Neuroimaging Changes and Treatment Outcome of Tubercular Meningitis- Experiences 22 Cases in a Tertiary Care Center

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Abstract:

Background: Tuberculous meningitis (TBM) is caused by Mycobacterium tuberculosis (M. tuberculosis) and is the most common form of central nervous system (CNS) tuberculosis (TB).The prevalence of TB meningitis remains largely underestimated because clinical manifestations are nonspecific in early stages of the disease. Prompt diagnosis is critical for initiating appropriate therapy, facilitating measures to prevent dissemination of this highly contagious disease and to combat fatal complication in children

Aims: To evaluate the role of neuroimaging changes and treatment outcome of tubercular meningitis.

Methods: This prospective hospital-based cohort study was conducted in Department of Paediatric Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during January 2022 to December 2022. Children age belonged to 1 month to 10 year diagnosed as TBM during study period were enrolled in this study. Detailed history, clinical examination, CSF analysis and other relevant investigations were done. Data were recorded in standard questionnaire. Statistical analyses of the results were obtained by using window-based computer software devised with Statistical Packages for Social Sciences (SPSS-22).

Results: Total 22 diagnosed case of TBM was enrolled and evaluated. Among them two third (63.63%) children were in 5-10 year age group. Male (59%) were outnumbered than female (36.36 %).Male female ratio was 1.6:1. More than half (59%) of patients came from urban area. All of the patients were vaccinated. Cent percent (100%) patients were presented with fever followed by headache (77.27%), sign of meningeal irritation (54.54%), vomiting (54.54%) and seizures (50%). Most common complication was hemiparesis (45.45%) followed by cranial nerve palsy (40.90%), visual problem (9.09%) and hydrocephalus (4.54%). Abnormal neuroimaging changes were found in 100% cases. Common findings were hydrocephalus (40.90%), tubercloma (36.36%), basilar enhancement (18.18%), Benign enlargement of subdural space & cerebellar hyperintensity (9%) and thalamic infract was present in 4.54% cases. Anti TB and steroid treatment were given in 100% cases and among them18.18% cases were required shunt procedure.

More than one-third cases (40.90%) were completely normal without any no sequelae. Among abnormal sequelae found in two third (59%) cases. Speech impairment (36.36%) was most common followed by GDD (18.18%), hemiparesis (13.63%), quadriparesis (9.09%) and epilepsy in 9.09% cases.

Conclusion: In our study all children of TBM were presented with fever followed by other predominant clinical features headache, vomiting, seizures and sign of meningeal irritation. Abnormal neuroimaging changes were found in all cases. Common findings were basilar enhancement, hydrocephalus, tubercloma, benign enlargement of subdural space & cerebellar hyper intensity and thalamic infract. After treatment more than one-third cases were completely normal without any no sequelae.

Keywords: Tubercular Meningitis, Neuroimaging changes

(J Bangladesh Coll Phys Surg 2024; 42: 214-218)
DOI: https://doi.org/10.3329/jbcps.v42i2.72391

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Received: 16 Sept. 2023 **Accepted:** 5 Dec. 2023

Introduction

Tuberculous meningitis (TBM) is caused by Mycobacterium tuberculosis (M. tuberculosis) and is the most common form of central nervous system (CNS) tuberculosis (TB).

Globally, almost half a million children become sick with TB every year, 20-30 per cent being affected by extra pulmonary TB (EPTB). Almost 10-20 per cent of the children with TB live in high TB burden countries[1]. Even though TBM constitutes a small proportion of the total reported TB cases (around 1%), it causes a disproportionate amount of suffering with higher rates of mortality and morbidity, especially in young children[2]. Delay in diagnosis and effective treatment results in poor prognosis and sequelae in up to 25% of cases.[3,4]

The prevalence of TB meningitis remains largely underestimated because clinical manifestations are nonspecific in early stages of the disease.[5] The diagnosis poses a special challenge as it is often missed or misdiagnosed due to its variable presentation in children. Prompt diagnosis is critical for initiating appropriate therapy, facilitating measures to prevent dissemination of this highly contagious disease and to combat fatal complication in children. Apart from CSF study, neuroimaging plays a crucial role in the early and accurate diagnosis of tuberculous meningitis and its disabling complications.[6] There is still dearth of studies regarding clinico-radiological findings of TBM with relative outcome of tubercular meningitis in children in a high burden developing country.

So this Prospective hospital based cohort study was conducted to evaluate the clinical and radiological profile and treatment outcome of TBM cases.

Methods: This prospective hospital based Cohort study was conducted in Department of Paediatric Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, during January 2022 to December 2022. A total of 22 Infant and children, age belonged to 1month-10 year, who diagnosed as Tubercular meningitis during study period were enrolled and evaluated in this study. Detailed history, clinical examination, CSF analysis and other relevant investigations were done. Data were recorded in standard questionnaire. Statistical analyses of the results were obtained by using window-based computer software devised with Statistical Packages for Social Sciences (SPSS-22).

Results: Total 22 diagnosed case of TBM was enrolled and evaluated. Among them two third (63.63%) children was in 5-10 year age group. The mean age was 4.27±1.99 years ranged from 2 to 11 years). Almost two-third (59%) of patients were male and 36.36 % were female. More than half (59%) of patients came from urban area. Cent percent patients were vaccinated. Hundred percent (100%) patients presented with fever followed by headache (77.27%), sign of meningeal irritation (54.54%), vomiting (54.54%) and seizures (50%). Most common complication was hemiparesis (45.45%) followed by cranial nerve palsy (40.90%), visual problem (9.09%) and hydrocephalus (4.54%). High CSF protein was found in 40.90% cases followed by high cell count in 31.81% cases. Gene X-pert in CSF was positive in 22.72% cases.

Neuroimaging changes were found in 100% cases. Common findings were hydrocephalus (40.90%), tubercloma (36.36%) and basilar enhancement (18.18%) Benign enlargement of subdural space & cerebellar hyperintensity (9%) and thalamic infract was present in 4.54% cases. Anti TB and steroid treatment were given in 100% cases and among them18.18% cases were required shunt procedure.

More than one-third cases (40.90%) were completely normal without any no sequelae. Abnormal sequelae were found in about two third (59%) cases. Speech impairment (36.36%) was most common sequelae followed by GDD (18.18%), hemiparesis (13.63%), quadriparesis (9.09%) and epilepsy in 9.09% cases.

Results:

Table-I

Base line characteristics of study cases (n=22)

	Number	Percentage (%)
Age		
<1 year	3	13.63
1-5	5	22.72
5-10	14	63.63
Sex		
Male	14	63.63
Female	8	36.36
Residence		
Rural	13	59.09
Urban	9	40.90
Social Class		
Lower	9	40.90
Middle	13	59.09
Upper	0	0.00
TB Contact	8	36.36
BCG Vaccination	22	100.00

Table-I showed majority of study children (63.63%) were in 5-10 years age group. Male patient (63.63%) were

outnumbered than female (36.36%). Male and female ratio was 1.75:1. About 59% children were from rural area. 60% cases came from middle class back ground. About 36.36% case had history of contact with TB patient. All (100%) cases were BCG vaccinated.

Table-II

Distribution of study cases by clinical presentation (n=22)

Category	Number	Percentage (%)
Fever	22	100
Headache	17	77.27
Vomiting	12	54.54
Seizure	11	50.
Unconsciousness	1	4.54
Sign of meningeal irritation	12	54.54

Table II showed 100% patients presented with fever followed by headache (77.27%), sign of meningeal irritation (54.54%), vomiting (54.54%) and seizures (50%).

Table-III

Distribution of the study cases by Complication (n=22)

Category	Number	Percentage (%)
Hemiparesis	10	45.45
Cranial nerve palsy	9	40.90
Hydrocephalus	1	4.54
Aphasia	1	4.54
Visual problem	2	9.09

Table III showed that most common complication was hemiparesis (45.45%) followed by cranial nerve palsy (40.90%), visual problem (9.09%) and hydrocephalus (4.54%).

Table-IV

Distribution of the study cases by CSF finding (n=22)

Category	Number	Percentage (%)
High protein	9	40.90
High cell count	7	31.81
Low sugar	5	22.72
Gene X-pert	5	22.72

Table IV showed abnormal CSF findings among the study cases. High CSF protein was found in 40.90% cases followed by high cell count in 31.81% cases . Gene X-pert in CSF was positive in 22.72% cases.

Table-V

Distribution of the study cases by Neuroimaging changes (n=22)

Category	Number	Percentage (%)
Normal	0	0.00
Abnormal	22	100
Hydrocephalus	9	40.90
Tubercloma	8	36.36
Thalamic Infract	1	4.54
Basilar enhancement	4	18.18
Bening enlargement of subdural space	2	9.09
Cerebellar hyperintensity	2	9.09

Table V showed Neuroimaging changes in 100% cases. Common findings were hydrocephalus (40.90%), tuberculoma (36.36%) and basilar enhancement (18.18%) Benign enlargement of subdural space & cerebellar hyperintensity (9%) and thalamic infract was found in 4.54% cases of TBM.

Table-VI

Distribution of the study cases by Treatment (n=22)

Category	Number	Percentage (%)
Anti TB drug+Steroid	22	100.00
Anti TB drug+Steroid+ shunt	4	18.18

Table VI showed Anti TB and steroid were given in 100% cases and among them18.18% cases need VP shunt.

Table-VII

Distribution of the study cases by follow up of TBM cases (n=22)

Category	Number	Percentage (%)
Normal (no sequelae)	9	40.9
Abnormal (sequelae)	13	59.09
Hemiparesis	3	13.63
Quadriparesis	2	9.09
Speech impairment	8	36.36
Epilepsy	2	9.09
Global developmental delay (GDD)	4	18.18

Table VII showed after 1 year follow up, 40.90% cases were normal with no sequelae. Among abnormal sequelae developmental regression was most (36.36%) followed by GDD (18.18%), hemiparesis (13.63%), quadriparesis (9.09%) and epilepsy in 9.09% cases.

Discussion:

TBM is a fatal but still preventable and treatable disease among children. Death and disability eventually follow if remain untreated. Here the study had included 22 TBM cases with clinical and radiological profile along with their outcome.

In this study majority of study children (63.63%) were in 5-10 years age group. According to surveillance data from Germany, of the total pediatric TB patients, TBM occurred in 3.9 per cent of the children in less than five-year age group, 2.2 per cent in 5 to 9 yr of age and 1.3 per cent in 10 to 14 year of age[7]. A bit difference to our study may be attributed to the geographical variation along with improved diagnostic modality in that region. Male patient (63.63%) were more than female (36.36%) male and female ratio was 1.75:1. In a study in Afghanistan by Rahimi BA et al reported among 818 children with TBM had female predominance.[8] Poor implementation of vaccination program along with religious tabu may be a contributing factor to the female in that region.

In the current study about 36.36% case had history of TB contact with TB patient. In another study in South Africa it was reported that 70% (21/30) had household contact with an adult TB source case.[9] Lack of appropriate investigation facilities and proper tracing of index cases may be the causative factors of undetermined contacts.

All of study populations presented with fever followed by headache (77.27%), sign of meningeal irritation (54.54%), vomiting (54.54%) and seizures (50%). In a study by Wang DM et al. concluded that the most common symptoms of culture-confirmed children's patients with TBM included fever (90.5%), headache (71.4%), neck stiffness (83.3%), vomiting (52.4%), cough (45.2%), disturbance of consciousness (33.3%) and varying degrees of convulsions, weight loss and night sweats[10]. This study findings support our findings.

The most common complication encountered was hemiparesis (45.45%) followed by cranial nerve palsy (40.90%), visual problem (9.09%) and hydrocephalus (4.54%). In another study by Mania A et al. observed focal weakness, cranial nerve palsy, hydrocephalus were the most common complications[11]. Findings suggest same results like the current study.

Neuroimaging changes in our study was evidenced in 100% cases. Common findings were hydrocephalus (40.90%), tuberculoma (36.36%) and basilar enhancement (18.18%). In a study by Azeemuddin M et al. observed CT scans, tuberculomas were found in 25 (12%), infarction in 54 (25%), basal meningeal enhancement in 29 (14%), and hydrocephalus in 84 (40%). Additionally, their study showed development of new lesions on subsequent neuroimaging suggesting a dynamic and progressive nature of the disease process in some individuals[12]. Although our study had a similar neuroimaging finding but subsequent neuroimaging findings were lacking to reveal the progressive nature of the disease.

In the current study high protein in CSF was present 40.90% cases followed by high cell count (31.81%) and low sugar. Gene X-expert in CSF was positive in 22.72% cases. However, this 'typical' CSF pattern (elevated protein, lymphocytic pleocytosis, and low glucose) cannot reliably distinguish TBM from other forms of sub-acute meningitis[13]. While Israni AV et al. observed patients dying of TBM had higher mean CSF protein values and also CSF lymphocytic pleocytosis compared to those who survived[14]. Thus, CSF findings may contribute to the prognosis of the disease.

18.18% of our studied cases needed VP shunt. The rate of ventriculoperitoneal shunting was lower (8.4%) in other study[15]. Early diagnosis, early initiation of treatment may contribute to less requirement of shunt surgery.

Among abnormal sequelae developmental regression was most (36.36%) followed by GDD (18.18%) and focal motor deficit in our study. In a study done in South Africa observed 36.6% of TBM cases suffered some form of disability in terms of motor, visual and hearing deficit. Patients who responded to treatment did well despite initial depressed neurological function, and almost half the cohort made a good clinical recovery attributed to prompt appropriate treatment[16]. The neurodevelopmental outcome is influenced by disease pathology in combination with social, educational, and environmental factors.

This was a single center study with a small sample of study participants. It may not reflect the adequate scenario of TBM. But all the study participants had abnormal neuroimaging findings mostly along with adverse outcomes. This may provide insights towards the importance of neuroimaging in this group of population with an additional need of early management to prevent the mortality and morbidities as well.

Conclusion

In our study abnormal neuroimaging changes were found in all cases. Common findings were basilar enhancement, hydrocephalus, tubercloma, benign enlargement of subdural space & cerebellar hyperintensity and thalamic infract. After treatment more than one-third cases were completely normal without any sequelae. Abnormal neurological sequelae, speech impairment, hemiparesis, epilepsy and GDD were found in about two third cases of TBM.

Recommendation: Despite the progress about Neuroimaging and new generation antibiotic, we still cannot treat TBM early and promptly. So multiple sequelae may be the consequence. So further extensive studies is needed to identify the early clue for diagnosis of TBM and appropriate management.

Acknowledgement

We are very thankful to all faculties and residents of Pediatric Neurology Department of BSMMU for their continuous support. We also thankful to Department of Biochemistry and Radiology & Imaging department of BSMMU.

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