

Original Research Article


To study the combined use of pleural fluid lymphocyte/ neutrophil ratio and ADA for the diagnosis of tuberculous pleural effusion

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	International Archives of Integrated Medicine, Vol. 4, Issue 9, September, 2017. Copy right © 2017, IAIM, All Rights Reserved. Available online at http://iaimjournal.com/ ISSN: 2394-0026 (P) ISSN: 2394-0034 (O)	
	Received on: 30-07-2017	Accepted on: 12-08-2017
	Source of support: Nil	Conflict of interest: None declared.
How to cite this article: Ramasamy Suresh, Victor Theophilus Premkumar. To study the combined use of pleural fluid lymphocyte/ neutrophil ratio and ADA for the diagnosis of tuberculous pleural effusion. IAIM, 2017; 4(9): 1-5.		

Abstract

Background: Pulmonary tuberculosis is the most frequent cause of death by an infectious agent worldwide. Among the extra pulmonary presentations after tuberculous lymphadenitis, pleural TB is the second most frequent 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. Hence, this study was aimed to determine whether combined use of pleural fluid lymphocyte neutrophil ratio and ADA activity would provide a more efficient means for diagnosing tuberculous pleurisy than the use of ADA levels.

Aim: To determine whether the combined use of ADA activity and lymphocyte/neutrophil ratio would provide a more efficient means for diagnosing tuberculous pleural effusion than with the use of ADA alone.

Materials and methods: Present study was hospital based prospective observational study carried out from February 2016 to July 2016. All the patients with pleural effusion admitted in medical ward at GRH Madurai. Information collected through preformed and pretested proforma. The qualifying patients were undergoing detail history, clinical examination and investigation. Patients were classified as exudative and transudative pleural effusion based on light's criteria Patients with MRS score of 5 and 6 were declared as very poor outcome and MRS of 3 and 4 as poor outcome. Patients

with MRS 0, and 1 were considered as good outcome. Statistical analysis was done by One way ANOVA, Pearson correlation and Chi square test.

Results: There was significant correlation between the combined use of ADA along with L/N ratio than ADA alone for diagnosing tuberculous Pleural effusion.

Conclusions: The combined use of ADA along with L/N ratio would provide a more efficient means for diagnosing tuberculous Pleural effusion than the use of ADA alone.

Key words

Pleural effusion, ADA, Lymphocyte neutrophil ratio.

Introduction

Pulmonary tuberculosis is the most frequent cause of death by an infectious agent worldwide. Among the extra pulmonary presentations after tuberculous lymphadenitis, pleural TB is the second most frequent 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 [1].

Conventional methods have proven to be insufficient for diagnosis of pleural TB. Direct examination of pleural fluid is inefficient because sensitivity is about 1% [2]. 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], as raised levels are also associated with a number of other diseases including malignancies (especially those of hematologic origin), bacterial infections (Q-fever, brucellosis), empyemas, and 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 [4].

Hence this study is aimed to determine whether combined use of pleural fluid lymphocyte neutrophil ratio and ADA activity [5] would provide a more efficient means for diagnosing tuberculous pleurisy than the use of ADA levels.

Pleural effusion is a very common clinical presentation of diseases. A correct diagnosis of the underlying disease is essential for the management of pleural effusion. A limited number of diseases causes transudative pleural effusions [6, 7], whereas exudative effusions require more extensive diagnostic investigations. Therefore, the first step is to classify them as transudates or exudates, even if this differentiation does not contribute to the etiological diagnosis.

Many criteria have been used to distinguish them, but none of them have been found to be satisfactory. Light's criteria is the most commonly used method. The criteria are one or more of the following for diagnosing exudates.

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

It was found that even Light's criteria misclassified a large number of effusions, 25% of transudates as exudates.

Materials and methods

Study Population

Patients diagnosed as having pleural effusion on the basis of clinical feature and chest radiography

in Government Rajaji Hospital, Madurai over a period of six months were chosen for the study.

Inclusion criteria

All exudative pleural effusion cases.

Exclusion criteria

- Patients with transudative pleural effusion.
- Patients with malignant pleural effusion.
- Patients with immuno deficient states like HIV, those on chemotherapy were excluded.

Ethical Committee Approval: Obtained.

Study protocol

The study was conducted on 50 patients with pleural effusion admitted in medical ward GRH Madurai. Patients will be classified as exudative and transudative pleural effusions based on Light's criteria. All the exudative pleural effusion cases were studied. Pleural fluid adenosine deaminase levels of $> 50\text{U/L}$ [8] were considered as positive for tuberculous pleural effusion. Pleural fluid Lymphocyte /neutrophil ratio >0.75 were taken as positive for tuberculous pleural effusion. Patients were treated with antitubercular therapy based on clinical features and pleural fluid analysis and followed up.

The sensitivity, specificity, positive predictive value, negative predictive value for pleural fluid ADA $>50\text{ U/L}$ alone and combined pleural fluid ADA and lymphocyte neutrophil ratio of >0.75 were calculated and compared using student t-test. History, physical examination and lab investigations like Hb, LFT, ADA, LDH were done.

Statistical analysis

Mean and standard deviation for continuous variables and proportions for categorical variables are reported. Ada alone, L/N and ADA values were the combined with various L/N ratios by calculating sensitivity, specificity, PPV, NPV and efficiency. An interactive dot diagram

was used for cut-off points and plot versus criteria values graph used. SPSS version 16.0 was used for statistical analysis.

Results

In this study, 50% of patients were between 40 60 years of age. Only 20% of them were above 60 years of age. Tuberculous pleural effusion was more common in males (64%) and more common in smokers (56%).

Use of ADA alone was positive in 34 patients of tuberculous effusion. Only 6 patients of TB effusion were ADA negative (**Table – 1**).

Lymphocyte/neutrophil ratio was positive in 40 patients of tuberculous effusion.

Combined use of ADA and lymphocyte/ neutrophil ratio was positive in 34 patients of TB effusion.

Combined use of ADA and L/N ratio has increased sensitivity, specificity, positive predictive value and negative predictive value and increased efficiency (**Table – 2**).

Table – 1: ADA alone (n=50).

ADA alone (U/L)	TB pleural effusion	Non-TB pleural effusion	Total
>50	34	6	40
<50	6	4	10
Total	40	10	50

Table – 2: Combined ADA and L/N ratio (n=50).

ADA and L/N ratio	TB pleural effusion	Non-TB pleural effusion	Total
>50 and >0.75	34	2	36
<50 and <0.75	–	11	11
Total	34	13	47

Discussion

Increased ADA activity in pleural effusion [9] is classically associated with tuberculosis. However it may occur due to a number of causes and this may negatively affect the diagnostic utility of ADA measurements and decrease its specificity in the diagnosis of TB [2]. 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 [3]. When the L/N ratio's was considered together with ADA activity, the results improved considerably for the diagnosis of tuberculosis pleuritis [4]. Pleural fluid lymphocytes is also found in malignant conditions, collagen vascular disease, heumaticpleuritis, sarcodosis and up to o third of all transudates. Parapneumonic and empyematous effusions are characterised by neutrophil-predominant, exudative effusions. In the cases and 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 [10].

TB pleurisy is traditionally diagnosed by either identification of M tuberculosis in pleural fluid and/or biopsy specimen cultures or from the presence granulomas in the pleural biopsy tissue [11]. Pleural fluid cultures have sensitivity of 20-30%, pleural biopsy specimen 50-80%, depending upon the clinician's proficiency. Because of the long culture periods required, clinical and therapeutic decisions are often made before the lab results become available. Polymerase chain reaction, having a sensitivity of 78% for active disease, has not been found to be an efficient alternative.

Conclusion

In conclusion, it is suggested that the combined use of adenosine deaminase activity [12] along with lymphocyte neutrophil ratio would provide a more efficient means for diagnosing tuberculosis pleuritis [13] than ADA alone [14].

Acknowledgements

We express our sincere thanks and gratitude to the Dean, Government Rajaji Hospital and Madurai Medical College for permitting us to conduct this study. We express our deep sense of gratitude to HOD of respiratory medicine and biochemistry for their support in the study.

We are extremely grateful to all our Assistant Professors and PG Residents of Department of Medicine for their constant source of cheer and encouragement throughout the study. We thank all our patients who have formed the backbone of my study, without them this work would not have been possible. We are also thankful to paramedical staff of all departments for their concern.

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