Original Research Paper

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Pulmonary Medicine

DIAGNOSTIC VALUE OF SERUM ADENOSINE DEAMINASE (ADA) LEVEL IN TUBERCULOSIS

Dr. Gaurav R. Dubey	Associate Professor Department of Pulmonary Medicine, Dr. Panjabrao Deshmukh Memorial Medical College, Amravati
Dr. Vijay R. Kapse	Professor & Head Department of Pulmonary Medicine, Dr. SCGMC, Nandeed.
Dr. Sanjiv Vithalrao Zangde	Assistant Professor Department of Pulmonary Medicine, SCGMC Nanded

ABSTRACT **Background:** Although the standard diagnosis of PTB is based on M. tuberculosis isolation or direct observation of AFB in sputum examination yet, other diagnostic methods with shorter duration and acceptable sensitivity and specificity are essential. **Materials & methods:** This present hospital based cross sectional study was conducted on 68 study subjects. Blood sample from all study subjects were collected and serum ADA level was measured. **Results:** Mean serum ADA value in patients of tuberculosis was 26.93 + 16.44 U/L when compared to mean serum ADA value of 17 + 5.78 U/L in patients of non-tubercular diseases group, showed higher significant mean difference between two groups and was also statistically significant with a p value of 0.04386. **Conclusion:** The best cut-off point of Serum ADA was 15 U/L in which sensitivity and specificity were 85.7 % & 33.3% respectively.

KEYWORDS : Tuberculosis, ADA, Diagnosis

INTRODUCTION

A definite diagnosis of pulmonary tuberculosis can be made with sputum smear examination showing the presence of acid fast bacilli. Chest radiograph provides only a probable analysis.[1] Problem arises when sputum is repeatedly negative for acid fast bacilli, and sputum culture is a time consuming process. ELISA, PCR and interferon are very expensive tests, the measurement of serum adenosine deaminase is one of the biochemical methods.[2]

Adenosine deaminase (ADA) is an enzyme ten times higher in concentration in lymphocytes than erythrocytes involved in purine metabolism. Adenosine deaminase is a significant indicator of active cellular immunity. The level of serum ADA increases in various diseases where cell mediated immunity is stimulated like tuberculosis, enteric fever, infectious mononucleosis, brucellosis and bronchogenic carcinoma.[3] The level of ADA in tuberculosis is higher than any other non tubercular pulmonary diseases. Its sensitivity and specificity are very high. The serum ADA value is sufficiently useful in identifying those patients in whom the diagnosis of pulmonary tuberculosis should be actively considered.[4]

Determination of ADA is cost effective and not time consuming, therefore it is recommended that adenosine deaminase estimation should be done routinely, especially if the diagnosis of tuberculosis is in doubt, and also used to differentiate pulmonary tuberculosis from non tubercular pulmonary diseases.[5] Thus, present study was conducted to assess diagnostic value of serum adenosine deaminase level in tuberculosis.

MATERIALS & METHODS

The present hospital based cross sectional observation study was done in Department of Respiratory Medicine, Dr. Panjabrao Deshmukh Memorial Medical College, Amravati, tertiary care teaching hospital. The study was carried on total 68 patients, to assess diagnostic value of serum adenosine deaminase level in tuberculosis. The study was conducted between Periods Jan 2022-June 2022.

In the present study, 68 patients highly suspected of having tuberculosis attending OPD & IPD of hospital during above mentioned study period were selected on the basis of inclusion and exclusion criteria and were subjected to further investigation by using sputum AFB, X ray chest & CBNAAT.

Patients above 18 years of age with clinically suspected to have TB were included in the study. Patients with combined lung malignancy and pulmonary tuberculosis, Patients with previous history of extra-pulmonary or pulmonary tuberculosis or on TB treatment were excluded from study.

TB detection was done using Sputum AFB, X ray Chest & CBNAAT. All specimens were processed according operating manual given by central TB Division, government of India. Lung malignancy diagnosed by CT chest, FNAC and physician records.

An informed written consent was taken before collecting the sample. 5 ml of plain venous blood sample was drawn from the median cubital vein from all 68 study subjects before the start of the tretment. This was followed by centrifugation and then sample was processed for ADA immediately. Then diagnosis of patients was done by diagnostic tests as described above & then comparison of serum ADA level was done. Student's t test was applied to compare mean values of ADA from tuberculosis & non tuberculosis patients, p value less than 0.05 was considered significant at 95% confidence interval. ROC curve, Sensitivity, specificity, positive & negative predictive values were calculated using SPSS software, trial version 20.

RESULTS

Table No.1: distribution of study subject according to age & gender

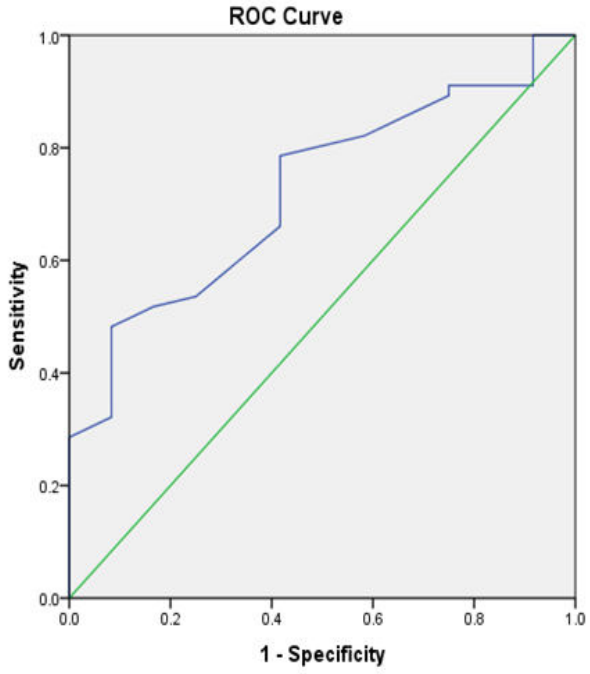
AGE GROUP (IN YEARS)	MALE	FEMALE	TOTAL
<20	3 (4.4%)	3 (4.4%)	6 (8.8%)
21-40	13 (19.1%)	16 (23.5%)	29 (42.6%)
41-60	8 (11.8%)	15 (22.1%)	23(33.8%)
>61	3 (4.4%)	7 (10.3%)	10 (14.7%
TOTAL	**27 (39.7%)**	**41 (60.3%)**	**68 (100%)**

In this present study total 68 study subjects were studied, among this more than half were female (60.3%) and 39.7 % were male. Mean age of study subjects were 41.61 $\pm$ 15.89, majority study subjects were young adults i.e. in age group 21-40 years (42.6%)

Table No. 2: Distribution of study subjects according to presence of disease

DISEASE	MALE (%)	FEMALE (%)	TOTAL (%)
PULMONARY TB	17 (25)	21 (30.9)	38 (55.9)
TUBERCULAR PLURAL EFFUSION	8 (11.8)	10 (14.7)	18 (26.5)
COPD	0 (0)	5 (7.4)	5 (7.4)
PNEUMONIA	0 (0)	2 (2.9)	2 (2.9)
MALIGNANCY	2 (2.9)	0 (0.0)	2 (2.9)
BRONCHITIS	0 (0)	1 (1.5)	1 (1.5)
SARI	0 (0)	1 (1.5)	1 (1.5)
LUNG ABSCESS	0 (0)	1 (1.5)	1 (1.5)
TOTAL	**27 (39.7%)**	**41 (60.3%)**	**68 (100%)**

Microbiologically confirmed pulmonary tuberculosis cases were found to be 55.9% and confirmed tubercular plural effusion cases were 26.5%. Other than tuberculosis COPD was diagnosed in 7.4% cases, pneumonia & malignancy in 2.9 % cases.



Area Under the Curve				
Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.722	0.071	0.016	0.582	0.863

In the present study, the mean serum ADA value in patients of tuberculosis was 26.93 ± 16.44 U/L when compared to mean serum ADA value of 17 ± 5.78 U/L in patients of non-tubercular diseases group, showed higher significant mean difference between two groups and was also statistically significant with a p value of 0.04386. The best cut-off point was 15 U/L in which sensitivity and specificity were 85.7 % & 33.3% respectively.

Table No.3: Distribution of study subject according to presence of disease & test results.

TEST	TUBERCULOSIS		TOTAL
	PRESENT	ABSENT	
POSITIVE	48 (85.7%)	8 (66.7%)	56 (82.4%)
NEGATIVE	8 (14.3%)	4 (33.3%)	12 (17.6%)
TOTAL	56 (100)	12 (100)	68 (100%)

Out of 68 study subjects it was found that 56 study subjects were having Tuberculosis. Among 56 confirmed tuberculosis patients test were positive in 48 patients, thus sensitivity of serum ADA to diagnose Tuberculosis was 85.7%.

Among 12 cases in which Tuberculosis was not present, test detected 4 cases as negative for tuberculosis, thus specificity of this test was 33.3 %. Positive predictive value of Serum ADA to diagnose tuberculosis was 85% & negative predictive value was 33 %

DISCUSSION

Early diagnosis and treatment is the most important aspect of the evaluating tuberculosis. Diagnosis of Tuberculosis is based on clinical findings, radiographic changes and sputum smear examination for acid fast bacilli. But there are some variations between clinical and radiological findings and that may become false negative. Therefore it is of vital importance to do some rapid and useful tests for the detection of tuberculosis.

In present study, serum ADA level was a suitable index for diagnosing tuberculosis. High sensitivity was observed in serum level of 15 U/L. For that reason, serum ADA could be used for diagnosis of tuberculosis.

Estimation of Adenosine deaminase (ADA) is a useful surrogate marker for tuberculosis in serosal fluids. There are several studies also suggested that the use of serum adenosine deaminase levels in pulmonary tuberculosis and showed that the serum ADA levels is significantly higher in pulmonary tuberculosis patients than other non-tuberculous respiratory diseases such as lung cancer, chronic obstructive pulmonary disease, pneumonia.[6]

Adenosine, a purine nucleotide which is generated at sites of injury and inflammation and interacts with G protein coupled receptor to regulate their function. CD26-Adenosine deaminase interaction is a key role in cell mediated immunity. The enzyme adenosine deaminase is predominately a T lymphocyte enzyme and its plasma activity is high in various diseases where cell mediated immunity is stimulated such as tuberculosis.[7]

In this study, the mean serum ADA value in patients of sputum positive pulmonary tuberculosis was 26.93 ± 16.44 U/L when compared to mean serum ADA value of 17 ± 5.78 U/L in patients of non-tubercular respiratory diseases group, showed higher significant mean difference between two groups and was also statistically significant with a p value of 0.04386. Similarly Meena Verma et al[8], Jhamaria Jp et.al[9], also showed in their study significant higher mean difference of serum adenosine deaminase levels between sputum positive pulmonary tuberculosis and non tuberculous respiratory diseases like chronic obstructive pulmonary diseases, pneumonia with a statistically significant raised serum ADA values in pulmonary tuberculosis.

In present study, sensitivity and specificity were 85.7 % & 33.3% respectively. Diagnostic value of serum ADA in pulmonary TB has been assessed only in few numbers of studies. Pairs et al.[10] reported an increase in ADA level in TB pleural effusion; other studies have also confirmed such an increase in TB pericardial effusions, peritoneum, and central nervous system (CNS). The main reason for the increased ADA levels in pleural effusion is the movement of T lymphocytes toward this area. Increase in ADA level is the result of a tropical inflammatory reaction caused by monocytes and macrophages. When alveolar macrophages are infected by mycobacterium, this enzyme could be found in serum during active pulmonary disease. When TB infection is controlled, growth-markers of lymphocytes decrease; leucocytes will decrease in serum ADA levels concurrent with the decrease in lymphocytes. Because of this, serum ADA level could be utilized as a treatment response index.[11]

In this present study, the best cut-off point was 15 U/L in which sensitivity and specificity were 85.7 % & 33.3% respectively& Positive predictive value of Serum ADA to diagnose tuberculosis was 85% & negative predictive value was 33 %. In Gupta et al.'s study[12] sensitivity, specificity, positive predictive value, and negative predictive value were 92.8%, 90%, 92.8%, and 90%, respectively, for diagnosis of TB in pleural effusion with an ADA level of more than 40. In Conde et al.'s study[13] ADA level of 14 U/L was chosen as cut-off point. Stevanovic et al [14] assessed serums of extra-pulmonary TB patients and in a cut-off point of 24, sensitivity and specificity were 94.3% and 92.2%, respectively; in their study, serum ADA level decreased as treatment started.

CONCLUSIONS

According to this study, serum ADA level is proposed as a proper index for TB diagnosis; in a cut-off point of 15, its sensitivity and specificity are calculated as 85.7 % & 33.3% respectively

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