Original Article

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A Cross-Sectional Study Comparing Adenosine Deaminase Levels in Pleural Effusion of Tuberculous versus Non-Tuberculous Aetiology

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Abstract

Background: Tuberculous pleural effusion (TPE) is a common condition in developing countries compared to developed countries. It is one of the most prominent characteristics of extrapulmonary tuberculosis. The enzyme Adenosine deaminase (A.D.A.) is highly active in diseases that induce cellular immunity. Therefore, the present study was designed to evaluate the accuracy of A.D.A. levels in diagnosing pleural effusion caused by tubercular etiology. **Subjects and Methods :** The study was a cross-sectional type and was conducted at the tertiary care institute from July 2019 to March 2020. A total of one hundred thirty-five patients with pleural effusion were recruited for the study. Among which eighty-nine pleural effusion patients were suffering from tuberculosis, and forty-six pleural effusion patients were without tuberculosis. A p-value < 0.05 was taken as statistically significant. For calculations, IBM SPSS Statistics 21 manufactured by I.B.M., U.S.A was used. **Results:** Findings of the present study have shown a significant difference between A.D.A. levels of tubercular effusion patients (69.3±27.22) compared to non-tubercular pleural effusion patients (20.46±7.34). Further, there was a significant difference between Lactate dehydrogenase (L.D.H.) levels of the tubercular effusion patients (172.72±25.7) in comparison to non-tubercular pleural effusion patients (81.91±6356). However, there was no significant difference between total protein (p>0.05), glucose level (p>0.05) and total cells (p>0.05) level of both the groups. **Conclusion:** From this study, it was inferred that the A.D.A. level was considerably high in pleural effusion patients with tubercular aetiology in comparison to non-tubercular pleural effusion.

Keywords: Tuberculosis, A.D.A., L.D.H.

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Introduction

Adenosine deaminase (A.D.A.) is an enzyme that is highly active in diseases that induce cellular immunity. A.D.A. catalyzes the reaction of conversion of adenosine to inosine; moreover, it is associated with the differentiation of lymphoid cells.[1] Various studies have suggested different cut-off values ranging from 30-100 IU/L for A.D.A. level.[1,2] Tuberculous pleural effusion (TPE) is a widespread condition in developing countries and a common characteristic of extrapulmonary tuberculosis.[3–5] The mycobacterium tuberculosis bacteria's detection is an important diagnostic tool for pleural tubular effusion (P.T.E.) detection. However, this an invasive process, and mycobacterium growth is too slow in the culture. Therefore, diagnosis of P.T.E. is still challenging for clinical evaluation of pleural effusion.[6]

However, pleural biopsy has been considered a promising diagnostic method for suspecting TPE in orthodox clinical practice. On the other hand, thoracocentesis is a similar yet complicated process of pleural tissue biopsy. The examination TPE can be considered an alternative of pleural therapy for confirming tubercular pleural effusion.[7] Estimation of A.D.A. level is one of the methods for screening and diagnosing tuberculous pleural effusion in patients of T.B.[8] A recent study showed that 2 to 3 million people die every year due to tuberculosis, and 10 million new tuberculosis cases are adding every year. Moreover, H.I.V. patients are more susceptible to tubercular infections.[9] In more than 70% of pleural effusion cases, T.B. has been found, this incidence has decreased up to 1% in developed countries.[10] T.B. can be classified into two types pulmonary and extrapulmonary.[11]

Mycobacterium tuberculosis stimulates the various inflammatory processes which in turn induce synthesis of A.D.A. in pleural fluid.[12–14] Lian QL et al. observed that A.D.A. was a potential marker for diagnosing tubercular pleural effusion.[15] A.D.A. has been found associated with the differentiation and proliferation of lymphocytes, especially T lymphocytes.[16] Research has noted that in a TB patient, an increased

response of the immune system and activity in T lymphocyte may consequently raise the action of A.D.[17]

It was found that the activity of A.D.A can raise up by 12 times because of T lymphocytes compared to those by L lymphocytes (which is believed to be active in mycobacterium tuberculosis infection).[18]

Therefore, this study was designed to evaluate the accuracy of A.D.A. levels in diagnosing pleural effusion caused by tubercular aetiology.

Subjects and Methods

A cross-sectional type of study was conducted at a tertiary care institute in the Department of Respiratory Medicine from July 2019 to March 2020. A total of one hundred thirty-five patients of pleural effusion were recruited for the study, among which eighty-nine pleural effusion patients were suffering from tuberculosis, and forty-six pleural effusion patients were not. The ethical committee approved this study of the tertiary care institute. Written informed consent was taken from each and every participant before they enrolled for this study.

Location: The exact location and optimal site for puncture were superior to a rib where the percussion note became dull and tactile fremitus lost.[19–21]

Procedure: Skin was sterilized with an antiseptic solution, after which one sterilized drape with a central hole was taped on the back of the subject while another drape was placed on the bed. After the anesthesia was administered, the procedures of skin, periosteum, and parietal pleura were conducted.[22] A 20/50 ml syringe with 1 ml anticoagulant was used to aspire the pleural fluid.

Pleural fluid was used to investigate the following parameters: Total Cell count (T.L.C.), Glucose level, Total proteins, A.D.A., and Lactate dehydrogenase (L.D.H.).

Statistical Analysis

All the results were presented as mean ± S.D. p-value < 0.05 was considered to be statistically significant. For calculations, IBM SPSS Statistics 21 manufactured by I.B.M. U.S.A was used.

Results

One hundred thirty-five cases of pleural effusion were recruited for this study, out of which 65.92% were tubercular pleural effusion patients and 34.07% non-tubercular cases. Further, out of forty non-tubercular effusion cases, 17.77%, 9.62%, 0.07%, and 2.22% of cases were due to malignancy, pneumonia, congestive cardiac failure, and rheumatoid arthritis respectively [Table 1].

The present study results reflect a significant difference between A.D.A. levels of tubercular effusion patients (69.3±27.22) compared to non-tubercular pleural effusion patients (20.46±7.34). Also, there was a significant difference between L.D.H. levels of the tubercular effusion patients (172.72±25.7) in comparison to non-tubercular pleural effusion patients (81.91±6356). However, there was no difference between total protein ($p>0.05$), glucose level ($p>0.05$), and total cells ($p>0.05$) level was observed in both groups [Table 2].

Discussion

Tubercular pleural effusion is still an undiagnosed condition even though there is a tremendous advancement in disease and diagnostic research. Results of the study reveal that one of the most common causes of pleural effusion were Tb (65.92%), malignancy (17.77%), and pneumonia (9.62 %). Previous research conducted by Lima D et al.[23]also noted similar findings of pleural effusion. Even Valdes et al.[21] observed that tuberculosis was the cause of about 62.8% of pleural effusions. Contrary to this finding, Reechaipichitkul W et al.[24] and Barger Wet et al.[25] found malignancy to be the most widespread cause of pleural effusion as opposed to other factors.

Further, the present study shows that there were only a few cases of pleural effusion, possibly due to other reasons, including congestive cardiac failure, rheumatoid arthritis, and pneumonia.

Recent studies show that A.D.A. is a vital tool for the diagnosis of tubercular pleural effusion.[26–28] In the present study, A.D.A. has been found significantly high ($p<0.01$) in tubercular effusion patients (69.3±27.22) in comparison to non-tubercular pleural effusion patients (20.46±7.34). The findings of the present study are very similar to the findings of the prior studies of Ungerer J.P.J. et al.[13] and Miserochi G et al.[26] Further, Leuallen EC et al.[27] and Paddock FK,[29] observed a similar significant difference A.D.A. in tubercular pleural effusion patients and non-tubercular effusion patients. Enzyme A.D.A. found elevated in pleural fluid of tuberculosis patients.[13]

However, A.D.A. found higher in pleural fluid of a patient with malignancy. It has a positive correlation with tuberculosis and can be used to diagnose pleural effusion of tubercular aetiology.[24,26,27]

L.D.H. level ($p<0.01$) was significantly high in tubercular effusion patients in comparison of non-tubercular pleural effusion patients. These findings are very similar to the findings of the previous studies of Burgess LJ et al,[20] Valdes L et al,[30] and De Oliveira HG,[31] in which they observed significantly high L.D.H. level in pleural effusion cases

Table 1: Distribution of study population among pleural effusion cases.

Diagnosis	Number of cases (%)
Tuberculous pleural effusion	89 (65.92%)
Non Tuberculous pleural effusion	46 (34.07%)
Malignancy	24 (17.77%)
Neumonia	13 (9.62%)
Rheumatoid arthritis	1 (0.07%)
Congestive cardiac failure	3 (2.22%)

Table 2: Comparison of all markers in both groups.

Variables	Tubercular pleural effusion		Non-tubercular pleural effusion		P-value
	Mean±SD	S.E.M.	Mean±SD	S.E.M	
ADA (IU/L)	69.3±27.22	±2.968	20.46±7.34	±1.84	<0.01
LDH	172.72±25.7	±5.14	81.91±6356	±7.39	NS
Total Protein	3.75±0.572	±0.5	3.89±0.62	±.061	NS
Glucose(mg/dl)	82.64±18.98	±12.026	79.47±23.27	±9.02	NS
T. cell count (/Cumm)	4012±1418.17	-	4262.96±1392	-	NS

with tubercular etiology in comparison of without tubercular etiology.

Furthermore, the results revealed that there was no significant difference in total proteins (p>0.05), glucose (p>0.05), and total cells (p>0.05) counts which is very similar to the findings of Valdes et al.[30]

Conclusion

The present study's findings showed that the A.D.A. level was significantly high in pleural effusion patients with tubercular etiology compared to non-tubercular pleural effusion.

The current study results suggest that A.D.A. level can be an essential marker for diagnosing tubercular pleural effusion. The estimation of A.D.A. level is rapid, minimally invasive, and above all economical for diagnosing tubercular pleural effusion.

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