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Original Article

Value of Adenosine Deaminase Level for the Differential diagnosis various meningitis.

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ABSTRACT

Objective :- Tuberculosis kills 3.70 lakh patients in India every year, out of which 7-12 % are with meningeal involvement. Delay in its diagnosis and initiation of treatment results in poor prognosis and sequelae in up to 25% of cases. The aim of the present study is to look for a simple, rapid, cost effective and fairly specific test in differentiating tubercular etiology from other causes of meningitis. In the present study we measured the adenosine deaminase (ADA) activity in cerebrospinal fluid (CSF) of TBM and non-TBM patients. Material and method : 150 patients were studied and divided into four groups: TBM culture positive, TBM culture negative pyogenic meningitis and viral meningitis, depending upon the accepted criteria. CSF was drawn and ADA Value estimated. Results : Out of 65 tubercular patients, 64 had CSF ADA at or above the cutoff value while one had below. Out of 85 non- tuberculous patients, two had ADA levels at or above the cutoff value while 83 had below this value, Cut off value of test was 9 IU. For diagnosis of Tuberculous Meningitis specificity of the test is 97.65 Sensitivity is 98.46; positive predictive value is 98.81 with negative predictive value of 96.97. Conclusion :- It can be concluded that ADA estimation in CSF is not only simple, inexpensive and rapid but also fairly specific method for making a diagnosis of tuberculous etiology in TBM, especially when there is a dilemma of differentiating the tuberculous etiology from non-tuberculous ones. For this reason ADA estimation in TBM may find a place as a routine investigation.

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1. Introduction

Tuberculous meningitis (TBM) is an endemic disease in developing countries [1] At present 1/5th of the global annual new cases occur in India. Tuberculosis claims 100 lives per day, out of them 20% patients have TBM. Tuberculosis is became a social problem because it has emerged in the patients of AIDS and multidrug resistant tuberculosis. Tuberculous meningitis is a most dangerous form of tuberculosis. In region of Vadodara and Peripheral districts have found 226 suspected cases of MDR TB in a period of oct09- to march-10. It kills 3.70 lakh patients in India out of which approximately 10% patients have tuberculous meningitis [2] Incidence of TBM in developing countries is 7-12%. Delay in diagnosis and so in the start of effective treatment results in poor prognosis and sequelae in up to 25% of cases [3]. Available methods of diagnosis of TBM were evaluated [4] and all of them were found

to have low sensitivity and specificity There are several methods to diagnose tuberculous meningitis with accuracy like CSF culture, CSF PCR, but this methods are time consuming and costly respectively. In the developing countries which have lower socio-economic patients, which cannot afford expensive laboratory investigation. So we required a diagnostic stool for inexpensive and early detection of tuberculous meningitis.

Adenosine deaminase (ADA) is an enzyme in the purine salvage pathway that catalyzes the conversion of adenosine and deoxyadenosine to inosine and deoxyinosine respectively with the release of ammonia. It plays important role in differentiating lymphoid cells and is present in abundance in active T-lymphocytes whose concentration is inversely proportional to the degree of differentiation [5]. Its levels are ten times higher in T-lymphocytes than in erythrocytes. ADA is released by T cells during cell mediated immune response (CMI) to the tubercle bacilli. ADA is now being recognized as a marker of cell mediated immunity particularly as a marker of T lymphocyte activation. Adenosine deaminase levels (ADA) have also been considered by several researchers to differentiate tubercular disease from non-tubercular [6-10].

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2. Material and methods

In this study we have included 150 patients of age range 1 day to 65 years admitted to Dhiraj Hospital, Piparia during 2010-2011. Clinical and laboratory evidence was taken as inclusion criteria. Enzyme activity was measured in CSF and divided in four groups of patients. These four groups were characterised as given below.

- 1) Tuberculous meningitis culture positive
- 2) Tuberculous meningitis culture negative
- 3) Pyogenic meningitis
- 4) Viral meningitis

Specimen: CSF Obtained by Lumber Puncture with all aseptic precautions by clinician. Method: spectrophotometric method or the sensitive colorimetric method of Galanti and Gusti.[11]

2.1. Statistical Analysis : Data from the study was analysed separately using statistical Package for Social Sciences. Results are presented as Mean ± SD (Standard deviation).

Table No. 01: No. Cases in various types of meningitis

Type	Male	Female	Total	Percentage	Ratio M:F
TBM culture +ve	26	23	49	32.67%	1.13:1
TBM culture -ve	10	6	16	10.67%	1.67:1
Pyogenic meningitis	13	7	20	13.33%	1.86:1
Viral meningitis	43	22	65	43.33%	1.95:1
Total	92	58	150	100%	1.59:1

Table No.01 shows that TB meningitis is more common than Non TB meningitis. And in each type of meningitis Male are more affected than Female.

Table No. 02: Age distribution in various meningitis groups

AGE	TBM CULTURE +VE		TBM CULTURE -VE		PYOGENIC MENINGITIS		VIRAL MENINGITIS		TOTAL	
	NO.	%	No	%	NO.	%	No.	%	NO.	%
0-6 months	6	12.2	5	31.3	4	20.0	9	13.8	24	16.00
7-12 months	2	4.1	2	12.5	1	5.0	5	7.7	8	5.33
1yr- 5yr	7	14.3	0	0.0	0	0.0	6	9.2	16	10.67
5yr-10yr	2	4.1	1	6.3	0	0.0	3	4.6	6	4.00
10yr-18yr	8	16.3	1	6.3	1	5.0	10	15.4	18	12.00
18yr-50yr	20	40.8	6	37.5	13	65.0	30	46.2	71	47.33
>50yr.	4	8.2	1	6.3	1	5.0	2	3.1	7	4.67
Total	49	100	16	100	20	100	65	100	150	100

Table No. 02 shows that tuberculous meningitis is more common in 18 to 50 yr. of age.

Table No. 03 ADA (Mean ±SD), Sugar, Protein and cell count in various meningitis groups

TYPE OF MENINGITIS	MEAN ±SD ADA	ADA RANGE	MEAN SUGAR	MEAN PROTEIN	MEAN TOTAL COUNT	LYMPHO CYTE %
TBM CULTURE POSITIVE	25.08	8-112	29.87	96.95	130	88
TBM CULTURE NEGATIVE	9.80	09-48	28.81	94.81	56	91
PYOGENIC	5.42	2.0-14.78	32.45	425.95	1735	27
VIRAL	4.65	2.0-9.0	66.10	24.81	6	97

(p < 0.01) shows a highly significant difference between the tuberculous and non-tuberculous groups.

Table No.3 Shows that ADA level are higher in TB meningitis then Non TB meningitis

Table No. 04 Comparative analysis of disease wise distribution in meningitis

Type	Rajesh Baheti et al. [12]	O.P.mishra et al. [13]	Rajendra Prasad et al. [14]	Choi S. H. et al. [15]	P.Chaturvedi et al. [16]	Rajpalkashyap et al. [17]	N.Selva kumar et al. [18]	Gupta et al [19]	Present study
PYOG	07	19	15	09	24	41	61	21	20
ENIC	(14.2%)	(27.5%)	(19.7%)	(04.9%)	(43.60%)	(14.59%)	(53.5%)	(52.5%)	(13.33%)
TBM	24 (48.9%)	27 (39.1%)	29 (38.15%)	36 (19.78%)	24 (43.60%)	117 (41.6%)	26 (22.8%)	19 (47.5%)	65 (43.33%)
VIRAL	07 (14.2%)	10 (14.4%)	12 (15.78%)	130 (71.42%)	-	19 (06.7%)	10 (8.7%)		65 (43.00%)
CONTROL	11 (14.2%)	10 (14.4%)	20 (26.31%)	-	07 (12.72%)	104 (37.1%)	17 (14.9%)	40	-
TOTAL	49 (100%)	66 (100%)	76 (100%)	182 (100%)	55 (100%)	281 (100%)	114 (100%)	(100%)	150 (100%)

Table No. 05: Comparison of range of ADA level in various meningitis

Type	Rajesh Baheti et al. [12]	O.P.mishra et al. [13]	Rajendra Prasad et al. [14]	Choi S. H. et al. [15]	P.Chaturvedi et al. [16]	Rajpalkashyap et al. [17]	N.Selva kumar et al. [18]	Gupta et al [19]	Present study
PYOGENIC	1.6-5.6	0.0-8.0	0.48-4.44	4.1-10.6	8.72-21.97	5.11-13.96	1.0-10.9	2.571	2.0-14.78
TBM	6.2-21.8	4.0-22.5	3.33-9.55	5.2-20.2	3.91-228.96	2.99-26.94	2.5-25.4	27.168	8.0-112.0
VIRAL	1.11-8.3	1.5-5.0	0.1-4.44	0.2-4.9		4.99-9.0	-	0-6	2.0-9.0
CONTROL	0.33-2.8	0.0-3.8	0.5-5.5				0.0-1.6	0-6	-

In present study 65 cases of Tuberculous Meningitis and 85 cases of Non Tuberculous meningitis groups were studied, to differentiate Tuberculous Meningitis from other types by the help of estimation of CSF- Adenosine Deaminase. Out of 150 cases 43.33% cases were Tuberculous Meningitis, 13.33% of Pyogenic Meningitis, 24% was of Viral Meningitis and 19.33% cases were control group. In Tuberculous Meningitis 35.4% cases were under 5 years of age while maximum 40% cases found in age group of 18-50 years age group.

Out of 150 cases of study 61.33% males & 38.67% females. Tuberculous Meningitis Male: Female ratio was 1.24: 1. CSF ADA was measured in all cases. Mean CSF ADA level 18.96 was significantly raised in Tuberculous Meningitis as compared to other types.

For diagnosis of Tuberculous Meningitis cut off value of CSFADA in our study was >9.0 U/L.

For diagnosis of Tuberculous Meningitis specificity of the test is 97.65 Sensitivity is 98.46; positive predictive value is 98.81 with negative predictive value of 96.97.

Overall accuracy of the test is 98.00.

5. Conclusion

Meningitis is a significant cause of morbidity or mortality in ICU patients, which occurs due to varying etiology but Tuberculous Meningitis is more prevalent in elderly age group of patients. As these patients have lower socioeconomic status, more exposure to patients and habits.

Quick diagnosis & effective treatment is key to life. But not a single procedure has emerged which has the required degree of sensitivity and specificity for rapid diagnosis and differentiation of Tuberculous Meningitis and other types.

Following conclusions can be drawn.

- Prevalence of Tuberculous Meningitis is increasing day by day because of MDR TB and dangerous prevalence in AIDS patients.
- Males are more prevalent than Females.
- Tuberculous Meningitis is most frequently seen in 18-50 years of age group.
- CSF ADA is a cost effective highly sensitive; more specific single test to help a clinician for early and accurate diagnosis of Tuberculous Meningitis in association with clinic-pathological parameters.

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