Original Article

Study Of Correlation of Lymphocytes and ADA Levels in Suspected Cases of Bilateral Tubercular Pleural Effusion

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Abstract

Introduction: Pleural effusion is a prevalent medical disorder for which there are numerous potential causes. The causes of neutrophililic predominate exudative effusions are acute processes, such as acute pulmonary embolism or pneumonia, but the differential diagnosis for lymphocytic effusions is far lengthier. Nonetheless, malignancy and pleural tuberculosis are the most common causes of a lymphocytic pleural effusion in regions with a high TB incidence.

Objectives of the study: to determine the lymphocyte counts and ADA levels in patients with suspected bilateral tubercular pleural effusion.

Methodology: We included a total of 120 patients with and without bilateral tubercular pleural effusion. Patients with TPE are grouped as cases [TPE group], and patients without tubercular effusion as controls [Non TPE]. We had a total of 72 patients in Non TPE and 48 in TPE group.
Pleural fluid was collected in all the patients for biochemical analysis and cell counts. The biochemical investigations included total protein, albumin, glucose and ADA estimation.

Results and Conclusion: In the present study, we found statistically significantly elevated levels of ADA in TPE compared to Non TPE. Lymphocyte counts were elevated in both the groups but in the TPE group the association between ADA levels and lymphocytes counts was not statistically significant.

Key-words: tubercular pleural effusion, non-tubercular pleural effusion, lymphocytes, adenosine deaminase.

INTRODUCTION

Pleural effusion is a prevalent medical disorder for which there are numerous potential causes. The causes of neutrophillic predominate exudative effusions are acute processes, such as acute pulmonary embolism or pneumonia [1], but the differential diagnosis for lymphocytic effusions is

far lengthier [2]. Nonetheless, malignancy and pleural tuberculosis are the most common causes of a lymphocytic pleural effusion in regions with a high TB incidence [3, 4].
A closed pleural biopsy and pleural fluid analysis are essential components of the investigative work up of an exudative pleural effusion. Mycobacteria from pleural fluid cultures had a low yield of about 36% when used to diagnose tuberculous pleural effusions (TPE) [5]. Pleural biopsy is a relatively invasive procedure and involves a longwaiting time for mycobacteria culture results. Pleural fluid adenosine deaminase (ADA) has thus become an importantdiagnostic tool in the evaluation of exudative pleuraleffusions because it is inexpensive, rapid and has a high accuracywith sensitivity and specificity of up to 100% and %respectively for diagnosis of TPE [6].Mycobacteria from pleural fluid cultures had a low yield of about 36% when used to diagnose tuberculous pleural effusions (TPE) [5]. Biopsy tissue samples can have a joint sensitivity of up to 90% [5], however closed pleural biopsy is a more invasive process that requires a lengthy waiting period for mycobacteria culture findings. As a result, pleural fluid adenosine deaminase (ADA), which is quick, cheap, and accurate in diagnosing TPE with sensitivity and specificity of up to 100% and%, respectively, has become a crucial diagnostic tool in the assessment of exudative pleural effusions [6].The enzyme adenosine deaminase (ADA) is involved in the differentiation of lymphoid cells by catalysing the conversion of adenosine to inosine. In illnesses where cellular immunity is boosted, it is highly active [1]. Various investigations have employed ADA cut off values ranging from 30 to 100 IU/L, resulting in varying sensitivities and specificities [7]. The disparities in the results may be caused by the ADA analytic techniques used, the prevalence of tuberculosis in the different study populations, or variations in the characteristics of the study populations. Prior research has shown a relationship between CD4 lymphocyte counts and pleural ADA level [8], as well as a lower mean ADA level in Japanese patients with TPE [9]. This implies that the immunological condition of the patient as well aswell asdemographic factors may affect pleural fluid ADA levels.The present study is undertaken to estimate the levels of ADA and lymphocyte counts and to find out the correlation between ADA levels and lymphocyte counts in patients with bilateral tubercular pleural effusion.

MATERIALS AND METHODS

Study design: Hospital based observational study.
Duration: 1 year.
Inclusion criteria: We included a total of 120 patients with and without bilateral tubercular pleural effusion. Patients with TPE are grouped as cases [TPE group], and patients without tubercular effusion as controls [Non TPE]. We had a total of 72 patients in Non TPE and 48 in TPE group.

Methodology: Pleural fluid was collected in all the patients for biochemical analysis and cell counts. The biochemical investigations included total protein, albumin, glucose and ADA estimation.

RESULTS:

Table 1: Shows the demographic profile and baseline parameters comparison between TPE and Non TPE group

	TPE group [no=48]	Non TPE group [no=72]	
Males/Females	32/16	48/24	
Mean age	52.4 ± 18.6	54.2±20	
ADA (IU/L)	110.3 ± 32.24	32.6±9.82	<0.001 (HS)

Correlation coefficient between ADA and LDH, cell counts and lymphocytes		
	TPE	NTPE
Protein	r = 0.543, p<0.001	r = 0.346, p<0.001
LDH	r = 0.448, p<0.001	r = 0.864, p<0.001
Cell counts	r = 0.178, p>0.05	r = 0.632, p<0.001
Lymphocytes	r = 0.112, p>0.05	r = 0.522, p<0.001

DISCUSSION

Our study suggests that patient and pleural fluid characteristics need to be considered during interpretation of pleural fluid ADA as it decreases with age and increases pleural fluid protein.This study adds to a relatively small number of paperspublished on pleural fluid ADA performed on an Asianpopulation. Contrary to the study by Niwa et al. [9] whichshowed an ADA level of only 42.9 IU/L in patients withTPE and thus leading to a suspicion that ADA may be lessuseful in Asians, patients with TPE in our study had meanADA of 100 IU/L which was similar to that reported byRiantawan et al. [10].

Few studies have looked at the factors affecting pleuralADA. In our study age had the strongest correlation withpleural fluid ADA. We noted that the correlation betweenage and ADA was much weaker when examined withinthe subgroup of TPE patients. One possible explanation isthat the number of older patients aged > 55 years was relativelysmall in the TPE group resulting in a less representativepopulation. The relationship between age and ADAdemonstrated in our study was similar to that of Yeonet al. from Korea [11]. Their study showed a significantlyhigher ADA in patients with exudative pleural effusionswho were older than 65 yrs compared to those less than65 yrs and the ADA cut-off for the diagnosis of TPE in theolder group was also much lower than for the youngergroup (25.9 IU/L compared to 49.1 IU/L). Other authors have also shown that young patients with TPE have amuch higherlevel of pleural fluid ADA. In a group of patientsage ≤ 35 yrs the mean ADA level for those with TPEwas 111.1 IU/L, a similar figure to our study's youngerTPE group [12]. Merino studied a paediatric population(age < 18 yrs) with TPE and the mean ADA level obtainedwas 73.8 IU/L with all but 2 patients (%) having ADA lessthan 40 IU/L [13].

It may be possible that the decrease inADA with age does not occur as a continuum throughoutall ages but is evident only after a certain age.Lee et al. [14] examined patients with non-tuberculouslymphocytic effusions and found a fairly positive correlationbetween ADA, pleural protein and LDH, similar to our findings. In the study by Kashiwabara et al. [15] which consistedof a larger proportion (%) of parapneumonic effusionand mainly non-lymphocytic exudates, there was only positivecorrelation between ADA and LDH, but no significantcorrelation with protein or age. Our study showed a poorcorrelation between ADA and pleural cell count, and nocorrelation with blood lymphocyte count. This was similarto findings in other studies [10,14,16]. In fact,other authors have shown that the sensitivity of ADA was not affected by the CD4 count in pleural fluid and was still useful diagnosticallyin HIV positive patients [10,16].ADA has greatest activity in lymphoid tissues and isresponsible for the differentiation of lymphoid cells. Thereare 2 isoenzymes, ADA1 and ADA2, with ADA2 foundonly inmonocytes and macrophages. The high total levelof ADA in tuberculous pleural effusion is due largely tohigh ADA2 activity [17]. There is biologic plausibility ofthe negative correlation between ADA and age, attributableto the phenomenon of immunosenescence [18]. There isincreasing evidence that there is loss of immune functionin the elderly individual. We noted a weaker correlation betweenADA and age in the TPE subgroup compared to theoverall study population. Apart from the possible effect dueto a small sample size of elderly TPE patients mentionedearlier in the discussion, another postulation is that ageingmay affect monocytes and macrophages to varying degreescompared to lymphocytes and subsequently a

smaller effecton ADA2 isozyme production, which is the predominantisoenzyme in TPE. Pleural protein and LDH are both indicatorsof the degree of pleural inflammation [1] and therewould be conceivably more activated lymphocytes andADA production in the presence of greater pleural inflammation.Lee at al [11] previously offered an explanation forthe lack of association between ADA and pleural cell count.The standard ADA determination measures ADA activityand not the absolute amount of enzyme present. ADAactivity may be dependent more on the pathologic stimulus e.g. TB and rapidity of T lymphocyte proliferation, and not on amount of lymphocytes present.

CONCLUSION:

In the present study, we found statistically significantly elevated levels of ADA in TPE compared to Non TPE. Lymphocyte counts were elevated in both the groups but in the TPE group the association between ADA levels and lymphocytes counts was not statistically significant.

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Conflicts of interest
There are no conflicts of interest

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