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Original Research Article

Diagnosis of Tuberculous Pleural Effusion by analysis of Adenosine Deaminase in Serum and Exudative pleural effusion

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Abstract: Various enzymes has evaluated by analyzing pleural fluid to diagnose Tubercular pleural effusion. Among different enzymes, Adenosine deaminase has been proven with higher specificity and sensitivity, to be a good marker for tuberculosis. The aim of this study is to evaluate the utility of Adenosine deaminase in serum and pleural fluids in the diagnosis of HIV seronegative Tuberculous pleural effusion. A total of 120 patients with Exudative pleural effusion of known etiology with HIV seronegative status were selected to do this study. Out of 120 patients, 60 were with new cases of Tuberculous pleural effusion and those were considered as cases. Remaining 60 patients were with non Tuberculous pleural effusion, were considered as controls. Serum or Plasma and Pleural fluid samples were collected under aseptic precautions from selected groups and sent for investigation. After collection samples were analyzed for Adenosine deaminase by cross checking in Systronics UV spectrophotometer, spectrophotometer and Transasia semi auto analyzer with precinorm and precipath in duplicates. ADA was analyzed by Guisti G and Galanti Method. The mean value of ADA in serum samples of among tuberculous and non tuberculous pleural effusion patients was 75.12±2.83 and 17.43±3.62 respectively. The Mean value of ADA levels in pleural fluid among tuberculous and non tuberculous pleural effusion patients was 86.42±3.48 and 15.48±5.23 respectively. On analyzing the statistical significance of ADA levels between tuberculous and non tuberculous pleural effusion, shown that it was extremely statistically significant. ADA test have a higher degree of specificity and sensitivity, which is a simple, quick, less expensive and superior diagnostic test for exudative pleural effusion. ADA testing requires just a simple colorimeter.
Keywords: Adenosine deaminase, Pleural fluid, Serum, Tuberculous Pleural effusion

INTRODUCTION

Tuberculosis (TB) is caused by strict aerobe bacteria called Mycobacterium tuberculosis, which thrives best in tissues with high oxygen tension such as apex of the lung. Usually it is a chronic disease with varying clinical manifestations [1].

Pleural effusion is collection of fluid in the pleural space in more than normal volume that is actually present in the pleural space. Among exudative pleural effusions of immunocompetent patients, tuberculous pleural effusion is one of the most frequent causes. If we exclude patients with underlying pulmonary disease, TB is the most common cause of pleural exudates in many areas of the world [2]. Pleural TB is one of the most frequent extra pulmonary manifestations of tuberculosis [3]. With new infections being controlled, pleural disease now is seen more as a reactivation than a primary infection.

Pulmonary tuberculosis can be diagnosed by testing sputum for acid fast bacilli, sputum culture and radiological investigations. Diagnosing extra pulmonary tuberculosis is the main area of concern. Demonstration of bacilli in pleural effusion, genital tuberculosis, tubercular meningitis and other forms of extra pulmonary tuberculosis is quite difficult. In India the facilities of culture are located mostly at district headquarters. Most of the treatments of extrapulmonary tuberculosis are started on clinical evidence.

Various enzymes has evaluated by analyzing pleural fluid to diagnose Tubercular pleural effusion. Among different enzymes, Adenosine deaminase has been proven with higher specificity and sensitivity, to

be a good marker for tuberculosis. ADA is a very useful tool to diagnose tubercular effusions in India, where there are high prevalence and incidence rates of TB.

As pleural effusions can be caused by diseases in the chest, organ dysfunction or infections below the diaphragm, drugs and systemic disease, analysis should be carried out to detect the source and type of effusion. In Tuberculosis prevalent areas, ADA analysis plays a major role in diagnosis, as it is easy to perform, quick, low cost [4]. Pleural fluid analysis provides a safe and accessible means for diagnosing conditions that affect the pleural space.

The aim of this study is to evaluate the utility of Adenosine deaminase in serum and pleural fluids in the diagnosis of HIV seronegative tuberculous pleural effusion.

MATERIALS AND METHODS

After institutional ethical committee approval, study has conducted from March 2013 to may 2014 in the Department of General Medicine, Government General Hospital & Medical College, Ananthapuram. Study was explained to all the selected patients and informed consent was taken.

A total of 120 patients with Exudative pleural effusion of known etiology with HIV seronegative status were selected to do this study. Out of 120 patients, 60 were with new cases of tuberculous pleural effusion and those were considered as cases. Remaining 60 patients were with non Tuberculous pleural effusion, were considered as controls.

Serum (Fresh, unhemolysed / non turbid samples) or Plasma (Fresh EDTA, citrate, heparinised or oxalate anticoagulated) and Pleural fluid samples were collected under aseptic precautions from selected groups and sent to the Department of Biochemistry, Government Medical College, Ananthapuram for immediate processing.

After collection samples were analyzed for Adenosine deaminase by cross checking in Systronics UV spectrophotometer, spectrophotometer and Transasia semi auto analyzer with precinorm and precipath in duplicates.

ADA was analyzed by Guisti G and Galanti Method [5].

Reference range of ADA:

Specimen	Interpretation	Values U/L
Serum, Plasma, Pleural, Pericardial and Ascitic fluids	Normal	< 40
	Suspect	40 - 60
	Positive	> 60
CSF	Normal	< 10
	Positive	> 10

All the results were entered into spread excel sheet and analyzed.

RESULTS

A total of 120 patients, among which 60 were Tuberculous pleural effusion and 60 patients were with Non Tuberculous pleural effusion. The Mean age of tuberculous pleural effusion patients was 36±5.3 years and of non tuberuclous pleural effusion was 42±6.8. There was female predominance in both groups (Table No.1). Socioeconomic status was assessed by Modified Kuppuswamy's scale.

Table-1: Demographic profile of Tuberculous and Non tuberculous pleural effusion patients

Demographic data	Tuberculous Pleural effusion (n=60)	Non Tuberculous Pleural effusion (n=60)
Age in years	36±5.3	42±6.8
Sex	41	38
BMI	19±6.4	21±7.8
Socioeconomic status		
Upper class	4	8
Upper Middle class	12	15
Middle class	18	20
Upper Lower class	21	14
Lower class	5	3

On assessment of Adenosine Deaminase, the mean value of ADA in serum samples of among tuberculous and non tuberculous pleural effusion patients was 75.12±2.83 and 17.43±3.62 respectively. The Mean value of ADA levels in pleural fluid among tuberculous and non tuberculous pleural effusion patients was 86.42±3.48 and 15.48±5.23 respectively (Fig No.1).

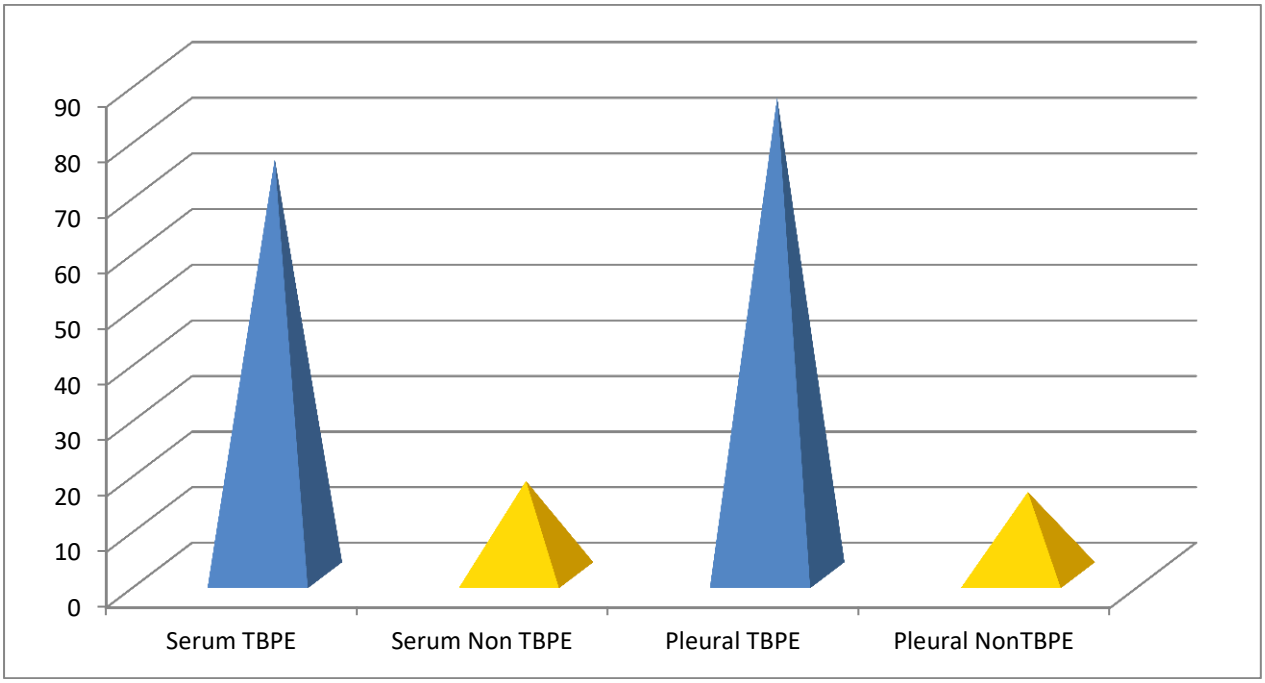

Fig-1: Diagrammatic representation of Mean values of ADA levels in serum and pleural fluid.

On analyzing the statistical significance of ADA levels between tuberculous and non tuberculous pleural effusion, shown that it was extremely statistically significant (Table No.2).

Table-2: Analyzing significance between tuberculous and non tuberculous pleural effusion

Mean Values	t value	p value	Significance
Serum Tuberculous Pleural effusion vs Serum Non Tuberculous pleural effusion	97.2519	<0.0001	ESS
Pleural Tuberculous Pleural effusion vs Pleural Non Tuberculous pleural effusion	87.4722	<0.0001	ESS
Serum Tuberculous Pleural effusion vs Pleural Tuberculous pleural effusion	19.5141	<0.0001	ESS
Serum Non Tuberculous Pleural effusion vs Pleural Non Tuberculous pleural effusion	2.3747	0.0192	SS

ESS - Extremely Statistically Significant; SS - Statistically Significant

DISCUSSION

Tuberculous pleurisy results from Mycobacterium tuberculosis infection of the pleura. It manifests as a pleural effusion with exudative characteristics and can be found either isolated or in association with pulmonary tuberculosis (TB).

There are 2 isoforms of ADA: ADA1 and ADA2. ADA1 is ubiquitous and is necessary for the breakdown of the substrate adenosine to 2′deoxyadenosine. This enzyme is important because a low level of 2′deoxyadenosine is essential for the proper functioning of immune cells. In contrast, ADA2 is not ubiquitous, and coexists with ADA1 only in monocytes and macrophages. In a tuberculous effusion, ADA-2 is the predominant isoforms accounting for over 80 percent of ADA activity, whereas ADA-1 accounts for approximately 70 percent of the activity of the total ADA activity in empyema [6].

The diagnostic cut-off points for ADA have been reported from 40 to 60 U/L [7]. Selecting a cut-off

point of 40 U/L will increase the sensitivity of ADA but decrease its specificity, while choosing a cut-off point of 60 U/L will increase specificity but decrease sensitivity.

In this study, the mean value of ADA in serum samples of among tuberculous and non tuberculous pleural effusion patients was 75.12±2.83 and 17.43±3.62 respectively. The Mean value of ADA levels in pleural fluid among tuberculous and non tuberculous pleural effusion patients was 86.42±3.48 and 15.48±5.23 respectively.

The serum levels of ADA in tuberculous effusions are in accordance with the studies of Jadhav *et al*. [8]. Who observed a mean ± SD of 38.58 ± 22.81 in serum. In another study by Meena verma *et al*. [9] the mean serum level of ADA was 39.97 ± 2.7 wih p value of < 0.001.

A study by Anand patel and Sushmita choudhury *et al*. [10] reported that mean level of 114.1 ± 61.36 in tuberculous effusion and 20.3± 23.42 in non tuberculous effusion. They had obtained that sensitivity of 97% and specificity of 93% by analyzing ADA activity of 40 IU / L in tuberculous pleural effusion patients and with > 35 IU/L as cut off value the sensitivity is 100 % and specificity is 93%.

Bharath kumar Gupta *et al*. [11] reported mean values of ADA levels in pleural fluids of tuberculous and non tuberculous groups obtained were 67.34 ± 22.85 and 18.60 ± 9.12 respectively.

Zay Soe *et al*. [12] observed that the best cut off level of ADA activity tested was at 42.5 IU/L when sensitivity was 87% and specificity was 89%. The mean ADA levels in their study were 73.90 ± 33.96. The positive predictive value (PPV) was 96 % and NPV was 83%.

Mathur PC *et al*. [13] studied that ADA Level in tuberculous pleural effusion ranged from 45-160 U/L with a mean level of 100 U/L while in non- tuberculous group it ranged from 5 to 33 U/L with the mean of 18 U/L ($p<0.001$, highly significant). The sensitivity and specificity for diagnosing tubercular effusion was 100% and 94.6% with positive and negative predictive values of 95.5% and 100% respectively.

ADA estimation should do routinely along with other investigations like culture, cytological studies, and radiological studies especially to diagnose extra pulmonary tuberculosis and in sputum negative tuberculous cases.

CONCLUSION

In tuberculosis prevalent areas like India and when there is a failure of conventional treatment of TB, there is a need of accurate diagnostic methods. ADA test have a higher degree of specificity and sensitivity, which is a simple, quick, less expensive and superior diagnostic test for exudative pleural effusion. ADA testing requires just a simple colorimeter.

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