



Diagnostic value of Adenosine Deaminase (ADA) in Tuberculous Pleural Effusion

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ABSTRACT

Tuberculosis is a common cause of pleural effusion in India. Pleural fluid adenosine deaminase (ADA) estimation is a quick test used for the diagnosis of tubercular pleural effusion. The sensitivity and specificity vary in different studies.

Aim of study: To find out the sensitivity and specificity of ADA in the diagnosis of tuberculous pleural effusion.

Methodology: The study was done as a diagnostic test evaluation. Total 120 patients, 60 each in TB and nonTB were included. Pleural fluid ADA estimation was done for all patients and the sensitivity and specificity were calculated.

Results: Pleural fluid ADA level was significantly high in patients with tuberculous pleural effusion. With ADA cut off value of 30U/L the sensitivity was 90% and specificity 83%. With a cut off value 42.5U/L sensitivity 80%; specificity 93% and cut off value 70U/L sensitivity 40% and specificity 97%.

Conclusion: Pleural fluid ADA estimation is a very useful test for the diagnosis of tubercular pleural effusion. As the ADA value increases, specificity increases but sensitivity decreases.

KEYWORDS : Pleural effusion, Tuberculosis, ADA

Introduction

Tuberculosis (TB) is a leading cause of preventable morbidity and mortality from an infectious agent worldwide. Tuberculous pleuritis is a common manifestation of extra pulmonary tuberculosis, second to TB lymphadenitis⁽¹⁾. The frequency of TB as a cause of pleural effusion depends on the prevalence of TB in that particular population⁽²⁾. Pleural effusion occurs in approximately 5% of patients with TB. Pleural TB occurs as a result of a TB antigen entering the pleural space, usually through the rupture of a sub pleural focus, followed by a local, delayed hypersensitivity reaction mediated by CD4+ cells⁽³⁾. The paucibacillary nature makes the diagnosis of TB pleural effusion a real challenge. Pleural aspiration and pleural fluid analysis for different tests are usually done to make a correct diagnosis of tuberculous pleural effusion. But the available investigations have its own recognized limitations for clinical use. Adenosine Deaminase (ADA) level estimation is one biochemical test widely used worldwide for diagnosis of tuberculous pleural effusion. Indian studies show variable sensitivity and specificity for the test. Hence a study was planned to assess the diagnostic value of ADA in tuberculous pleural effusion.

Aim of study

To find out the sensitivity and specificity of ADA in the diagnosis of tuberculous pleural effusion.

Study design

Diagnostic test evaluation.

Study population and setting

Cases of pleural effusion attending Department of Pulmonary Medicine, Medical College, Thiruvananthapuram.

Inclusion criteria

All patients with exudative pleural effusion willing to give consent were included in the study.

Exclusion criteria

Patients aged less than 12 years, Empyema, Hydropneumothorax and not willing to give consent were excluded from the study.

Sample size

60

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Calculated as 60 positive cases, using a software developed by CMC Vellore, nMaster 1.0LNK

Methodology

Total 120 patients were included in the study, 60 each in the TB and Non TB group. Detailed clinical history and physical examination done. All patients were subjected to Blood routine, RBS, Sputum AFB, mantoux test and CXR PA view. Thoracentesis & Pleural fluid sent for TC, DC, cytology for malignant cells, ADA, protein, sugar, AFB smear, gram stain, Culture & Sensitivity, pleural biopsy was done in feasible situations.

Based on a Departmental consensus 65 patients with probable tuberculous etiology were started on CATEGORY I ATT, to make the treatment uniform as there were 3 HIV positive & 6 sputum positive pulmonary TB patients in the study group and rest of the patients with alternate diagnosis treated accordingly. Follow up was done every month & response to treatment assessed clinically & radiologically and those not responding were further evaluated. Thus of the 65 TB patients, 5 did not respond to ATT & on further evaluation were found to be malignant. Documented response to ATT was taken as gold standard. The results of this study are analyzed and statistical analysis was performed using SPSS statistical software version 22.0.

Results

A total number of 120 patients were included in the study; 60 each in the TB & non TB group. Among the non TB, 37(30.8%) was malignancy, 15(12.5%) parapneumonic and connective tissue disorders 8(6.7%) (Table 1).

Table 1: Etiology of pleural effusion

| Diagnosis | Count | Percent |
|------------------|-------|---------|
| Tuberculosis | 60 | 50.0 |
| Malignancy | 37 | 30.8 |
| Parapneumonic | 15 | 12.5 |
| Others (SLE, RA) | 8 | 6.7 |

Among TB group, 47(78.3%) were males and 13(21.7%) females and non TB group 49(81.7%) were male and 11(18.3%) females (Fig 1).

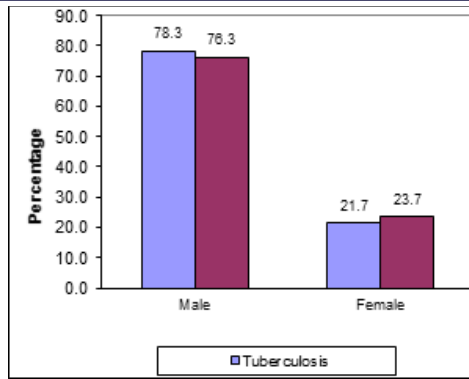


Fig.1 Association between occurrence of TB and gender

Among the clinical variables studied cough(91.7%) was the predominant symptom; fever & dyspnoea in 83%, chest pain in 60% patients. Study by Berger et al in 254 patients showed cough & chest pain as the predominant symptom ⁽⁴⁾ Among the clinical variables only the presence of fever was found to be statistically significant (p <.01). When chest X-ray findings were studied majority (93.3%) in the TB group had moderate effusion, only 4(6.7%) had massive effusion. Upon analyzing pleural fluid characteristics 85% of the TB group had straw colored effusion. Majority (83.3%) had lymphocyte predominant effusion (*ie* lymphocyte >50%).16.7 %had neutrophilic type; but differential count could not be repeated for these patients later. This was found to be statically significant.

ADA values were compared and analyzed for TB and nonTB effusion. ADA value of less than 30 was seen in 6(10%) of TB and 51(85%) of non TB effusion cases, ADA between 30-50 was obtained in 12(20%) of TB; 6(10%) of non TB cases. 18(30%) of TB and 2(3.3%) of non TB cases showed ADA value between 50 -70. ADA more than 70 was seen in 24(40%) of TB and 1(1.7%) of non TB effusions. ROC curve was plotted for ADA & sensitivity and specificity for various cut off points measured (Fig 2).

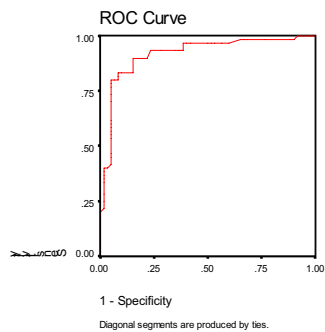


Fig.2 ROC curve for ADA on TB

- Cut off 30: sensitivity 90%; specificity 83%
- Cut off 42.5: sensitivity 80%; specificity 93%
- Cut off 70: sensitivity 40%; specificity 97%

As the ADA value increases, specificity increases but sensitivity decreases. On comparing the value of ADA among TB effusion and non TB effusion, there was statistically significant difference for ADA value in TB pleural effusion.

Discussion

TB pleural effusion is a common manifestation of extra pulmonary TB and is one of the common causes of pleural effusion in our country. But the diagnosis of pleural TB remains a challenge, as the conventional diagnostic tests such as microscopy, culture & biochemical tests of pleural fluid, histopathology & culture of pleural

tissue have known limitations. The diagnostic yield of thoracentesis alone varies from approximately 25- 75 %⁽⁵⁾. ADA is an enzyme in the purine salvage pathway that catalyzes the conversion of adenosine and deoxyadenosine to inosine and deoxyinosine with the release of ammonia. Piras and colleagues for the first time in 1978 reported high levels of ADA in patients with TB pleural effusions⁽⁶⁾. Subsequently, several studies have explored the usefulness of estimation of ADA activity in the diagnosis of TB pleural effusions^(7,8). Different authors have used various cutoff levels for the pleural fluid, ADA between 30 and 70 U/L for the diagnosis of pleural TB. The higher the pleural fluid ADA level, the more likely the patient is to have tuberculous pleuritis.

A meta analysis of 40 studies published from 1966 to 1999 concluded that the test performance of ADA (sensitivity range 47.1 to 100%, and specificity range 0% to 100%) in diagnosing TB pleural effusions is reasonably good and is adequate to avoid pleural biopsy in young patients from areas with high prevalence of TB⁽⁹⁾. Sensitivity & specificity of the test in Indian studies are not as good as in western studies. It is not clear whether the discrepancies in the results are due to the difference in the method of ADA analysis or a true ethnic variation⁽¹⁰⁾. Sharma SK and colleagues done a prospective study and using cut off value for ADA as 35U/L, the sensitivity was 83.3% and specificity was 66.7%⁽⁸⁾. Jose Banales and group when used a cut off value of 70U/L, the sensitivity was 98% and specificity 96%⁽¹¹⁾. Aoki et al obtained a sensitivity of 81% and specificity of 89% using ADA cut off value 45U/L⁽¹²⁾. In our study with ADA cut off value of 30U/L the sensitivity was 90% and specificity 83%, cut off of 42.5U/L had a sensitivity 80%; specificity 93% and for a cut off value 70U/L sensitivity 40% and specificity 97%.

Conclusion

Pleural fluid ADA estimation is a very useful test for the diagnosis of tubercular pleural effusion. In our study a cut off value of 42.5U/L has sensitivity 80%; specificity 93%. As the ADA value increases, specificity increases but sensitivity decreases.

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