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ORIGINAL RESEARCH

Factors associated with poor outcome in tuberculous meningitis; study from a tertiary care referral Center

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Abstract
Background: Tuberculosis (TB) caused by Mycobacterium tuberculosis is a leading cause of death globally. While TB commonly affects the lungs, it can also manifest in other parts of the body, leading to extra-pulmonary TB (EPTB).The objective of this study is to explore the factors that contribute to a negative outcome in children affected by tuberculous meningitis (TBM).
Materials & methods:A total of 50 children were enrolled. Complete demographic and clinical details of all the patients was obtained. Only those patients were enrolled which were confirmed cases of TBM. A questionnaire was obtained and following details were recorded:Duration of symptoms,Duration of hospital stay, Signs and symptoms, and Clinical staging of the disease. Radiographic findings of all the patients were recorded. Poor clinical outcome is defined as death. All the results were recorded in Microsoft excel sheet and was subjected to statistical analysis using SPSS software.
Results: Mean age of the patients was 16.2 years. Headache, fever, vomiting and anorexia was seen in 70 percent, 66 percent, 40 percent and 10 percent of the patients respectively. Cranial nerve palsy and altered sensorium was seen in 30 percent and 46 percent of the patients respectively. While conducting univariate analysis, it was seen that altered sensorium, elevated CSF pressure, MRC staging III on admission and presence of vasculitic infarcts were considered as significant risk factors associated with poor prognosis.
Conclusion: The Modified Rankin Scale (MRC) at admission is one of the independent variables that significantly influence the outcome upon discharge in cases of paediatric TBM.
Key words: Tuberculous meningitis, Poor outcome

Introduction

Tuberculosis (TB) caused by Mycobacterium tuberculosis is a leading cause of death globally. While TB commonly affects the lungs, it can also manifest in other parts of the body, leading to extra-pulmonary TB (EPTB).[1,2] Tuberculous meningitis (TBM), a form of EPTB, occurs when the M. tuberculosis bacteria spread to the meninges and cerebrospinal fluid, resulting in a serious and often fatal condition. Diagnosing TBM, especially in children, is a challenging task as the symptoms are nonspecific, and the available diagnostic tests are invasive and time-consuming. Current diagnostic methods involve analysing cerebrospinal fluid (CSF) for white cell count, total protein, and glucose levels.[3] In TBM, typical CSF findings include elevated total protein, decreased CSF-to-serum glucose ratio, and increased white blood cell count with lymphocytic pleocytosis. Distinguishing TBM from other forms of infectious meningitis caused by viruses, bacteria, and fungi is crucial but complicated.[4,5] The clinical management of TBM is challenging due to incomplete understanding of the immunopathogenesis underlying the disease.[6] The objective of this study is to explore the factors that contribute to a negative outcome in children affected by tuberculous meningitis (TBM).

Materials & methods

The present study was conducted for assessing the factors associated with poor outcome in tuberculous meningitis; study from a tertiary care referral centre. A total of 50 children were enrolled. TBM was defined if one of the following criteria was met: (1) definite: acid fast bacilli (AFB, +) on cerebrospinal fluid (CSF) microscopy, or CSF TB-PCR(+), or M.tuberculosis cultured from CSF. (2) conclusive: symptoms and signs of meningitis and CSF findings (such as total white cell count > 5 cells × 106/L, protein > 0.45 g/L, glucose < 2.2 mmol/L, and CSF/serum glucose ratio < 0.5), plus at least one of the following (i) TB suggested by abnormal radiographic features (chest, or cerebral imaging), (ii)

positive TB assays (such as AFB, PCR, and culture) using non-CSF samples.Complete demographic and clinical details of all the patients was obtained. Only those patients were enrolled which were confirmed cases of TBM. A questionnaire was obtained and following details were recorded:

- Duration of symptoms,
- Duration of hospital stay,
- Signs and symptoms, and
- Clinical staging of the disease

Radiographic findings of all the patients were recorded. Poor clinical outcome is defined as death. All the results were recorded in Microsoft excel sheet and was subjected to statistical analysis using SPSS software.

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A total of 50 children were enrolled. Mean age of the patients was 16.2 years. Headache, fever, vomiting and anorexia was seen in 70 percent, 66 percent, 40 percent and 10 percent of the patients respectively. Cranial nerve palsy and altered sensorium was seen in 30 percent and 46 percent of the patients respectively. While conducting univariate analysis, it was seen that altered sensorium, elevated CSF pressure, MRC staging III on admission and presence of vasculitic infarcts were considered as significant risk factors associated with poor prognosis.

Table 1: Clinical profile

Symptoms	Number	Percentage
Headache	35	70
Fever	33	66
Vomiting	20	40
Anorexia	5	10
Night sweats	4	8
Weight loss	20	40
Seizures	15	30
Cranial nerve palsy	15	30
Altered sensorium	23	46

Table 2: Factors associated with poorer outcome

Variable	OR	p-value
Altered sensorium	0.329	0.000 (Significant)
Elevated CSF pressure	0.315	0.000 (Significant)
MRC stage III on admission	-1.952	0.001 (Significant)
Vasculitic infarcts	0.448	0.000 (Significant)

Discussion

Tuberculous meningitis (TBM) poses a significant health threat, particularly in children, with the potential for substantial morbidity and mortality. Understanding the factors associated with poor outcomes in TBM is crucial for improving patient care and management of the disease. Therefore, research efforts are directed at identifying these factors to enhance the understanding of TBM's clinical course and to develop strategies that can help mitigate the risks associated with poor outcomes in affected individuals. [7]

Treating tuberculous meningitis (TBM) presents greater challenges and a higher risk of treatment failure compared to pulmonary TB. The insights gleaned from our data could play a pivotal role in enhancing the management of childhood TBM, thereby addressing the existing difficulties in treatment. Previous studies have underscored the detrimental impact of treatment delays on TBM outcomes. Consistent with findings from Verdon et al. and Sheu et al.,[8,9] delays in initiating TBM treatment have been linked to poorer prognosis, reinforcing the critical importance of timely intervention in optimizing patient outcomes.

A total of 50 children were enrolled. Mean age of the patients was 16.2 years. Headache, fever, vomiting and anorexia was seen in 70 percent, 66 percent, 40 percent and 10 percent of the patients respectively. Cranial nerve palsy and altered sensorium was seen in 30 percent and 46 percent of the patients respectively. While conducting univariate analysis, it was seen that altered sensorium, elevated CSF pressure, MRC staging III on admission and presence of vasculitic infarcts were considered as significant risk factors associated with poor prognosis.The elevated level of cerebrospinal fluid (CSF) protein in tuberculous meningitis (TBM) is an indicator of blood-brain barrier disruption and CNS circulation blockage associated with an intensified immunological response. [10] Additionally, the characteristic CSF findings in TBM patients, such as low glucose, high protein, and pleocytosis, are diagnostic criteria for the condition. A high level of CSF protein has been associated with adverse outcomes in both adult and childhood TBM cases. The study also highlighted recent findings suggesting that the faster normalisation of CSF parameters is associated with improved outcomes, while increased CSF protein levels may contribute to the formation of basal exudates, potentially leading to cranial nerve involvement.[11,12]Wang MS et al investigated the risk factors associated with poor outcome of childhood TBM. Between January 2006 and December 2019, consecutive children patients (≤ 15 years old) who had a diagnosis of TBM were included for the analysis. The demographic, clinical, laboratory, and radiographic data were collected from the electronic medical records retrospectively. Poor outcome was defined as death or transfer to a higher-level hospital. Patients were then divided into good and poor outcome groups. Subsequently, risk factors for poor outcome were estimated using univariate and multivariate logistic regression analysis. A total of 149 children with TBM was enrolled, twenty-two patients suffered poor outcome, including 16 transfers to a higher-level hospital and 6 deaths, and the remaining 127 patients were classified as good outcome group. Further multivariate analysis revealed that coma (age- and sex-adjusted OR = 6.425, 95% CI: 1.743, 23.676; $P < 0.01$) and cerebrospinal fluid (CSF) protein (> 1188.3 mg/L; age- and sex-adjusted OR = 4.680, 95% CI: 1.469, 14.902; $P < 0.01$) were associated with the poor outcome of childhood TBM. Childhood TBM remains to have a high mortality rate in China. High CSF protein and coma were identified as risk factors for poor outcome of childhood TBM.[13]

Conclusion

The Modified Rankin Scale (MRC) at admission is one of the independent variables that significantly influence the outcome upon discharge in cases of TBM.

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