

A Study on Adenosine Deaminase (ADA) Activity in Tubercular Serositis: As A Diagnostic Tool

Asraf¹, T. Manmadha Rao², K. Sreenivasa Rao³

Assistant Professor, Dept. of Respiratory Medicine, GEMS Hopsital, Ragolu.

Professor, Dept. of Respiratory Medicine, GEMS Hopsital, Ragolu

Senior Resident, Dept. of Respiratory Medicine, GEMS Hopsital, Ragolu.

Correspondence Author: Dr K Sreenivasa Rao, Senior Resident, Dept. of Respiratory Medicine, GEMS Hopsital, Ragolu.

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background: Adenosine deaminase has been proposed to be a useful surrogate marker for tuberculosis in pleural, pericardial and peritoneal fluids. Studies have confirmed high sensitivity and specificity of Adenosine deaminase for early diagnosis of extra pulmonary tuberculosis.

Aim: To assess the diagnostic level of ADA in tubercular serosal effusion and to determine its sensitivity and specificity.

Methods: The study was carried out on 120 patients suffering from serosal effusion (50 pleural, 50 peritoneal, and 20 cases of pericardial effusion). Detailed clinical history, physical examination and routine and relevant investigation of all patients including ADA estimation by enzymatic method was done.

Results: ADA Level in tuberculous pleural effusion ranged from 45-160 U/L with a mean level of 100U/L and sensitivity and specificity of 100% (p<0.001, highly significant). ADA level in tuberculous peritoneal effusion ranged from 35-135 U/L with a mean level of 92U/L and sensitivity and specificity of 100% and 95% respectively (p<0.001, highly significant). ADA level in tubercular pericardial effusion ranged from 63-117 U/L with a mean level of 90U/L and sensitivity and specificity of 100%

and 83.3% respectively (p<0.005, very significant). In toto serosal fluid ADA level estimation offers high degree of sensitivity and specificity of about 100% and 94.6% respectively,

Conclusion: ADA was found positive with a mean value of 100U/L, 92U/L and 90 U/L in tubercular pleural, peritoneal and pericardial effusion respectively with overall 100% sensitivity and 94.6% specificity and cutoff value of 40 U/L.

Introduction

Tuberculosis is one of the oldest and commonest infectious diseases also known as master of death or captain of death. Tuberculosis usually affects lung but extra pulmonary tuberculosis is also common, of which serosal tuberculosis is one.

Diagnosis of pulmonary tuberculosis is confirmed mainly by sputum examination of AFB. However, the diagnosis of extra pulmonary tuberculosis requires investigation of pleural fluid biochemistry, cytology and pleural biopsy. Positivity for AFB and Histopathological (HP) study of pleura is very low and culture is very time consuming. ELISA, PCR & Interferon are very expensive tests. Adenosine deaminase has been proposed to be a useful surrogate marker for tuberculosis in pleural, pericardial and peritoneal fluids. Studies have confirmed high

sensitivity and specificity of adenosine deaminase for early diagnosis of extra pulmonary tuberculosis.

Material and Methods

This study was carried out on 120 patients suffering from serosal effusion (pleural, peritoneal, and pericardial effusion) who attended OPD in Department of Respiratory Medicine at tertiary care hospital. Detailed clinical history, physical examination and investigation e.g. AFB, cytological examination, biochemical examination and, wherever possible, biopsy and histopathological examination, USG, X- ray chest, ECG, ECHO and other appropriate investigations including serosal fluid ADA were carried out in all patients.

Exclusion Criteria–Diagnosed cases of infectious mononucleosis, enteric fever, leprosy, viral hepatitis, HIV, CA urinary bladder and haematopoetic malignancy. ADA Estimation was done by enzymatic Method by ELISA.

Results

ADA Level in tuberculous pleural effusion ranged from 45-160 U/L with a mean level of 100U/ L and sensitivity and specificity of 100%. ADA level in tuberculous peritoneal effusion ranged from 35-135 U/L with a mean level of 92U/L and sensitivity and specificity of 100% and 95% respectively.

ADA level in tubercular pericardial effusion ranged from 63-117 U/L with a mean level of 90U/L and sensitivity and specificity of 100% and 83.3% respectively. Overall serosal fluid ADA level estimation offers high degree of sensitivity and specificity of about 100% and 94.6% respectively. Hence, along with other investigations like cytochemical analysis, radiological studies, serosal fluid samples should be subjected to ADA level routinely to differentiate between tuberculous and non tuberculous etiology.

Discussion

This study was carried out on total 120 cases of serosal effusion, in which 50 were of pleural effusion, 50 of peritoneal effusion and 20 cases of pericardial effusion.

ADA level in tuberculous pleural effusion ranged from 45 to 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). ADA level in tuberculous ascites ranged from 35 to 135 U/L with a mean level of 92 U/L while in non tuberculous group it ranged from 1 to 28 U/L with the mean of 12 U/L (p<0.001, highly significant). ADA level in tubercular pericardial effusion ranged from 63-117 U/L with a mean level of 90 U/L while in non tuberculous group it ranged from 1.5 to 29 U/L with a mean of 15.33 U/L (p<0.005, highly significant, Table 1).

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 in present study (Table 2). ADA, a product of T lymphocytes, has been

Table 1: ADA level in serosal fluid

Type		Range (U/L)	Mean (U/L)
Pleural Fluid	Tuberculous	45-160	100
	Non-tuberculous	5-33	18
Peritoneal Fluid	Tuberculous	35-135	92
	Non-tuberculous	1-28	12
Pericardial Fluid	Tuberculous	63-117	90
	Non-tuberculous	1.5-29	15.33

Table 2: Sensitivity and specificity of ADA for tuberculous effusion.

ADA	Tuberculous	Non-tuberculous
Positive	64 (a)	3 (b)
Negative	0 (c)	53 (d)

Sensitivity (%) = 100%, Specificity = 94.6%,

Positive Predictive value= 95.5%, Negative predictive value = 100% reviewed as an excellent marker for the diagnosis of tuberculous pleural effusion. Almost all research workers have shown sensitivity and specificity of 90% to 100% for the value of ADA in pleural fluid using different cut off levels. Gupta, D.K⁴ studied 53 cases of pleural effusion out of which 36 were of tuberculous etiology. The mean ADA level in tuberculous was 50.75 U/L while in malignant and parapneumonic effusion it was 14.47 U/L and 28.65 U/L respectively. The sensitivity and specificity for diagnosing tuberculosis were 100% and 94.1 % respectively.

Burgess L.J.⁷ showed ADA activity in tuberculous effusion was higher than in any other diagnostic group. At a level of 50U/L the sensitivity and specificity for the identification of tuberculosis was 90% and 89% respectively.

Strankinga W.F.⁸ investigated 10 patients with tuberculosis pleurisy and 76 patients with pleural effusions of other etiology. The ADA activity in the tuberculous patients was significantly higher than in the other groups while the exception of those with empyema. Specificity 87% and sensitivity 100% of this test for tuberculosis are high when a reference limit of more than 53 U/L is taken.

Significance of ADA activity and its iso-enzymes (ADA-1m, 1C and ADA-2) in pleural effusion was studied by Carstens ME et al.⁶ He concluded that determination of patterns of ADA isoenzymes doesn't enhance the overall diagnostic value of ADA activity in pleural effusion.

Value of ADA activity in pleural effusion was studied by Shibagaki T et al.⁹ He concluded that tuberculous pleural effusion had a much higher ADA activity than cancer effusion and total ADA activity in tuberculous pleural effusion decreases after anti tubercular therapy.

Voight² studied 41 cases with bacteriologically confirmed tuberculosis and 41 cases with other causes. The mean ADA level for tubercular etiology was 99.8 U/L with sensitivity and specificity for diagnosis tubercular ascites was 95% and 98% respectively. Dwivedi M³ studied 49 patients with ascites of which 19 were of tubercular etiology with mean ADA level of 98.8 U/L. At an ADA level > 33 U/L the sensitivity, specificity, positive and negative predictive values were 100%, 96.6%, 95% and 100% respectively.

24 ascites cases were studied by Gupta V.K.¹ of whom 7 were due to tubercular etiology with an ADA level of >30 U/L and sensitivity and specificity of 100% and 94.1% respectively. The sensitivity and specificity for tubercular ascites on the basis of ADA level were 100% and 97% respectively as per the study of Bhargawa D.K. Kwan G KK et al.¹⁰ studied pericardial fluid ADA level along with histopathology of pericardial biopsy and found a cut off ADA level of 40 U/L in pericardial fluid which has sensitivity of 93% and specificity of 97% in diagnosis of tubercular pericardial effusion.

In the present study, 100% sensitivity and 83.3% specificity of ADA level for diagnosis of tubercular pericardial effusion was found. In the present study, specificity of ADA for diagnosis of tubercular pericarditis was low that may be due to less number of

cases of pericardial effusion. It has been clearly shown that ADA levels are significantly high in tuberculosis as against non tuberculous causes. This test has 100% sensitivity and 94.6% specificity for diagnosing tuberculous etiology with positive and negative predictive values of 95.5% and 100% respectively.

The method of ADA estimation is easy, simple and doesn't require expensive equipment or elaborate laboratory arrangement except a simple colorimeter. It takes only 2 hours and it is also economical.

Conclusion

The present study shows that a simple, inexpensive, highly sensitive and specific test like ADA estimation should be employed routinely to differentiate between tubercular and non-tubercular etiology in patients of pleural, pericardial and peritoneal effusion.

References

1. Gupta VK, Mukerji S, Datta SK. Diagnostic evaluation of ADA in tuberculous peritonitis. JAPI 1992; 40 (6): 387-389.
2. Voight MD, Kalvaria L, Trey C, et al. Diagnostic value of ascites adenosine deaminase activity in tuberculous
3. Dwivedi M, Misra SP, Misra V, et al. Value of adenosine deaminase estimation in the diagnosis of tuberculous ascites. Am J Gastroenterology 1990; 85: 1123-5.
4. Gupta DK, Suri JC, Goel A. Efficacy of ADA in diagnosis of pleural effusions. Ind J Chest Dis 1990; 32 (4): 205-208.
5. Bhargava DK, Gupta M and Nijhawan S. Adenosine deaminase in peritoneal tuberculosis , diagnostic value in ascitic fluid and serum. Tubercle 1990; 71: 121-126.
6. Carstens ME et al. Isoenzymes of adenosine deaminase in pleural effusions: a diagnostic tool. Int J Tuberculosis Lung Dis 1998 Oct; 2 (10) : 831-835

7. Burgess L.J. Use of adenosine deaminase as a diagnostic tool for tuberculous pleurisy. Thorax 1995 June; 50 (6): 672-674.
8. Strankinga W.F. Adenosine deaminase activity in tuberculous pleural effusions: a diagnostic test. Tubercle 1987 June; 68 (2) : 137-140.
9. Shibagaki T. et al. Adenosine deaminase isoenzymes in tuberculous pleural effusion. J Lab Clin Med 1996 Apr., 127 (4): 348-352.
10. Kin JH et al. Adenosine deaminase and CEA in pericardial effusion. Circulation 1994; 89 (6): 2728-2735