Original article:

Adenosine DeaminaseLevels as a Tool for the Diagnosis of Tuberculous Pleural Effusion: A Cross-Sectional Study

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Abstract

Introduction: Tuberculous pleural effusion (TPE) is a common manifestation of extrapulmonary tuberculosis, and is the leading cause of pleural effusion in developing world regions, while it is much less common in developed countries.The aim of the study is to determine that the Adenosine Deaminase levels can use as a tool for the diagnosis of tubercular pleural effusion.

Materials and Methods: This cross-sectional study was conducted in one hundred ten cases of pleural effusion, in which seventy one cases were tubercular pleural effusion and thirty nine cases were non tubercular pleural effusion. A p-value < 0.05 was considered statistically significant. IBM SPSS Statistics 21 manufactured by IBM USA was used for entire calculations.

Result: In the present study the mean of ADA level was 173.3, LDH level was 184.91, T. Protein was 4.80, Glucose was 112.34 and the total cell count was 3996 in tuberculosis pleural effusion group. These variables are statistically significant (<0.05). This study has clearly shown that ADA levels are significantly high in patients with tubercular pleural effusion (173.3±34.93 U/L) compared to that (20.46±7.34 U/L) in non tuberculous group.

Conclusion: This study has clearly shown that ADA levels are significantly high in patients with tubercular pleural effusion compared to that in non tuberculous group.

Keywords: Tuberculous pleural effusion, Adenosine Deaminase, LDH.

Introduction

Adenosine deaminase (ADA) is an enzyme which catalysesthe conversion of adenosine to inosine and plays animportant role in the differentiation of lymphoid cells. activity is high in diseases in which cellular immunity is stimulated.[1] Different cut off values of ADA ranging from 30–100 IU/L have been used in various studies, with differing sensitivities and specificities.[2]

Tuberculous pleural effusion (TPE) is a common manifestation of extrapulmonary tuberculosis, and is the leading cause of pleural effusion in developing world regions, while it is much less common in developed countries.[3-5]The diagnosis of pleural TB is still challenging in clinical practice. The diagnosis of TPE depends on the demonstration of tubercle bacilli in pleural fluid, a pleural biopsy specimen or sputum, or the demonstration of granulomas in the pleura.[6] Due to the paucity of Mycobacterium tuberculosis in the pleural fluid, the performance of a pleural biopsy has historically been considered the most reliablemethod to confirm the diagnosis when tuberculousaetiology of a pleural effusion is suspected. However, since pleural tissue sampling is more difficult than simple thoracocentesis, pleuralfluid markers of TPE have been extensively

evaluated as an attractive alternative to pleural biopsy.[7] ADA is the most cost effective pleural fluid marker and is routinely employed as ascreening tool, in particular, in countries where tuberculosis is endemic.[3]

Recent estimates show that around 8-10 million new tuberculosis cases occur each year in theworld and 2-3 million die.[8] In developing countries, TB is one of thecommon opportunistic infections in people who are seropositive forhuman immunodeficiency virus (HIV).[9] Tuberculosis is classifiedas pulmonary, extrapulmonary, or both.[10] Pleural tuberculosis accounts for fewer than 1% of all exudative effusions in Westerncountries, occurring in only 3% to 5% of tuberculosis patientsand in developing countries like India, it is responsible for 30% to 80% of all pleural effusions encountered.[11]

Adenosine Deaminase Activity (ADA) in pleural fluid which identifies an inflammatory process triggered by MBT.[12-14]The most recent study, a metaanalysis by Lian QL and co-workers, shows a very good accuracy in measuring ADA in pleural effusion to diagnose TB pleural effusion. Nevertheless the best cutoff they found was 40 U/L given a positive likelihood (LH) of 9, 03 and negative LH ratio of 0,01 which are important values to consider.[15]

ADA is involved in the proliferation and differentiation of lymphocytes, especially T lymphocytes. [16] The increase in the ADA activity in patients with TB may indicate the cellular immune response and T lymphocyte activation in the disease.[17] T lymphocytes have ADA level 10 to 12 times higher than B lymphocytes. ADA activity varies depending on the proliferative status and maturity of cells.[18] The level of ADA is increased in TPE and this determination has acquired popularity as a diagnostic test in the high incidence area of TPE, because ADA measurement is a less expensive, minimally invasive, rapid and readily accessible test.

The main aim of the study is to determine that the Adenosine Deaminase levels can use as a tool for the diagnosis of tubercular pleural effusion.

Materials and Methods

This cross-sectional study was conducted in one hundred ten cases of pleural effusion, in which seventy one cases were tubercular pleural effusion and thirty nine cases were non tubercular pleural effusion. This study was done in department of pulmonary medicine,Smt. KashibaiNavale Medical College, Narhe, Pune, Maharashtra, India.The study protocol was approved from the ethical committee of college.Signed consent forms obtained from all the subjects included in this study. Parameters studied were total cell count, differential cell count, glucose, total proteins, lactate dehydrogenase, and adenosine deaminase.

Thoracocentesis was attempted at one inter space below the spot where tactile fremitus is lost and the percussion note becomes dull.[19] The excat location for the thoracocentesis attempt was just superior to a rib.[20,21]

Pleural fluid collect after the skin was cleaned with antiseptic solution. The sterile drape with the central hole was then taped to the patient`s back and another sterile drape was placed on the bed. Anaesthetization of the skin, the periosteum of the rib and the parietal pleura was done.[22] 20/50 ml syringe was used containing 1 ml heparin to prevent clotting of the pleural fluid. The fluid was placed in EDTA treated tubes, Pleural fluid is tested for: Total Cell count, Differential cell count, Glucose, Total proteins, Lactate dehydrogenase, and Adenosine deaminase. A p-value < 0.05 was considered statistically

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significant. IBM SPSS Statistics 21 manufactured by IBM USA was used for entire calculations.

Results

The total number of one hundred ten cases were recruited in this study in which tubercular pleural effusion cases were 64.54% and non-tubercular cases were 35.45%. Among the non-tubercular cases, 24 cases were due to malignancy, 11 were due to pneumonia, 3 cases were due to congestive cardiac failure and 1 due to rheumatoid arthritis. (Table 1, Figure 1)

Description of study of non-tuberculosis pleural effusion group and tuberculosis pleural effusion group were showed in Table 2 and 3. In the present study the mean of ADA level was 173.3, LDH level was 184.91, T. Protein was 4.80, Glucose was 112.34 and the total cell count was 3996 in tuberculosis pleural effusion group. These variables are statistically significant (<0.05). this study has clearly shown that ADA levels are significantly high in patients with tubercular pleural effusion (173.3±34.93 U/L) compared to that (20.46±7.34 U/L) in non tuberculous group.

Table 1: Distribution of study population among pleuraleffusion cases

Diagnosis	Number of cases (%)
Tuberculous pleural effusion	71 (64.54%)
Non Tuberculous pleural effusion	39 (35.45%)
Malignancy	24 (61.53%)
Neumonia	11 (28.20%)
Rheumatoid arthritis	1 (2.56%)
Congestive cardiac failure	3 (7.69%)

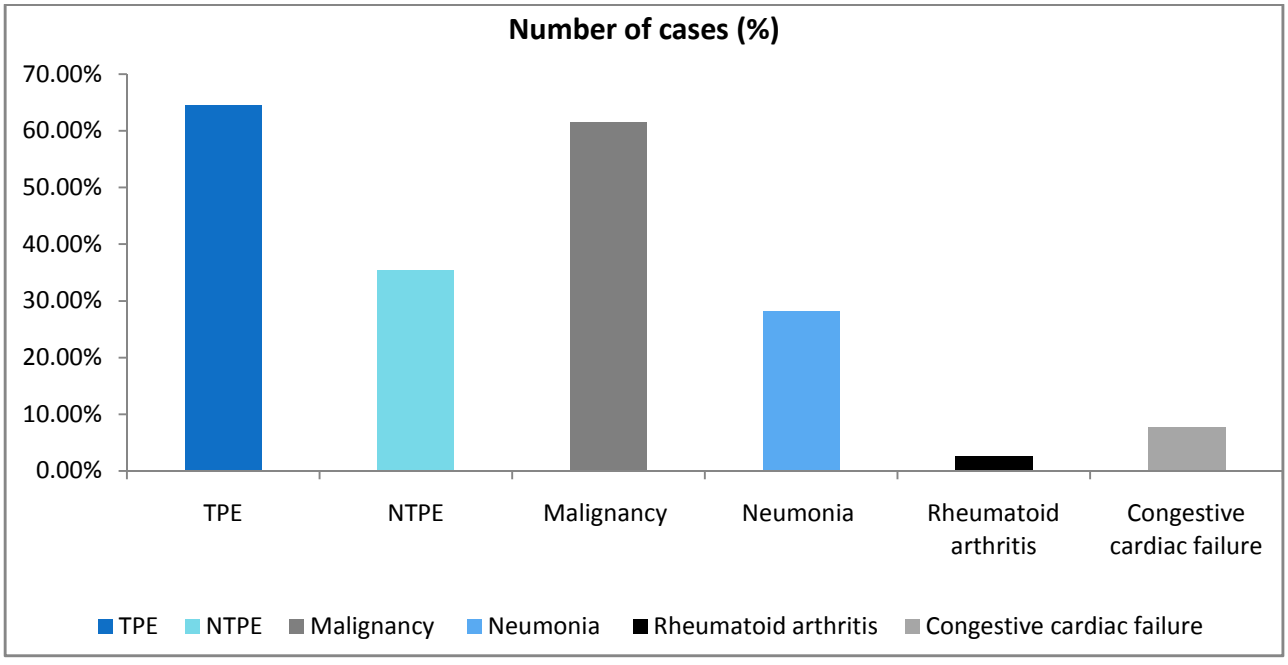

Figure 1: Distribution of study population among pleuraleffusion cases

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Table 2: Description of non-tuberculosis pleural effusion group

Variables	Mean	SEM	P value
ADA	20.46±7.34	±1.84	< 0.05
LDH	81.91±6356	±7.39	< 0.05
T. protien	3.97±0.749	±.041	< 0.05
Glucose	79.47±43.26	±9.02	< 0.05
Cell Count	4872.96±1712	-	NS

Table 3: Description of tuberculosis pleural effusion group

Variables	Mean	SEM	P value
ADA	173.3±34.93	±3.298	< 0.05
LDH	184.91±186.3	±28.94	< 0.05
T. protein	4.80±0.642	±0.1	< 0.05
Glucose	112.34±18.98	±4.026	< 0.05
Cell Count	3996±1324.67	-	<0.05

Discussion

This study has clearly shown that ADA levels are significantly high in patients with tubercular pleural effusion (173.3±34.93 U/L) compared to that (20.46±7.34 U/L) in non tuberculous group. Tubercular pleural effusion frequently represents a diagnostic problem even after extensive research.

Description of our study of non-tuberculosis pleural effusion group and tuberculosis pleural effusion group were showed in Table 2 and 3. In the present study the mean of ADA level was 173.3, LDH level was 184.91, T. Protein was 4.80, Glucose was 112.34 and the total cell count was 3996 in tuberculosis pleural effusion group.

These findings were similar to those observed in other studies.[23]However this finding is in contrast with some other studies[24] where they have found malignancy as the commonest cause of pleural effusion. Only a few cases of pleural effusion from congestive cardiac failure, rheumatoid arthritis and nephrotic syndrome were noted in the present study. Similar observations of rarity of pleural effusion by these diseases were also reported inBangladesh.[25]

Other studies also showed statistically significant elevation of dehydrogenase levels in tuberculous pleural effusion compared with non-tuberculous pleural effusion.[13,26-29] As per the results obtained the study was discussed under the following categories. Increased adenosine deaminase (ADA) enzyme levels in tuberculous pleural effusion than non tuberculous pleural effusion. Increased lactate dehydrogenase enzyme levels in tuberculous pleural effusion than non tuberculous pleural effusion .[20,30,31] There is not much of a difference in total protein levels of pleural fluid in tuberculous pleural effusion and non tuberculous pleural effusion. There is not much of a difference in glucose levels of pleural fluid of tuberculous pleural effusion and non tuberculous pleural effusion. There is not much of a difference in total count of pleural fluid - but in tuberculous pleural

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effusion there is lymphocytosis. ADAactivity values may be increased due to other clinical entities. Valdes et al.[30] have also reported high levels of ADA in patients with other causes of pleural effusions (mainly lymphomas, adenocarcinomas, systemic lupus erythematosus, and pneumonia).

Conclusion

This study has clearly shown that ADA levels are significantly high in patients with tubercular pleural effusion compared to that in non tuberculous group. The result indicated that the analysis of ADA levels in pleural effusion constitute a very useful marker for the diagnosis of TPE which, in addition, can be made quickly in a non- invasive way. So we concluded that this is very helpful test for the diagnosis of Tubercular pleural effusion.

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