Diagnostic Accuracy of Cerebrospinal Fluid Adenosine Deaminase Activity in Tuberculous Meningitis

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ABSTRACT
Tuberculous meningitis remains an important cause of morbidity and mortality in developing countries like India.It often poses diagnostic problem to the clinicians, and the prognosis of the disease depends on the stage at which the treatment is started. Adenosine deaminase (ADA) activity is a quick noninvasive method to diagnose of tuberculous meningitis.(TBM) compared to other methods which are less diagnostic and time consuming. The present study was conducted to evaluate the diagnostic accuracy of a cutoff point of 8IU/L of ADA activity in the cerebrospinal fluid for the diagnosis of tuberculous meningitis(TBM) .CSF from 85 patients suffering from meningitis and other CNS disorders were collected and ADA activity was determined..There was a significant elevation of ADA in TBM patients compared to Non TBM group which consisted of bacterial meningitis, encephalitis and other cases. The study showed a sensitivity, specificity and accuracy of of 95% ,92%and 92% respectively In conclusion ,the results of the present study confirms that CSFADA activity, withthe cut off value of 8 IU/L is found to have good sensitivity, specificity and accuracy and can be a good diagnostic marker for tuberculous meningitis. It is simple, inexpensive, takes less time to perform and thus can be considered as a rapid diagnostic test for tuberculous meningitis.
Key words: *ADA,CSF, tuberculous meningitis, T lymphocytes,*

INTRODUCTION

Tuberculous meningitis is an important cause of morbidity and mortality in developing country like India. It often poses diagnostic problem to the clinicians and the prognosis of the disease is closely related to the stage at which the treatment is started. The diagnosis of TBM depends upon the detection of acid fast bacilli in CSF and culture for mycobacterium tuberculosis which takes about 6-8 weeks. However, the sensitivity of CSF ZN staining is 2–87%, and CSF culture is positive for *M. tuberculosis* in 25–75% of cases [1-7]. The characteristic cytological and biochemical changes in the CSF are also variable and may even be absent. Newer methods for diagnosing tuberculosis are based on phenotypic and genotypic techniques. Because of the, high cost of these tests they cannot be used widely in developing countries. A simple and cost-effective test for the diagnosis of tuberculous meningitis patients

would help to make diagnosis easier.CSF ADA levels measurement can be utilized as rapid and inexpensive test to differentiate TBM from other causes of meningitis.

ADA is a purine catabolic enzyme ubiquitous in mammalian tissues. Catabolic pathways involving DA were first reported in 1984.ADA activity is found to be greatest in lymphoid tissue .It is required for the proliferation and differentiation of lymphocytes and the principle biological activity is seen in Lymphocytes.[8] Raised levels of the enzyme activity have been found in tubercular pleural[9] peritoneal [10] and pericardial fluids [11] and cerebrospinal fluid of patients with TBM.[12.13,14]

The present study was conducted with the following objectives: To study the usefulness of the current cut off point of 8 IU/L of ADA activity in the diagnosis of TBM by determining the sensitivity and specificity and accuracy.

MATERIALS AND METHODS

The study was conducted in a tertiary hospital in Bangalore.85 patients between the age group of 20-60, both males and females who were admitted in the hospital for various central nervous system problems were taken as subjects for this study. Cerebrospinal fluid was obtained by performing lumbar puncture on the patients by the physician and sent to biochemistry laboratory for various biochemical parameters including the estimation of ADA. The analysis of ADA was done immediately by the colorimetric procedure of Guisti and Galanti [158], employing reagents optimized by Kaplan [16]

The subjects were divided into two groups. Tuberculous meningitis group (TBM) and nontuberculous meningitis groups.(Non TBM). The TBM group consisted of 25 patients with the confirmed diagnosis of TBM with a positive CSF profile and positive culture and biopsy from any other site. The Non TBM group consisted of 60 patients who were diagnosed to have bacterial meningitis, encephalitis, and seizures of unknown origin.

STATISTICAL METHODS

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance, Student t test (Two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups and Inter group analysis.

STATISTICAL SOFTWARE

Diagnostic statistics viz. Sensitivity, Specificity, PPV, NPV and Accuracy have been computed to find the correlation of ADA for diagnosis with tuberculosis patients. Student t test (Two tailed, independent), Sensitivity and Specificity using standard statistical software package.[17,18,19]

RESULTS

Table 1: % of people in both tubercular and non tubercular group with ADA levels >8 IU/L OR < 8 IU/L

ADA U/L	Tuberculous meningitis (n=25)		Non TBM (n=60)	
	No	%	No	%
>8 IU/L	24	96	5	8.33
<8IU/L	1	4	55	91.67
Total	25	100	60	100

Inference: ADA levels were significantly elevated in TBM group compared to Non TBM group. P value<0.001

Table 2: Mean ADA levels in two groups of patients studied.

Group	Number of cases	Mean+/- SD
Tuberculousmenigitis	25	12.4+/-6.4
Non TBM	60	3.5+/-2.1

Inference: Mean ADA levels were significantly elevated in TBM group compared to Non TBM group.
P value<0.001

Table 3: Components of Diagnostic accuracy with a cut off point of 8IU/L of ADA activity.

Sensitivity	95%
Specificity	92%
Positive predictive value	83%
Negative predictive value	98%
Accuracy	92% (0.92)

Diagnostic value based on accuracy (0.9-1)= Excellent test.

DISCUSSION

The results of our study show a significant (P<0.001) rise in mean ADA levels in TBM group compared to Non TBM group. This shows that ADA levels in CSF are very useful in diagnosis of TBM and differentiate this disease from other diseases. The raised ADA activity could be due to the increased secretion of ADA by T Lymphocytes due to the mycobacterial antigenic stimulation. The raised activity of ADA under antigenic stimulation reflects a good cell mediated immunity. [20] Several studies have shown the use of CSF-ADA in diagnosing TBM, differentiating it from other forms of meningitis with different cut off points. [21,22,23,24]. In the present study a cut off level of 8IU/L was used which gave a sensitivity and specificity of 95% and 92% respectively. The accuracy value of 0.92 shows that it is an excellent test for the diagnosis of tuberculous meningitis. In conclusion, the results of the present study confirms that CSFADA activity, with the cut off value of 8 IU/L is found to have good sensitivity, specificity and accuracy and can be a good diagnostic marker for tuberculous meningitis. It is simple, inexpensive, takes less time to perform and thus can be considered as a rapid diagnostic test for tuberculous meningitis.

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