

A Prospective Study on Clinical Manifestations and Outcomes of Pediatric Tuberculous Meningitis in Relation to BCG Vaccination and Nutritional Status

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Abstract:

Background: Pediatric tuberculous meningitis (TBM) is a severe form of tuberculosis with high morbidity and mortality, particularly in young children. Factors such as BCG vaccination and nutritional status may influence disease severity and outcomes.

Aim: To prospectively evaluate the clinical manifestations and outcomes of pediatric TBM in relation to BCG vaccination status and nutritional status.

Methodology: A prospective study was conducted on 42 children aged 6 months to 12 years diagnosed with definite or probable TBM at Patna Medical College and Hospital. Clinical evaluation, cerebrospinal fluid analysis, and neuroimaging were performed. BCG vaccination was confirmed by scar presence, and nutritional status was assessed using the IAP classification. Patients were managed with standard anti-tubercular therapy and corticosteroids, and outcomes were assessed at three months.

Results: TBM predominantly affected children aged 1–5 years (42.9%) with male predominance (61.9%). Most patients presented in advanced stages (Stage II: 50%; Stage III: 31%). BCG-vaccinated children had higher complete recovery rates (16/28) and lower mortality (3/28) compared to unvaccinated children (4/14 recovery; 5/14 deaths). Nutritional status strongly influenced outcomes; children with normal nutrition had the best recovery, whereas severe malnutrition was associated with higher mortality and residual deficits.

Conclusion: Early diagnosis, BCG vaccination, and adequate nutrition significantly improve outcomes in pediatric TBM. Malnutrition and lack of vaccination are associated with severe disease and higher mortality.

Keywords: Pediatric tuberculous meningitis, BCG vaccination, Nutritional status, Clinical outcomes, Protein-energy malnutrition.

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Introduction

Tuberculosis remains one of the biggest global public health problems, most especially in developing countries. According to the World Health Organization, almost one third of the world's population is infected with *Mycobacterium tuberculosis*, with the highest prevalence from Asian countries [1]. In spite of the global control efforts being sustained, tuberculosis remains a big cause of morbidity and mortality, especially among children. Pediatric tuberculosis is an important yet neglected part of the overall TB burden because of difficulties in diagnosis coupled with the nonspecific nature of the clinical presentations.

The prevalence of childhood tuberculosis is widely underestimated. These are largely attributed to the

challenges faced in diagnosis, as children usually present with signs and symptoms that are nonspecific and vague. Clinical manifestations such as lethargy, fever, vomiting, weight loss, altered mental status, and photophobia usually closely resemble those of other prevalent conditions during childhood, particularly in the early stages of illness. As a result, tuberculosis infection in children is often misdiagnosed, underdiagnosed, or paradoxically over-treated. Even in tertiary care institutions, only about 30–40% of childhood TB cases are bacteriologically confirmed [2]. The diagnostic limitations notably delay the institution of treatment, thus increasing the risk for severe forms of the disease and poor outcomes.

The immature immune status makes young children particularly susceptible to severe and disseminated forms of tuberculosis. Younger children are at a greater risk of serious complications such as tuberculous meningitis (TBM) and disseminated tuberculosis compared to their older peers and adults [3]. TBM is the most dangerous and devastating form of extrapulmonary tuberculosis. It accounts for approximately 7–12% of tuberculosis cases in our country and has a high fatality rate despite treatment with effective antitubercular chemotherapy. Survivors often suffer from long-term neurological sequelae, making TBM a major cause of chronic disability in children.

Results for tuberculous meningitis depend on many factors: age, nutritional condition, timing of diagnosis, stage of disease at presentation, and the prompt institution of appropriate antitubercular therapy. Delayed diagnosis and advanced disease at the time of presentation are strongly associated with increased mortality and grave neurological impairment. Malnutrition, common in many developing countries, further compromises host immunity and has an adverse influence on disease progression and treatment response.

The BCG vaccine has been widely used in many national immunization programs to prevent tuberculosis, especially the more severe forms of the disease seen in children. However, the protective efficacy of BCG vaccination has varied widely, between 0 and 80%, in different clinical trials. The efficacy of BCG remains one of the most controversial topics in tuberculosis research [4,5]. Although BCG vaccination does not protect against pulmonary tuberculosis in a consistent way, it is generally believed to offer protection against severe disseminated forms of TB, such as tuberculous meningitis.

BCG vaccination prevents hematogenous spread of *Mycobacterium tuberculosis*, leading to localization of the disease. Because of the increasing vaccinations, particularly in children, the neuro-tuberculosis clinical spectrum seems to be changing. Atypical presentations are increasingly common in BCG-vaccinated and well-nourished children. The modified presentations include serous tuberculous meningitis and localized tubercular lesions in the meninges and brain parenchyma. Such presentations show extensive variability in their clinical manifestations depending on the anatomical site of involvement [6]. These atypical and localized forms often pose diagnostic challenges and result in delayed treatment.

In contrast, the protective effect of BCG vaccination is considered to be significantly reduced in malnourished children. In our country, the results of BCG vaccination are usually disappointing in malnourished children. Severe forms of tuberculosis such as classical or generalized tuberculous meningitis, miliary tuberculosis, disseminated TB and other serious

complications of primary infection continue to occur even in BCG-vaccinated children who are poorly nourished [7]. Malnutrition not only increases susceptibility to infection but also impairs the immune response required for effective vaccine-induced protection.

In the backdrop of these observations, there is an imperative need to understand the changing patterns of tuberculous disease in children in terms of their BCG vaccination status and nutritional status. Changing disease presentation, severity, and outcome may reflect interactions between vaccination coverage, nutritional factors, and improved diagnostic modalities. The role of nutritional status in modifying disease progression and vaccine efficacy deserves particular attention in regions with high prevalence of childhood malnutrition.

Indeed, there is a limited number of literature studies focused on the clinical manifestations and outcomes of tuberculous meningitis in children, especially with regards to the status of BCG vaccination [8]. Additionally, the influence of the nutritional status on disease presentation and outcome has not been studied in detail during a clinical prospective study. In the last two decades, advanced neuroimaging techniques, like computed tomography (CT) scan and neuro-sonography, have become more available. These studies have improved the understanding of the clinical features, complications, and management of TBM. These diagnostic modalities enable the detection of complications like hydrocephalus, infarctions, and tuberculomas much sooner, with the result that treatment strategies and outcomes are influenced.

In this regard, the current prospective study was conducted to systematically determine the clinical manifestations and outcomes of pediatric tuberculous meningitis. This study further proposes to explore possible differences in disease presentation, severity, and outcome among BCG-vaccinated versus non-vaccinated children and among well-nourished versus poorly nourished children. Understanding such associations is important in improving early diagnosis, optimally managing patients, and guiding public health interventions at reducing morbidity and mortality associated with pediatric TBM.

Methodology

Study Design: This study was designed as a prospective case series study conducted to evaluate the clinical manifestations and outcomes of pediatric tuberculous meningitis (TBM) in relation to BCG vaccination status and nutritional status.

Study Area: The study was conducted in the Department of Pediatrics, Patna Medical College and Hospital (PMCH), Patna, Bihar, India.

Study Duration: The study was conducted over a period of 8 months from March 2025 to October 2025

Sample Size: A total of 42 children diagnosed with definite or probable tuberculous meningitis were included in the study.

Study Population: The study population consisted of children aged 6 months to 12 years admitted to the pediatric emergency ward and pediatric units of PMCH with a diagnosis of tuberculous meningitis during the study period.

Inclusion Criteria

- Children aged 6 months to 12 years admitted with a clinical diagnosis of tuberculous meningitis.
- Patients fulfilling the clinical case definition of tuberculous meningitis, based on history, clinical features, and neurological examination.
- Demonstration of acid-fast bacilli (AFB) in cerebrospinal fluid, OR
- Patients fulfilling the following essential CSF criteria:
 - Predominant lymphocytic pleocytosis >50 cells/mm³
 - CSF protein level >60 mg/dL
 - CSF glucose level $<$ two-thirds of the corresponding blood glucose level
- Along with the essential CSF criteria, presence of two or more supportive clinico-investigational features, such as:
 - History of fever lasting ≥ 2 weeks
 - Positive family history or contact with tuberculosis
 - Generalized lymphadenopathy
 - Mantoux test (5 TU) >10 mm
 - Radiological evidence of tuberculosis elsewhere in the body
 - Isolation of AFB from gastric lavage or other sites
 - CT scan evidence of basal exudates or central nervous system tuberculosis
 - Histopathologically proven tubercular lymphadenitis
- Children whose parents or legal guardians provided informed written consent for participation in the study.

Exclusion Criteria

- Children with neurological symptoms due to confirmed alternative etiologies, such as:
 - Pyogenic (bacterial) meningitis
 - Japanese encephalitis
 - Cerebral malaria
 - Viral or fungal meningitis with proven diagnosis

- Children with CSF findings diagnostic of non-tubercular infections.
- Children with neurological manifestations are secondary to metabolic, toxic, or traumatic causes.
- Children whose parents or guardians did not provide consent for participation in the study.

Data Collection: Data were collected prospectively from consecutive pediatric patients diagnosed with definite or probable tuberculous meningitis and admitted to the Department of Pediatrics, Patna Medical College and Hospital, Patna, during the study period. After obtaining informed written consent from parents or legal guardians, detailed information was recorded using a predesigned proforma. This included demographic details, clinical history with emphasis on duration of fever, contact with tuberculosis, immunization status, and nutritional history. All patients underwent thorough general, neurological, and fundoscopic examinations. Laboratory investigations included complete hemogram, erythrocyte sedimentation rate, Mantoux test (5 TU), biochemical parameters, and cerebrospinal fluid analysis following lumbar puncture. Neuroimaging studies such as CT scan of the brain and/or transcranial neuro-sonography were performed wherever feasible to detect features of chronic meningitis and its complications. BCG vaccination status was determined by the presence of a visible BCG scar over the left deltoid region, and nutritional status was assessed using the Indian Academy of Pediatrics (IAP) classification.

Procedure: All enrolled children were evaluated clinically at the time of admission and were staged according to the clinical severity of tuberculous meningitis. Based on neurological findings, patients were classified into Stage I, Stage II, or Stage III of classical tuberculous meningitis, or into modified forms of TBM where applicable. Following diagnosis, all patients were initiated on anti-tubercular therapy according to body weight using the standard regimen of 2HRZE followed by 10HRE. Adjunctive corticosteroid therapy was administered for a duration of 6-8 weeks, and anti-edema measures along with supportive care were provided as required. Patients were closely monitored during hospitalization for clinical improvement, development of complications, or adverse drug reactions. Outcome assessment was performed at the time of discharge and again at three months of follow-up, and outcomes were categorized as complete recovery, partial recovery with residual neurological deficits, or death based on the modified British Medical Research Council criteria.

Statistical Analysis: The collected data were compiled and entered into a master chart and analyzed using appropriate statistical methods. Descriptive statistics such as mean, percentages, and proportions

were used to summarize demographic variables, clinical features, nutritional status, BCG vaccination status, and outcomes. The Chi-square test was applied to assess the association between tuberculous meningitis outcomes and BCG vaccination status as well as different grades of nutritional status. A p-value of less than 0.05 was considered statistically significant, and a p-value of less than 0.001 was considered highly significant.”

Result

Age Group (years)	Number of Cases (n)	Percentage (%)
< 1 year	6	14.3
1–5 years	18	42.9
6–10 years	12	28.6
>10 years	6	14.3
Total	42	100

Table 2 shows the sex distribution of 42 children with tuberculous meningitis. Males predominated, with 26 children (61.9%), while females accounted

Table 1 presents the age distribution of 42 children with tuberculous meningitis (TBM). The largest proportion of cases, 18 children (42.9%), were aged 1–5 years, followed by 12 children (28.6%) in the 6–10 years group. Infants under 1 year and children over 10 years each accounted for 6 cases (14.3%). Overall, Table 1 indicates that TBM predominantly affects young children, particularly those between 1 and 5 years of age.

for 16 children (38.1%). This indicates a higher proportion of male participants in the study population.

Sex	Number (n)	Percentage (%)
Male	26	61.9
Female	16	38.1
Total	42	100

Table 3 presents the BCG vaccination status among 42 children with tuberculous meningitis (TBM). The majority of children, 28 (66.7%), were vaccinated as evidenced by the presence of a BCG scar, while 14

children (33.3%) had not received the vaccine. This indicates that one-third of the TBM cases occurred in unvaccinated children, highlighting the continued risk of TBM in this subgroup.

BCG Vaccination Status	Number (n)	Percentage (%)
Vaccinated (scar present)	28	66.7
Not vaccinated	14	33.3
Total	42	100

Table 4 shows the nutritional status of 42 children according to the IAP classification. Nearly a quarter of the children (10, 23.8%) had normal nutrition, while the majority exhibited some degree of protein-energy malnutrition (PEM). Grade I PEM was observed in 12 children (28.6%), Grade II in 11

children (26.2%), Grade III in 6 children (14.3%), and the most severe Grade IV in 3 children (7.1%). Overall, Table 4 indicates that more than three-quarters of the children admitted had varying degrees of malnutrition, highlighting a significant burden of PEM in this population.

Nutritional Status	Number (n)	Percentage (%)
Normal nutrition	10	23.8
Grade I PEM	12	28.6
Grade II PEM	11	26.2
Grade III PEM	6	14.3
Grade IV PEM	3	7.1
Total	42	100

Table 5 indicates that the majority of children with tuberculous meningitis presented in Stage II at

admission (21 cases, 50%), followed by Stage III in 13 children (31%), while only 8 children (19%) were

diagnosed in the early Stage I, suggesting that most patients presented with moderate to advanced disease.

Clinical Stage	Number (n)	Percentage (%)
Stage I	8	19
Stage II	21	50
Stage III	13	31
Total	42	100

Table 6 shows that at the 3-month follow-up of children with tuberculous meningitis, nearly half achieved complete recovery (20 cases, 47.6%), while one-third had partial recovery with residual

neurological deficits (14 cases, 33.3%). Mortality remained substantial, with 8 children (19.1%) succumbing to the illness, highlighting the serious prognosis of TBM despite treatment.

Outcome Category	Number (n)	Percentage (%)
Complete recovery	20	47.6
Partial recovery with residual deficits	14	33.3
Death	8	19.1
Total	42	100

Table 7 demonstrates that children who had received BCG vaccination had better clinical outcomes compared to those who were not vaccinated. Among vaccinated children, complete recovery was observed in 16 of 28 cases, with fewer deaths (3 cases),

whereas non-vaccinated children showed lower complete recovery (4 of 14) and a higher number of deaths (5 cases), suggesting a protective association of BCG vaccination with improved outcomes.

BCG Vaccination Status	Complete Recovery	Partial Recovery	Death	Total
Vaccinated	16	9	3	28
Not vaccinated	4	5	5	14
Total	20	14	8	42

Table 8 shows a clear association between nutritional status and clinical outcome among the 42 children, with better outcomes observed in those with normal nutrition. Complete recovery was highest in children with normal nutritional status (7/10) and declined with worsening protein-energy

malnutrition, while mortality increased from 1 case in the normal group to 3 cases in Grade I–II PEM and 4 cases in Grade III–IV PEM, indicating that severe malnutrition was associated with poorer recovery and higher risk of death.

Nutritional Status	Complete Recovery	Partial Recovery	Death	Total
Normal	7	2	1	10
Grade I–II PEM	11	9	3	23
Grade III–IV PEM	2	3	4	9
Total	20	14	8	42

Discussion

The current study puts into perspective the clinical manifestations and outcomes of pediatric TBM in relation to BCG vaccination and nutritional status. Our findings indicate that TBM was more common among the younger children, with 42.9% of the cases occurring within the age group of 1–5 years and almost three-fourths below the age of five. This is in agreement with previous studies that have stated that young children are more prone to the severe forms

of disease because of their immature immune system. Benakappa et al. (1975) [9] also found that the majority of the children with TBM were below five years of age, although Udani et al. (1994) [4] found a slightly lower percentage of young children being afflicted, indicating that regional and demographic factors may influence age-related susceptibility of children (Chandrashekar, 1999) [10]. The male preponderance found in our study, with a male-to-female ratio of 1.6:1, corroborates the findings of Garg

(1981) [11] and Kennedy and Fallon (1979) [12], who have reported a higher incidence among males. This could be due to biological factors, such as sex-specific immune responses, as well as sociocultural factors that include preferential healthcare-seeking for male children.”

BCG vaccination: 66.7% of our cohort were vaccinated, but TBM still occurred among the vaccinated, indicating that BCG provides partial protection rather than complete immunity. Similar observations were noted by Girgis et al. (1998) [13] as prior vaccination with BCG did not completely prevent TBM, though the disease was less severe and the outcome much better. Our data further support this finding; complete recovery among the vaccinated was higher, 57.1%, mortality lower, 10.7%, when compared to unvaccinated children, where mortality was 35.7%. Conversely, Degefie (2003) [14] in a cohort of pediatric TBM in Ethiopia showed an overall immunization rate to be as low as 33%, indicating variable immunization rates in different parts of the world. Although Udani et al. (1994) [4] mentioned differences in clinical manifestations in vaccinated and non-vaccinated children, we did not note statistically significant variability in presenting features, which could be related to the small sample size and more children presenting with advanced disease.

Nutritional status emerged as a critical determinant of disease severity and outcome in our study. Malnutrition was present in 76.2%, whereas 21.4% suffered from severe malnutrition (Grades III and IV). Children who had severe malnutrition had a poor outcome as only 22.2% recovered completely while mortality was as high as 44.4%, while in well-nourished children, the recovery rate was 70% with mortality of 10%. This is in agreement with Gupta and Chopra (1981) [15], who found that malnourished children were prone to develop more severe TBM and its complications, and Al-Abasil (2002) [16], who reported higher mortality among pediatric malnourished populations. Malnutrition could heighten disease severity by weakening the immune response, thereby leading to delayed recovery and increased neurological sequelae. Our findings also align with those of Kalita and Misra (1999) [17], who stated that nutritional deficiencies, particularly protein-energy malnutrition, decisively influenced prognosis in TBM.

Clinical presentation in our series consisted predominantly of fever, altered mental status, and vomiting. This is consistent with a number of previous studies (Ramachandran et al., 1970; Benakappa et al., 1975; Udani et al., 1999) [18,9,4]. However, convulsions were relatively less common in this population, as compared to those described by Kennedy and Fallon (1979) [12], perhaps due to a difference in the stage of disease at presentation or possibly due to genetic and environmental factors. Meningeal irritation

signs were less common than described in several previous series, but McEwan's sign and tense anterior fontanel were more common. In general, these findings suggest that there is some variation between series in the clinical identification and recording of subtle neurological signs (Benakappa et al., 1975; Chandrashekar, 1999) [9,10]. Meningeal tuberculomas, one of the atypical presentations, were present in one-third of the cases, which adheres to the findings by Kondo and Ito (2003) [19] showing that atypical presentations of TBM are increasingly being identified with newer imaging.

Outcomes were strongly influenced by stage at presentation: half the children presented in Stage II and 31% in Stage III, reflecting delayed diagnosis, which is a common challenge in resource-limited settings. All survivors of Stage III disease had residual neurological deficits. This trend is consistent with findings from Girgis et al. (1998) [20] and Al-Abasil (2002) [16] who showed that advanced-stage TBM at presentation was the most significant predictor of poor outcome. Overall, the case fatality rate of 19.1% in our study is lower than the reports by Malik et al. (2002) [21] and Afzal (2003) [22], but higher than in some studies from better-resourced regions, underscoring the persistent challenge of reducing TBM-related mortality despite standard therapy.

Overall, our study highlights the disparities across pediatric TBM presentations, given the inclination towards younger age, male gender, malnutrition. While BCG vaccination and nutritional status were associated with good outcomes, delayed presentation and advanced stage of disease remain major contributors to morbidity and mortality. These findings are consistent with other studies, although there are some variations because of geographic, socioeconomic, and methodological differences. Improvement in BCG coverage, nutritional status, and early recognition and treatment of TBM are essential steps in reducing mortality and long-term neurological sequelae among affected children.

Conclusion

This prospective study demonstrates that pediatric tuberculous meningitis mainly affects young children, with male preponderance, and usually presents in advanced clinical stages at the time of admission, which adversely affects the outcomes. A significant proportion of children were undernourished, pointing to malnutrition as an important correlate of the severity of the disease and prognosis. BCG vaccination was found to be associated with better outcomes in the form of higher complete recovery rates and lower mortality, indicating protection against severe forms of the disease. In contrast, unvaccinated children and those with severe grades of protein-energy malnutrition showed poor outcomes manifested by higher residual neurological deficits and death.

Overall, the study emphasizes the critical role of early diagnosis, timely initiation of appropriate treatment, adequate nutritional support, and universal BCG vaccination in the improvement of clinical outcomes and reduction of morbidity and mortality in pediatric tuberculous meningitis.

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