



ORIGINAL RESEARCH PAPER

Pathology

DIAGNOSTIC SIGNIFICANCE OF ADENOSINE DEAMINASE AND LYMPHOCYTES IN SUSPECTED TUBERCULOUS PLEURAL EFFUSION

KEY WORDS: Adenosine deaminase, Biomarker, Diagnostic accuracy, Tuberculous pleural effusion.

Radhika T M	Junior Resident, Basaveshwara Medical College and Hospital, Chitradurga.
Narayana Murthy C*	Head of the Department and Professor, Basaveshwara Medical College and Hospital, Chitradurga. *Corresponding Author
Ruhi salma Naagar	Assistant professor, Basaveshwara Medical College and Hospital, Chitradurga.

ABSTRACT

CONTEXT: Tuberculosis is a major public health problem in India. Tuberculous pleural effusion is a paucibacillary manifestation of the Tuberculosis, so isolation of Mycobacterium tuberculosis is difficult, biomarkers being an alternative for diagnosis. Pleural fluid Adenosine deaminase (ADA) level is being used in diagnosis of Tubercular pleural effusion. The combination of ADA and pleural fluid lymphocyte count is being recognized as a better method for increasing the specificity of ADA test. **AIM:** The present study was conducted to analyze the diagnostic usefulness of ADA alone ($\geq 40U/L$) compared with the combination of ADA and pleural fluid lymphocyte count ($\geq 50\%$). **SETTINGS AND DESIGN:** Retrospective study. **METHODS AND MATERIAL:** Study was conducted for a period of one year from May 2017 to April 2018. A total of 110 pleural fluid samples data was analysed. **STATISTICAL ANALYSIS USED:** SPSS 20 statistical software. **RESULTS:** ADA level in Tuberculous pleural effusion ranged from 40U/L to 112U/L with mean value of 69.4U/L. Sensitivity, Specificity, Positive predictive value (PPV) and Negative predictive values (NPV) for ADA alone were 93.2%, 76.4%, 82% and 90.6% respectively. For ADA and lymphocyte count the Specificity and PPV increased (98% and 98.1% respectively) with hardly any decrease in sensitivity or NPV (89.8% and 89.5% respectively). **CONCLUSION:** Combined use of ADA and pleural fluid lymphocyte count increases the specificity and PPV when compared to the specificity of ADA test alone in diagnosing Tubercular pleural effusion.

INTRODUCTION:

Tubercular pleural effusion (TPE) accounts 30-60% of pleural effusion worldwide.^[1] TPE is paucibacillary manifestation, Acid fast bacilli seen on smears in 10-25%, cultures are positive in 25-75% cases. Adenosine deaminase concentration in pleural fluid is useful screening test. Tuberculosis can be ruled out when ADA values are low. The specificity of the ADA test can be increased with pleural fluid lymphocyte count which helps to avoid the invasive procedures.^[2-10]

AIMS AND OBJECTIVES

The present study was conducted to analyse the diagnostic usefulness of ADA ($\geq 40U/L$) and compared with the combination of ADA ($\geq 40U/L$) and pleural fluid lymphocyte count ($\geq 50\%$ of total count).

SUBJECTS AND METHODS

Retrospective study was conducted from May 2017 to April 2018 in our Tertiary care centre. A total number of 110 pleural fluid samples data was collected and analysed. A detailed clinical history and pleural fluid data which includes Total pleural fluid leukocyte count, Differential count, Protein, Glucose and ADA level were analysed. Radiological, Sputum analysis and Culture report were also analysed where ever feasible. A cut off value of ADA level ($\geq 40U/L$) and pleural fluid lymphocyte count $\geq 50\%$ of total count was taken for diagnosing Tubercular pleural effusion.

RESULTS

The present study had 59 cases (53.6%) pleural effusion of tubercular and 51 cases (46.3%) non- tubercular pleural effusion.

Table I: Pleural Fluid ADA Levels In Tuberculous And Non Tuberculous Pleural Effusion:

VARIABLES	ADA $\geq 40U/L$	ADA $< 40U/L$	TOTAL NUMBER OF CASES
TUBERCULAR PLEURAL EFFUSION	55	4	59

NON TUBERCULAR PLEURAL EFFUSION	12	39	51
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Table II: Pleural Fluid Lymphocyte Count In Tuberculous And Non Tuberculous Pleural Effusion:

Variables	Pleural fluid lymphocyte count $\geq 50\%$ of total count	Pleural fluid lymphocyte count $< 50\%$ of total count	Total number of cases
Tubercular pleural effusion	58	1	59
Non tubercular pleural effusion	17	34	51

Table III: Usefulness Of ADA Alone Compared With Combination Of ADA And Pleural Fluid Lymphocyte Count In Tuberculous And Non Tuberculous Pleural Effusion:

VARIABLES	ADA $> 40U/L$	ADA $> 40U/L$ Lymphocytes $> 50\%$
TUBERCULAR PLEURAL EFFUSION	55/59	53/59
NON-TUBERCULAR PLEURAL EFFUSION	12/51	01/51

Table IV: Comparison Of Sensitivity, Specificity, PPV And NPV Of ADA Alone And Combination Of Both ADA And Pleural Fluid Lymphocyte Count:

VARIABLES	ADA	ADA AND PLEURAL FLUID LYMPHOCYTE COUNT
SENSITIVITY	93.2 %	89.8%
SPECIFICITY	76.4%	98%
PPV	82%	98.1%
NPV	90.6%	89.5%
P VALUE: 0.03%.		

DISCUSSION

Tuberculosis is the commonest cause of exudative pleural effusion in India.⁽¹¹⁾ Tubercular pleural effusion is a

paucibacillary manifestation which is resultant of delayed type hypersensitivity to Tubercular bacillary protein.^[12,13]

Adenosine deaminase (ADA) is an enzyme involved in the purine metabolism, catalysis adenosine to inosine. ADA has two isoforms: ADA 1 and ADA 2. ADA 1 is ubiquitous and ADA 2 is present in monocytes and macrophages. Tubercular pleural effusion has ADA 2 isoform. ADA helps in the proliferation and maturation of T lymphocytes. It is also involved in transformation of monocyte to macrophage. Tubercle bacilli stimulate T lymphocytes, which leads to increase ADA concentration in pleural effusion.^[14-19]

The biomarker ADA test has high sensitivity 92% and specificity 89% can be used for early diagnosis extrapulmonary tuberculosis like Tuberculous pleuritis, pericarditis, ascitis and meningitis.^[20]

The present study had male predominance compared to females. Out of 110 cases, 69 cases (62.7%) were males and 41 cases (37.3%) were females. A study conducted by Modi SD had male predominance.^[21]

In the present study, total of 110 cases of pleural effusion were analysed and diagnosed as 59 cases of tubercular pleural effusion and 51 cases of non-tubercular pleural effusion.

In the present study, among 59 cases of tubercular pleural effusion 55 cases (93.2%) had ADA level above >40U/L which correlates with the conclusion by Castro et al and Pande K et al.^[23] Castro et al stated that ADA level <40U/L excludes TPE in lymphocyte predominant effusion. Four cases of Tubercular pleural effusion had ADA level <40U/L, out of four cases, three patients belongs to elderly age group. A review article by Vorster MJ et al had stated that low ADA level is seen in elderly patients and smokers with Tuberculous pleural effusion.^[18]

In the present study, ADA level in Tuberculous Pleural effusion ranged from 40 U/L to 112 U/L with mean value of 69.4 U/L. The mean value ADA level in non-Tuberculous effusion was 44.86U/L which was lower than the tuberculous pleural effusion. A study by Khowean N et al had mean value of ADA in tubercular effusion was 38.17 and in non-tubercular effusion was 14.83 which was lower than the tubercular effusion.^[9] A study by Modi et al had mean ADA value in TPE was 85.09 and in Parapneumonic effusion was 51.2IU/L.^[21]

A study by Mathur PC et al had sensitivity and negative predictive value of 100% for ADA test which almost correlates with the present study.^[8]

In the present study, among 59 cases of Tubercular pleural effusion, 58 cases had Pleural fluid lymphocyte count \geq 50% and one case had <50% of total count. Among 51 cases of Non-tubercular pleural effusion, 17 cases showed Pleural fluid lymphocyte count \geq 50% and 34 cases had <50%. More than 50% of lymphocytes in pleural effusion can be seen in malignancy, cardiac failure, lymphoma, chronic rheumatoid pleurisy, sarcoidosis and late post coronary artery bypass graft surgery effusions.^[22-27]

In the present study, the specificity and positive predictive value of ADA alone was 76.4% and 82%, which increased to 98% and 98.1% respectively with addition of pleural fluid lymphocyte counts with hardly any effect on sensitivity and negative predictive value.

A study by Zamalloa et al had specificity and PPV of ADA was 92.7% and 69.2% respectively which increased to 98.3% and 90% with pleural fluid lymphocyte counts which was well correlated with the present study.^[15]

A study by Pande K et al had specificity and PPV of ADA was 92% and 80% respectively which increased to 87% and 83%

with increase in NPV of 100% with pleural fluid lymphocyte counts.^[23] A study by Mathur PC et al had sensitivity and negative predictive value of 100% for ADA test which almost correlates with the present study.^[8]

High ADA level in lymphocytic pleural effusion is also seen in Rheumatoid arthritis, lymphoma, Broncho-alveolar carcinoma, mesothelioma and SLE. In present study one case of non TPE showed malignant cells.^[28,29]

CONCLUSION:

The use of adenosine deaminase biomarker along with the pleural fluid lymphocyte count is more specific in diagnosing suspected tubercular pleural effusion cases. ADA test offers simple, easy, reliable and cost effective diagnostic tool for Tubercular Pleural Effusion.

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