ORIGINAL RESEARCH PAPER

Volume-7 | Issue-4 | April-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CORRELATION OF THE INITIAL LEVELS OF CSF-ADA WITH ADVERSE NEUROLOGICAL OUTCOME IN TUBERCULOUS MENINGITIS

Medical Science

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KEYWORDS

TBM is a syndrome of sub-acute lymphocytic meningitis in majority of patients. In developing countries TB meningitis is still a disease of childhood with the high incidence in the first three years of life. Tuberculous meningitis (TBM) can occur as the sole manifestation of TB or with pulmonary or other extra pulmonary sites. [1-3] The presumptive diagnosis of TBM is made when CSF shows lymphocytic pleocytosis with high protein and decreased sugar and is found to be sterile on the basis of absence of usual organisms on Gram staining and routine aerobic culture. The diagnosis is further supported by the score given by the Thwaites criteria [4]

[TABLE 1]. TB meningitis displays some clinical and radiological characteristics but the "gold standard" for diagnosis remains the identification of Mycobacterium tuberculosis in the CSF by direct staining of culture. Direct staining, however, is rarely successful and culturing of M. Tuberculosis can take 4 to 8 weeks. The yield of CSF culture and of direct demonstration of AFB in CSF is particularly low. To overcome this dilemma, a multitude of new tests are coming into vogue. Some of these include CSF-PCR for AFB, CSF – ADA levels, Adenosine Deaminase enzyme is produced by lymphocytes and monocytes and reflects cell mediated immunity. The enzyme is estimated easily by the colorimetric method. Isoenzyme ADA 2 is present only in macrophages and monocytes and they release it when stimulated in the presence of live microorganisms in their interior. This explains why ADA 2 is increased in biological fluids in the course of infectious diseases characterised by microorganisms infecting the macrophages. So, more the CSF ADA, more the inflammation. The aim of our study is to correlate the levels of CSF ADA levels at the initial diagnosis and the extent of neurological deficits, at the diagnosis and at the discharge. The neurological deficits were assessed by the MODIFIED RANKINS SCORE. [5,6,7] **[TABLE 2]**

MATERIALS AND METHODS

The study was a prospective study, done in the department of medicine and department of neurology from September 2015 to August 2016. The patients who got admitted with clinical picture commensurate with Meningitis in Medicine and Neurology department were assessed on Thwarts Criteria and those found to be likely cases of T.B.M, as per the criteria were included in the study.

INCLUSION CRITERIA:

Those subjects who gives informed consent for the study.
Patients fulfilling the diagnostic criteria of TBM based on the Thwarts criteria.

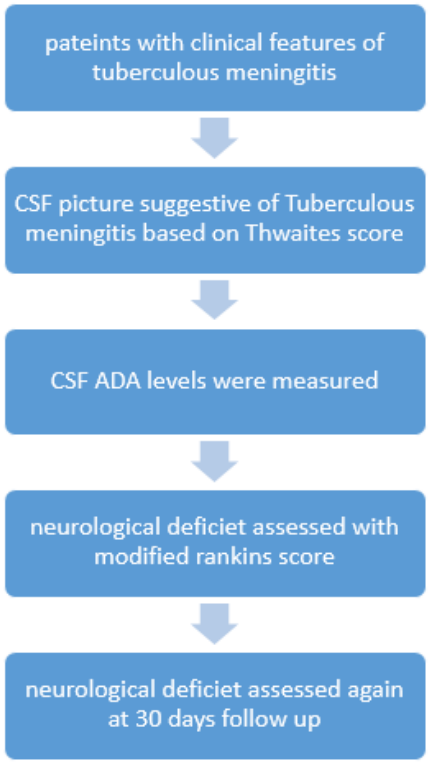
EXCLUSION CRITERIA:

1.Patients/attendants refusing consent.
2.Patients not fulfilling the Thwaites criteria.
3.Brain abscess
4.Head trauma

STUDY DESIGN:

Patients who presented with history and clinical features suggestive of TBM were included in this study. A criteria suggested by Thwarts et al [4] was used to label these patients to be suffering from TBM.

Patients satisfying the criteria thus, labelled as TBM were further evaluated. CSF-ADA values were measured in these patients, and values above 10 IU/L were taken to be positive. These patients were treated for TBM as per the standard protocol, and the morbidity and mortality were assessed at discharge and 30 days using the Modified Rankin Scale [5,6,7].



RESULTS

Table 3: ADA levels (Overall and Stage wise)

ADA values ranged from 3 to 251 units with a mean value of 32.97±40.86. Stage I & II had lower mean value (17.66±19.13) whereas Stage III had higher mean value (37.87±44.69). Statistically, this difference between two groups was significant (p=0.034).

Table 4: ADA Correlation with Thwaite's Score

ADA levels of patients with Thwaite's score -3 to 0 were significantly lower (19.20±14.41) as compared to those of patients with Thwaite's score -5 (43.54±50.54). Statistically, this difference was significant too (p=0.003).

Table 5: ADA Correlation with MRS-D Scores

Mean ADA values of patients with lower MRS-D scores (0 to 2) were

significantly lower as compared to those of patients with MRS-D scores 4 and 5 (p<0.001)

Table 6: ADA Correlation with MRS-30 Scores
Mean ADA values of patients with lower MRS-D scores (0 to 2) were significantly lower as compared to those of patients with MRS-D scores 4 and 5 (p<0.001).

DISCUSSION

TBM, is an important cause of chronic meningitis in our country with significant morbidity and mortality and early diagnosis and treatment are essential to decrease the adverse outcomes. Despite years of experience, it is over and under diagnosed. The subjects of the study were patients who were admitted with the clinical syndrome of meningitis and were diagnosed to be suffering from TBM based on the THWAITES CRITERIA. The mean value of ADA in patients who presented with advanced stages of TBM (Stage III) was significantly higher than those presented who presented in Group I and II -37.87% vs 17.66. there was statistically significant relation (p=0.034). The lower the Thwaites score, the more is its predictive value in the diagnosis of TBM. Patients with the lowest possible Thwaites score (-5, n=56) had mean ADA of 43.54. Those with higher score (-3 and more) had mean ADA at 19.20. This was statistically significant too(p=.003).

At discharge mean ADA value was significantly higher in patients with higher MRS scores (4 and 5). Similar trend was seen at 1 month. Mean ADA levels of patients who expired were significantly higher as compared to those patients who survived (p<.001).

CONCLUSION

ADA levels correlated well with the stage of the disease. Patients with advanced stages of TBM (Stage III and above) had mean ADA values significantly higher than patients with less advanced TBM Patients with lower Thwaites scores, had higher probabilities to be suffering from TB. Patient with lowest possible score had higher mean ADA. Patients were analysed at discharge and at 1 month. Mean ADA values were significantly higher in the patients with higher MRS scores. Also the mean ADA values of patients who expired were significantly higher than those who survived. This suggests that the higher the ADA levels, the worse the prognosis and greater the disability.

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