

## Original Research Article

# Clinical profile of tuberculous meningoencephalitis in pediatric patients at a tertiary care center

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## ABSTRACT

**Background:** Tuberculous meningoencephalitis (TBME) is the most severe form of childhood tuberculosis and is associated with high mortality and long-term neurological sequelae. Despite availability of effective anti-tubercular therapy, delayed diagnosis, malnutrition, and poor immunization status continue to adversely affect outcomes in children.

**Methods:** This prospective observational study was conducted from January 2023 to June 2024 in the paediatric wards and pediatric intensive care unit of a tertiary care centre in western India. Children aged 1 month to 12 years diagnosed with TBME were included. Detailed clinical evaluation, laboratory investigations, neuro imaging, Bacillus Calmette–Guérin (BCG) vaccination status, nutritional status, complications, and outcomes were recorded using a pre-structured proforma.

**Results:** A total of 75 children with TBME were studied. Majority of patients (68%) were below five years of age. Fever, seizures, vomiting, and altered sensorium were the most common presenting features. BCG-vaccinated children had milder disease and better outcomes. Malnutrition was significantly associated with advanced disease stage, increased complications, and poor neurological outcome. Hydrocephalus was the most common complication. Mortality was higher in children with severe malnutrition and advanced stage of disease.

**Conclusion:** TBME remains a serious and life-threatening illness in children. BCG vaccination and good nutritional status play a protective role. Early diagnosis, prompt initiation of antitubercular therapy, and aggressive management of complications are essential to reduce morbidity and mortality.

**Keywords:** Tuberculous meningoencephalitis, Childhood tuberculosis, BCG vaccination, Malnutrition, Hydrocephalus

## INTRODUCTION

Tuberculosis (TB) continues to be a major public health problem in developing countries, including India, with a significant contribution to childhood morbidity and mortality. Children are particularly vulnerable to severe and disseminated forms of tuberculosis due to immature immune responses.<sup>1</sup>

Tuberculous meningoencephalitis (TBME) is the most severe manifestation of extra pulmonary tuberculosis in children and accounts for substantial mortality and long-

term neurological sequelae.<sup>2</sup> It results from hematogenous dissemination of *Mycobacterium tuberculosis* from a primary focus, most commonly pulmonary or lymph node tuberculosis, to the central nervous system.<sup>3</sup>

The clinical presentation of TBME in children is often insidious and nonspecific in the early stages, with symptoms such as fever, vomiting, and irritability. As the disease progresses, children may develop seizures, altered sensorium, focal neurological deficits, and features of raised intracranial pressure.<sup>4</sup> Delay in diagnosis and

initiation of antitubercular therapy is a major determinant of poor outcome and increased mortality.<sup>5</sup>

Children below five years of age are at a higher risk of developing TBME and tend to present with more severe disease. Younger age has been consistently associated with advanced stage at presentation, higher frequency of complications, and worse neurological outcomes.<sup>6</sup>

Bacillus Calmette–Guérin (BCG) vaccination has been shown to offer protection against severe forms of tuberculosis such as TB meningitis and miliary tuberculosis, although its efficacy against pulmonary tuberculosis is variable. Several studies have demonstrated reduced severity of illness and better outcomes among BCG-vaccinated children with TBME.<sup>7</sup>

Malnutrition is another important risk factor influencing susceptibility, severity, and outcome of childhood tuberculosis. Malnourished children have impaired cell-mediated immunity, which predisposes them to severe and disseminated disease. The coexistence of malnutrition and TBME has been associated with increased complications, prolonged hospital stays, and higher mortality.<sup>8</sup>

Despite availability of effective antitubercular therapy and improved supportive care, TBME remains a diagnostic and therapeutic challenge in paediatric practice, particularly in resource-limited settings. There is limited recent data from western India describing the clinical profile, complications, and outcomes of childhood TBME in relation to BCG vaccination and nutritional status.<sup>9</sup>

Therefore, the present study was undertaken to evaluate the clinical profile and outcome of tuberculous meningoencephalitis in children admitted to a tertiary care centre, with special reference to BCG vaccination status and nutritional status.

## **METHODS**

### ***Study design and setting***

This was a hospital-based prospective observational study conducted in the Department of Pediatrics, Civil Hospital, Ahmadabad, Gujarat, a tertiary care referral center.

### ***Study population and sample size***

A total of 75 children aged 1 month to 12 years, diagnosed with tuberculous meningoencephalitis, were included in the study. All eligible children admitted during the study period who fulfilled the inclusion criteria were enrolled.

### ***Data collection***

After obtaining informed consent, data were collected using a pre-structured proforma. Demographic details, clinical features, nutritional status, and BCG vaccination status were documented. Nutritional status was assessed

using WHO growth standards, and BCG vaccination status was confirmed by history and presence of BCG scar.

### ***Inclusion criteria***

Children aged 1 month to 12 years, diagnosed with tuberculous meningoencephalitis based on clinical features, cerebrospinal fluid analysis, and neuroimaging findings were included and written informed consent obtained from parents or legal guardians.

### ***Exclusion criteria***

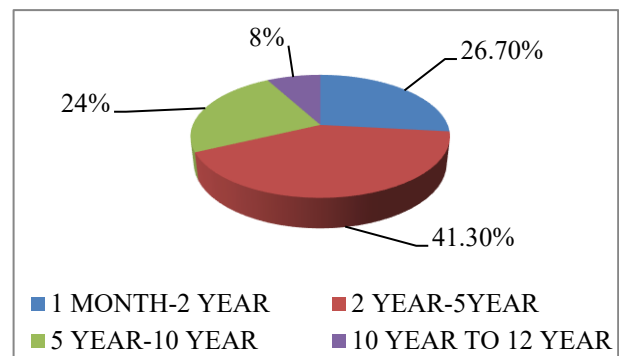
Children with human immunodeficiency virus (HIV) infection, children with congenital neurological disorders, and children with other chronic systemic illnesses were excluded.

### ***Statistical analysis***

Data was analyzed using statistical package for the social sciences (SPSS) software (version 25.0). Descriptive statistics were used for demographic and clinical variables. Chi-square tests were used for categorical variables to assess crude associations. Binary logistic regression was performed, including all variables with a  $p < 0.1$  in the univariate analysis. A  $p < 0.05$  was considered statistically significant.

## **RESULTS**

The majority of children with TBME were below five years of age (68%), with the highest number of cases observed in the 2–5-year age group (41.3%). This highlights the increased vulnerability of younger children to severe forms of tuberculosis (Figure 1).



**Figure 1: Age distribution of study subjects (n=75).**

A male predominance was observed, with males accounting for 58.6% of cases, giving a male-to-female ratio of approximately 1.4:1 (Table 1).

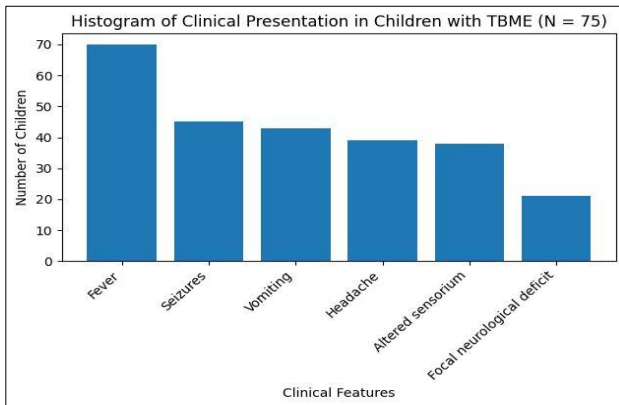
Table 2 and Figure 2 presents the frequency distribution of clinical features observed at presentation among children with TBME. Fever was the most common symptom, present in 93.3% of cases, reflecting the infective nature of

the disease. Neurological manifestations were prominent, with seizures observed in 60% of children, followed by vomiting (57.3%) and headache (52%). Altered sensorium was noted in 50.6% of cases, indicating significant central nervous system involvement at admission. Focal neurological deficits were seen in 28% of children, suggesting advanced disease in a considerable proportion of patients.

**Table 1: Sex Distribution of study subjects.**

Present study	Gender	
	Male (%)	Female (%)
<b>Tuberculous meningoencephalitis</b>	58.6	41.4

Table 3 presents an analysis of malnutrition in children with tuberculous meningitis, categorized according to the Indian Academy of Pediatrics (IAP) classification.



**Figure 2: Clinical features at presentation.**

**Table 2: Clinical features at presentation.**

Symptoms	Present study (n=75) (%)
<b>Fever</b>	93.3
<b>Seizure</b>	60
<b>Vomiting</b>	57.33
<b>Headache</b>	52
<b>Altered sensorium</b>	70.6
<b>Focal neurological deficit</b>	28

Among children  $\leq 5$  years old, 90.2% were undernourished, with the majority falling into grade 2 (25.5%) and grade 3 (43.1%), while only 9.8% had normal nutritional status. In children  $> 5$  years, 75% were undernourished, and 25% had normal nutrition. Both age groups show a high prevalence of undernutrition, but younger children ( $\leq 5$  years) were more severely affected.

The nutritional status among TBME patients in this study reveals a strong correlation between young age and severe undernutrition. Children under 5 years old not only had a higher rate of undernutrition, but also exhibited more severe grades (grade 2 to grade 4). This may be attributed

to their greater physiological vulnerability, dependence on caregivers, and susceptibility to infections.

**Table 3: Nutritional status of children with TBME.**

Age group	Grading	Number	Percentage
<b>&lt;5 year</b>	Grade 1	5	9.8
	Grade 2	13	25.5
	Grade 3	22	43.1
	Grade 4	6	11.8
	Normal	5	9.8
<b>&gt;5 year</b>	Undernutrition	18	75
	Normal	6	25

In the present study, a majority of the patients with tuberculous meningoencephalitis were unvaccinated (69.4%), while only 30.6% had received the BCG vaccine. The  $p < 0.005$  indicates that this difference is statistically significant, suggesting a strong association between lack of BCG vaccination and the occurrence of tuberculous meningoencephalitis. This highlights the potential protective role of BCG vaccination against severe forms of tuberculosis in children (Table 4).

**Table 4: BCG vaccination status.**

BCG vaccination status	Present study, % (N)
<b>Vaccinated</b>	30.6 (23)
<b>Unvaccinated</b>	69.4 (30)

In the present study, a history of contact with a known case of tuberculosis was documented in 48% (36/75) of children, while 52% (39/75) had no known contact (Table 5).

**Table 5: History of tuberculosis contact.**

History of TB contact	Present study, % (N)
<b>Yes</b>	48 (36)
<b>No</b>	52 (39)

Neuroimaging in patients with tuberculous meningoencephalitis revealed that hydrocephalus was the most common lesion, seen in 78.6% (59 patients), indicating that raised intracranial pressure and cerebrospinal fluid flow obstruction are major complications in this condition. Infarcts were observed in 36% (27 patients), suggesting vascular involvement and ischemic damage as common pathological consequences.

Basal exudates were found in 29.3% (22 patients), which are characteristic of TB meningitis and can lead to cranial nerve palsies and obstructive hydrocephalus. Leptomeningeal enhancement was present in 24% (18 patients), supporting active meningeal inflammation. Tuberculomas were detected in 14% (11 patients), representing localized granulomatous lesions often found in chronic or subacute TB cases (Table 6).

In the present study of 75 patients with tuberculous meningoencephalitis, the majority were diagnosed in stage 3 (50.7%), followed by stage 2 (36%), and only a small proportion were identified in stage 1 (13.3%).

This indicates that most patients presented at an advanced stage. Early identification and intervention are crucial to improving outcomes in tuberculous meningoencephalitis. As our center is a tertiary healthcare facility, the patients presenting to our department often exhibit more severe and advanced stages of illness compared to the general population (Table 7).

The outcome analysis indicates that tuberculous meningitis remains a serious condition with significant mortality and morbidity: Survival rate was 60%, suggesting that a majority of patients responded to treatment and were discharged alive.

However, the mortality rate was high at 29.3%, reflecting the severe nature and complications associated with TBM, such as hydrocephalus, infarcts, and delayed diagnosis or treatment. Additionally, 10.6% of patients left against medical advice (DAMA), which may impact the true assessment of treatment outcomes and highlights challenges in continuity of care (Table 8).

**Table 6: Analysis of CT/MRI finding in tuberculous meningoencephalitis (n=75).**

Type of lesion	Present study (CT/MRI), % (N)
Hydrocephalus	78.6 (59)
basal exudates	29.3 (22)
Infarct	36 (27)
Tuberculomas	14 (11)
leptomeningeal enhancement	24 (18)

**Table 7: Stage of presentation of tuberculous meningoencephalitis.**

Tuberculous ingoencephalitis stage	Number of patients, % (N)
Stage 1	13.3 (10)
Stage 2	36 (27)
Stage 3	50.7 (38)
Total	75

**Table 8: Outcome of patients of tuberculous meningoencephalitis (n=75).**

Outcome	Tuberculous meningoencephalitis, % (N)
Survival	60 (45)
Expired	29.3 (22)
LAMA	10.6 (8)

**DISCUSSION**

TBME continues to be a major cause of morbidity and mortality in children. In the present study (n=75), 68% children (n=51) were below five years of age, indicating increased vulnerability in early childhood. A similar age distribution has been reported by Abdella et al (n=62), where 64% of children were under five years, and by Israni et al (n=54), who reported 61% cases in this age group.<sup>10,11</sup> This confirms that TBME predominantly affects younger children across different settings.

A male predominance of 58.6% (n=44) was observed in the present study. Comparable findings were reported by Abdella et al (56%; n=62) and Seth et al (60%; n=80), suggesting that sociocultural factors and healthcare-seeking behavior may contribute to this trend.<sup>12</sup>

Fever was the most common presenting symptom in the present study (93.3%; n=70), followed by seizures (60%; n=45) and altered sensorium (50.6%; n=38). Vyas et al (n=50) reported fever in 92% and seizures in 58% of pediatric TBME cases, which closely correlates with the findings of the present study.<sup>13</sup>

In the present study, 50.7% children (n=38) presented in stage 3 TBME, reflecting delayed diagnosis and referral. Similar proportions of advanced disease at presentation were observed by Abdella et al (48%; n=62) and Israni et al (45%; n=54). Advanced stage at presentation has consistently been associated with poor outcomes in pediatric TBME.

Malnutrition was a significant associated factor in the present study, with more than 90% of children below five years and 75% of children above five years being undernourished (n=75). Abdella et al reported moderate to severe malnutrition in approximately 80% (n=62) of children with TBME, while Indian studies by Seth et al (n=80) also demonstrated a strong association between malnutrition and disease severity.

BCG vaccination appeared to have a protective effect in the present study, as 69.4% children (n=52) were unvaccinated and vaccinated children had relatively milder disease.

Neuroimaging findings in the present study showed hydrocephalus in 78.6% (n=59) of cases. Comparable findings were reported by Vyas et al (n=50), where hydrocephalus was the most common radiological abnormality in TBME.<sup>12</sup>

The overall mortality in the present study was 29.3% (n=22). Similar mortality rates have been reported by Abdella et al (25–30%; n=62) and van Well et al (20–35%; n=107).<sup>9,12</sup> Mortality was higher in children presenting with advanced disease stage, malnutrition, and neuroimaging complications.

## Limitations

### Single-center design

This study was conducted at Civil Hospital, Ahmedabad, and therefore may reflect regional epidemiological and healthcare access patterns with limited external validity for other populations or settings.

### Lack of long-term follow-up

The study has assessed short-term outcomes and acute complications, with limited details on long-term neurological sequelae, cognitive outcomes, or quality of life.

## CONCLUSION

Tuberculous meningoencephalitis continues to be a serious and life-threatening illness in children, particularly in those below five years of age. The disease is frequently diagnosed at an advanced stage, leading to high mortality and significant neurological morbidity.

BCG vaccination and good nutritional status play a crucial protective role in reducing disease severity and improving outcomes. Malnutrition significantly worsens disease progression and prognosis, emphasizing the need for integrated nutritional support in TB control programs.

Early recognition of symptoms, prompt neuroimaging, timely initiation of antitubercular therapy, and aggressive management of complications such as hydrocephalus are essential to reduce mortality and long-term sequelae. Strengthening routine immunization coverage, improving nutritional status, and increasing awareness among caregivers and primary healthcare providers are key strategies to improve outcomes in childhood TBME.

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