%	6.7%	50.0%	11.8%
Total	Count	45	6	51
	%	100.0%	100.0%	100.0%

Sensitivity = 93.3%, Specificity = 50%, Positive predictive value = 93.3%, Negative predictive value = 50%, Accuracy rate = 88.2%, X<sup>2</sup> = 14.234, p<0.001 vhs

**Table – 2:** Adenosine Deaminase (ADA) individual sensitivity and specificity.

ADA		Sputum for AFB		Total
		Positive	Negative	
Positive	Count	41	3	44
	%	91.1%	50.0%	86.3%
Negative	Count	4	3	7
	%	8.9%	50.0%	13.7%
Total	Count	45	6	51
	%	100.0%	100.0%	100.0%

X<sup>2</sup>=7.556 p<0.-001 vhs

**Table – 3:** Combined sensitivity and specificity.

Combined		Sputum for AFB		Total
		Positive	Negative	
Positive	Count	44	2	46
	%	97.8%	33.3%	90.2%
Negative	Count	1	4	5
	%	2.2%	66.7%	9.8%
Total	Count	45	6	51
	%	100.0%	100.0%	100.0%

Sensitivity = 97.8%, Specificity = 66.7%, Positive predictive value = 95.7%, Negative predictive value = 80%, Accuracy rate = 94.2%, X<sup>2</sup> = 24.864, p<0.001 vhs

### **ADA value individual sensitivity and specificity**

In our study, the cut-off values for the same were taken as 50 IU/ML. When taken alone, the individual sensitivity was 91.1% and the specificity was 50% as shown in the **Table – 2** (P value = <0.001).

### **Combined sensitivity and specificity taking together ADA and lymphocyte/ neutrophil ratio**

In our study, the combined sensitivity and specificity had been increased when we had considered ADA and L/N ratio together. The overall sensitivity had increased to 97.8%, and the specificity to 66.7%. The positive predictive value 95.7% and the accuracy rate was 94.2 (**Table – 3**).

### **Discussion**

In India, Tuberculous effusion is most common cause of exudative pleural effusion. This is similar to observation in another study from India Maldhure, et al. [1] where they showed that tubercular effusion constitute 66% and malignancy 15% of all exudative pleural effusion. This is consistent with the finding that India has a high prevalence of tuberculosis in general population. In this study, out of 50 patients with Tubercular pleural effusion, 60 percent were males and 40% were females which is comparable to the study conducted by Bijayak Behara, et al. [11]. The most common symptom experienced by our tuberculosis patients were fever 80%, cough 96% and pleuritic chest pain 70%. These findings are consistent with the studies done earlier by Moudgil, et al. [5]. This was also agreeable with the findings of study conducted by Maher GG, Berger JW, et al. [8], 96% of TB effusion had lymphocyte predominance. Our results are similar to the study done by Valdes, et al. [6] where they have also encountered lymphocyte predominance and neutrophil predominance in only 6.7% of TB effusion.

When we applied cut off of ADA 50IU/L the sensitivity for diagnosis of tubercular effusion is 92.98% , the specificity is 50.80%, PPV 91.38% and NPV 90% with accuracy of 83-98.05%, by applying Fischer Exact test, the test was statistically significant at  $p < 0.05$ .

Here we obtained a sensitivity of 92.98% and specificity of 50.80% in our study. This is more consistent with observation by S K Sharma, et al. [7] from AIIMS New Delhi where the sensitivity and specificity at ADA level of 35IU/l was 83% and 66% respectively. This was again supported by the study done by Behera, et al. [11], in which they found that the mean ADA value was 42.5U/Land the sensitivity of it alone in determination of pleural effusion was 91.4%. When we used pleural fluid ADA with L:N ratio >75% we found that there is increase in sensitivity and specificity in diagnosis of tubercular pleural effusion. When ADA more than 50 IU/ml was considered, the individual sensitivity was 91.1% and the specificity was 50%.

In our study, we aimed at combining L/N ratio and ADA in combination for diagnosis of tubercular pleural effusion, which will substantially raise the sensitivity and specificity which is consistent with the work done by Ramaswamy Suresh, et al. [10].

The study done showed that the sensitivity of taking the lymphocyte by neutrophil ratio alone in determining tubercular pleural effusion was 93.3% and the specificity was 50%. Similarly, when taking in account of Adenosine deaminase (ADA), alone the sensitivity was 91.1%, and the specificity was 50% [9]. But when we take both these parameters together, the sensitivity and specificity will increase significantly, sensitivity 97.8% and the specificity 66.7%, Positive predictive value of 95.7%, accuracy rate of 94.2%, P value <0.001.

### **Conclusion**

Tuberculosis which is a commonly encountered disease entity in our country, the need for early diagnosis and treatment has shown to cut-down mortality and morbidity significantly. The need for quick and cheap diagnostic tests are needed and in our study it was found that the combination of L/N ratio and ADA when combined together has significantly increased the sensitivity and specificity of diagnosing the disease.

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