Review Article

Diagnostic Value of Adenosine Deaminase Activity in Detection of Tuberculous Pleural Effusion

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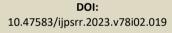***Corresponding author's E-mail:** vyankatesha78@gmail.com

ABSTRACT

Pleural effusion is very well known complication of pulmonary tuberculosis. There are several medical diseases like anaemia, hypo-proteinemia, chronic renal disease, chronic heart disease; liver cirrhosis etc. develops transudative pleural effusion. The common diseases like pneumonia, lung malignancy, tuberculosis etc. gives rise to exudative pleural effusion. In spite of the success in treatment modalities in past many decades, tuberculosis (TB) is still the leading cause of death for infectious disease in the world. The confirmative diagnosis of pulmonary tuberculosis is made via the identification of M. tuberculosis bacilli in sputum, pleural fluid, or pleural biopsy specimens. However, these traditional diagnostic methods have low accuracy for the diagnosis of TB. The elevated levels of adenosine deaminase (ADA) in pleural fluid have been shown to be useful in the diagnosis of TB. In the present study, accuracy of Adenosine deaminase (ADA) for detection of tuberculous pleural effusion was analyzed. The 100 pleural effusion cases were included in the study. The TB cases and non - tuberculous pleural effusion etiological diseases like pneumonia, lung malignancy, anaemia, hypo-proteinemia, chronic renal disease and chronic heart disease were confirmed with clinical history along with laboratory and radiological investigations. Out of 100 cases, 62 cases were tuberculous pleural effusion. The accuracy of ADA for detection of tuberculous pleural effusion was 96 % with cut off of 40 IU/L. Hence, present study concluded that ADA level detection is simple, reliable, cheap, single test, rapid diagnostic modality for diagnosis of tuberculous pleural effusion.

Keywords: Adenosine deaminase (ADA), TB, pleural effusion.

INTRODUCTION

Tuberculosis (TB) is still major cause of morbidity and mortality in the world. As per World Health Organization (WHO) India, China and India contributes to one quarter burden of TB in the world. Tuberculous pleural effusion is one of the common manifestations of extra pulmonary TB, with or without pulmonary TB.[1]

The diagnosis of tuberculous Pleural effusion is done by conformation of TB bacilli in pleural fluid or histopathology findings of TB in pleural biopsy specimen.[2] The confirmation of TB in pleural effusion is diagnostic challenge, in view of, low accuracy of microbiological investigations, for TB confirmation rates with pleural fluid analysis.[3, 4] The recent diagnostic methods like polymerase chain reaction-based techniques and rapid molecular tests also have suboptimal diagnostic accuracy. The low sensitivity of conventional traditional methods delays the diagnosis and management of TB. [5] With the evolution of multidrug resistance, in addition to the high rates of co-infection like HIV, there has been a need of simple, reliable, rapid, cost effective diagnostic test, for early detection of tuberculous pleural effusion.

Piras et al. first observed about elevated levels of ADA in pulmonary TB. [6] Several authors confirmed and supported his findings. [7, 8] The ADA level with cut off 40 U/L found to be having maximum accuracy for detection of TB. However, some studies showed that ADA is not that much useful, for differentiation of tuberculous and non tuberculous pleural effusion.[9, 10] The present study was done to analyze accuracy of pleural fluid ADA level for TB detection.

MATERIALS AND METHODS

The study was conducted in tertiary care hospital central laboratory for the period from January 2022 to June 2022.

Pleural fluid analysis: The pleural fluids received in the laboratory were analyzed for biochemical tests like protein, albumin, sugar, LFT, RFT, lipid profile long with ADA level. For malignancy cases, cytology for malignant cells was done. The case was labeled as TB case, when one of the following criteria was fulfilled by said case. 1. Microbiological confirmation of TB with pleural fluid or lung/ lymph node biopsy or sputum specimen with Ziehl-Neelsen stain and culture 2. Histopathology confirmation of TB for biopsy sample 3. Clinical history, radiology investigations confirming diagnosis of TB

The cases were labeled as anemia, chronic heart failure (CHF), chronic renal failure (CRF), Liver cirrhosis, pneumonia, malignancy as per the clinical history and investigations.

As described by Guisti, ADA level estimation done by colorimetric method. [11] ADA level cut off of more than 40 IU/ L were utilized to label the case as tuberculous exudates. Statistical analyses were done with the SPSS software and ADA level accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) was analyzed for detection of tuberculous pleural effusion.

RESULTS AND DISCUSSION

Out of 100 pleural effusion samples, 66 were from male and 34 from female patients and their age ranges from 19 to 76 years. As per etiology, total 62 were tuberculous and 38 were non-tuberculous pleural effusion. The causes of

non- tubercular effusions were pneumonia, malignancy, anaemia, chronic heart failure (CHF), chronic renal failure (CRF), Cirrhosis. (Table 1)

Table 1: Etiological distribution of pleural effusion

Disease	Number of cases (n)
Tuberculosis	62
Pneumonia	04
Malignancy	03
Anaemia	10
CHF	03
CRF	05
Cirrhosis	13
Total	100

Table 2: ADA test evaluation for tuberculous and non- tuberculous pleural effusion

	Tuberculous effusion	Non- tuberculous effusion	Total	Predictive value (PV)
ADA Positive	59	01	60	**PPV (98.33 %)**
ADA Negative	03	37	40	**NPV (92.5 %)**
Total	62	38	100	
	Sensitivity (95.16 %)	**Specificity (97.36 %)**	**Accuracy (96 %)**	

With ADA cut off level 40 IU/L, the evaluation of ADA activity was done for all 100 pleural effusion samples. ADA level 40 IU/L and above were considered as ADA positive and ADA level less than 40 IU/L were considered as ADA negative. (Table 2)

Out of 62 cases of tuberculous effusion, 59 cases showed ADA level more than 40 IU/ L and 3 cases showed ADA level less than 40 IU/L. Out of 38 non- tuberculous effusions, one malignancy case showed ADA fluid level more than 40 IU/L. Hence, with the cut of 40 IU/L, the ADA showed Sensitivity, Specificity, Accuracy, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of 95.16 %, 97.36 %, 96 %, 98.33 % and 92.5 % respectively. (Table 2)

Adenosine deaminase (ADA) is a zinc-containing metalloenzyme and is expressed in high levels by lymphocytes and monocytes and hence, it is elevated in pulmonary TB. It was first observed by Piras et al.[6] The rupture of sub pleural foci of TB lesion leads to development of pleural TB. The TB antigens activate macrophages which releases ADA in pleural fluid. Hence, the tuberculous pleural fluids have higher level of ADA, as compared to ADA level increase in pleural fluid, due to other diseases. In the present study, we found the accuracy of ADA level for TB detection in pleural fluid was 96 %. Similar type of ADA level high accuracy rate was found by Diacon HA et al [11] and Chen et al[12] for TB detection in pleural fluid.

In the conditions like empyema and malignancy, the large numbered proliferated neutrophils and lymphocytes may increase ADA level in pleural effusion and results to false positivity. [13] In the present study, we found that, out of 3 malignancy cases, one malignancy case showed the ADA level of more than 40 IU/L in pleural fluid and resulted into false positivity. Similar type of findings were reported by Zemlin et al.[8]

The ADA cut off is used from 30 IU/L to 50 IU/L in many studies. In the studies done by Lewinsohn DM et al and Aggarwal AN et al showed that ADA in pleural fluid (with a cutoff of 40 U/L) gave sensitivity and specificity values above 86%, as well as predictive values above 88% for TB diagnosis in pleural fluid.[14, 15] Hence, in the present study, the cut off of 40 IU/L was utilized to increase the accuracy of ADA level for TB detection in pleural fluid.

The present study has following limitations. As per Verma SK et al, the determination of ADA is more sensitive than histopathology (HP) examination of pleural tissue for diagnosis of TB. [16] In the present study, HP of lung/ pleural biopsy was not available for all cases and hence, comparison between these diagnostic modalities was not done.

Mishra OP et al and Wu YH et al presented that ADA measurement do not gave promising results for TB detection in pediatric patients. [9, 10] In the present study, all patients were adults. Hence, comparison of ADA level accuracy, in adults and pediatrics patients for TB diagnosis,

was not possible in this study. Fischer GB et al states that in cases of suspected false-negative or false-positive results measurement of ADA isoenzymes ADA1 and ADA2 is helpful. The said isoenzymes measurement is not done in this study.

CONCLUSION

The measurement of pleural fluid ADA (cut off 40 IU/L) is an excellent tool with good diagnostic accuracy, to confirm a tubercular etiology of pleural effusion. Because of good precision rate, it is recommended for its continued use as a rapid diagnostic modality of tuberculous pleural effusion, in a middle and low income country having high TB/HIV burden. It is suggested that all the cases of pleural effusion, should be screened to exclude tuberculosis with simple, reliable, cost effective pleural fluid ADA measurement test.

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