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Clinical outcomes and predictors of poor prognosis among children with probable and confirmed bacterial meningitis in Northwest Ethiopia: a prospective multicenter cohort study

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Article

Keywords: Pediatric bacterial meningitis, Poor clinical outcome, Northwest Ethiopia, Malnutrition, Delayed hospital admission

Posted Date: July 29th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9986495/v1

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Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Scientific Reports on October 28th, 2026.
See the published version at https://doi.org/10.1038/s41598-026-78091-3.

Abstract

Background

Pediatric bacterial meningitis remains a major cause of mortality and neurological disability in low-resource settings despite improvements in vaccination. The majority of studies conducted in Ethiopia previously have been retrospective and single-center studies with little information about the prognosis of the disease. This prospective multicenter cohort study evaluated clinical outcomes and identified independent predictors of poor prognosis among children with bacterial meningitis.

Methods

A prospective multicenter cohort study was conducted from June 3, 2024, to May 25, 2025, at Felege Hiwot Comprehensive Specialized Hospital and Tibebe Ghion Specialized Teaching Hospital. Patients aged 0 to 14 years with meningitis that was clinically suspected and met criteria for probable and confirmed bacterial meningitis according to the World Health Organization (WHO) guidelines were recruited serially from the time of admission to discharge. Patients with probable bacterial meningitis had clinical presentation that was compatible with the disease together with either leukocytosis in the CSF (> 100 cells/mm³ or 10–100 cells/mm³ in conjunction with increased protein concentration (> 100 mg/dL) or decreased glucose (< 40 mg/dL). Poor outcome was categorized as mortality, neurological complications on discharge, or prolonged hospital stay (> 14 days).

Results

Poor outcomes occurred in 28.4% of patients (n = 97). Independent predictors included delayed hospital admission (AOR = 3.1, 95% CI: 1.9–5.2), coma at presentation (AOR = 4.6, 95% CI: 2.6–8.1), malnutrition (AOR = 2.8, 95% CI: 1.5–4.9), and positive CSF culture (AOR = 2.5, 95% CI: 1.1–5.8).

Conclusion

Nearly one-third of children experienced poor discharge outcomes. Late presentation, severe neurological impairment, malnutrition, and positive bacterial culture results were strongly associated with poor outcome. Improved recognition, referral pathways, nutritional support, and diagnostic techniques could greatly decrease morbidity and mortality due to childhood meningitis in developing countries.

Introduction

Bacterial meningitis is an acute, life-threatening inflammation of the meninges. Despite global advances in immunization, it remains a significant cause of mortality and long-term morbidity, particularly in the

"African Meningitis Belt" (1, 2). Due to high rates of malnutrition, delayed healthcare seeking, and inadequate diagnostic infrastructure, children in low-resource environments like Ethiopia face a disproportionate burden (3–5).

Children who survive bacterial meningitis often experience long-term neurological complications, including epilepsy, hearing loss, and cognitive impairments (1, 6). Despite the development of conjugate vaccines, common causal bacteria including *Streptococcus pneumoniae* and *Neisseria meningitidis* are still prevalent, underscoring the need for better prevention and treatment measures (7–9).

Clinical outcomes of pediatric bacterial meningitis remain highly variable, according to recent data from sub-Saharan Africa. These outcomes are impacted by a number of factors, including delayed hospital presentation, malnutrition, low diagnostic capacity, and heterogeneity in treatment approaches (10–12). However, there is a shortage of reliable prospective data on indicators of poor outcomes in Ethiopian children with bacterial meningitis. The majority of current research is single-center, retrospective, and generally focuses on microbiological results rather than clinical prediction. As a result, there is little data to inform medical professionals and decision-makers about the variables linked to poor outcomes in hospitalized children with bacterial meningitis in Ethiopia (10, 13).

Therefore, this study aimed to prospectively assess the clinical outcomes of children with probable and confirmed bacterial meningitis and to identify independent predictors of poor prognosis among pediatric patients admitted to two tertiary hospitals in Northwest Ethiopia. This evidence is intended to support earlier recognition of high-risk patients, strengthen clinical management, and inform context-specific strategies to reduce meningitis-related morbidity and mortality.

Methods

Study setting and design

A prospective multicenter cohort study was conducted from June 3, 2024 to May 25, 2025 at Felege Hiwot Comprehensive Specialized Hospital and Tibebe Ghion Specialized Teaching Hospital, two tertiary referral hospitals located in Bahir Dar, Northwest Ethiopia. These hospitals serve a combined catchment population of more than seven million people in the Amhara region (11).

Study population and sample size

The study population consisted of children aged 0–14 years who were admitted to the pediatric wards of the study hospitals with clinically suspected meningitis and fulfilled the World Health Organization (WHO) criteria for probable or confirmed bacterial meningitis. Probable bacterial meningitis was defined based on compatible clinical features together with cerebrospinal fluid (CSF) abnormalities, whereas confirmed bacterial meningitis was established by positive CSF Gram stain and/or bacterial culture.

Children with confirmed or clinically suggestive viral, fungal, or tuberculous meningitis were excluded based on clinical presentation, CSF characteristics, and available laboratory findings.

The sample size was determined using a single population proportion formula:

$$n = (Z\alpha/2)2\ P\ (1 - P)/\ d2$$

Based on a previous proportion (p = 30%) (10), 95% CI (Z = 1.96), and 5% margin of error (d = 0.05), the minimum size was 323. To account for potential data loss or incomplete follow-up, 10% was added, resulting in a final cohort of 342 patients.

Inclusion criteria

Children aged 0–14 years that fulfilled WHO criteria for probable or confirmed bacterial meningitis were included.

Exclusion criteria

We excluded patients with confirmed or highly probable tuberculous, fungal, or viral meningitis based on specific laboratory evidence (e.g., clear fluid with lymphocytic predominance, positive GeneXpert, or negative bacterial indicators combined with suggestive imaging/clinical course).

Data collection and operational definitions

Trained pediatric residents collected data using a standardized, pre-tested checklist adapted from WHO meningitis protocols (1).

- **Case definition of pediatric bacterial meningitis**: Children aged 0–14 years were eligible if they had clinically suspected meningitis (fever, neck stiffness, altered consciousness, bulging fontanelle, seizures, or meningeal signs) and fulfilled WHO-compatible criteria for probable or confirmed bacterial meningitis.
- **Probable bacterial meningitis**: CSF leukocyte count > 100 cells/mm³, or 10–100 cells/mm³ with either CSF glucose < 40 mg/dL or protein > 100 mg/dL.
- **Confirmed bacterial meningitis**: Positive CSF Gram stain and/or bacterial culture. Children with confirmed or clinically suggestive tuberculous, fungal, or viral meningitis were excluded using CSF profile, clinical assessment, and available laboratory evidence.
- **Poor outcome**: The primary endpoint was an overall poor clinical outcome, defined as a composite of in-hospital mortality, acute neurological complications at discharge, or a prolonged hospital stay (> 14 days).
- **Delayed admission**: Presentation to the hospital > 48 hours after the onset of the first symptom.

- **Malnutrition**: Malnutrition was defined as a weight-for-age Z-score (WAZ) < − 2 standard deviations according to the WHO Child Growth Standards (12).

Follow-up procedures

All enrolled children were prospectively followed from the time of hospital admission until discharge or death. Clinical status was assessed daily during hospitalization. Information on treatment response, neurological complications, and clinical progression was recorded using a standardized data collection form. The final clinical outcome, including survival status, presence of neurological sequelae, and duration of hospitalization, was documented at the time of discharge.

Laboratory procedures

Lumbar punctures were performed upon admission. CSF samples underwent immediate macroscopical examination, biochemical analysis (glucose and protein), and microbiological testing (Gram stain and culture on Blood and Chocolate agar) (14, 15).

Statistical analysis

Data were analyzed using SPSS version 26. Descriptive statistics summarized the cohort. Factors with $p < 0.25$ in bivariable analysis were entered into a multivariable logistic regression model. Multicollinearity was assessed using variance inflation factors (VIF < 10). Model fitness was evaluated using the Hosmer–Lemeshow goodness-of-fit test. Results are reported as Adjusted Odds Ratios (AOR) with 95% Confidence Intervals (CI).

Ethical consideration

Ethical clearance was obtained from the Institutional Review Board of the College of Medicine and Health Sciences, Bahir Dar University (Ref: CMHS 1039/2024). Written informed consent was obtained from parents or legal guardians, and verbal or written child assent was secured based on age and developmental maturity Participant confidentiality was ensured using coded data. The study followed the Declaration of Helsinki and received support letters from relevant institutions.

Results

A total of 398 children with suspected meningitis were admitted during the study period. After applying the inclusion criteria, 342 children with probable and confirmed bacterial meningitis were enrolled in the study and followed until discharge or death. The participant selection process is summarized in Fig. 1.

Patient characteristics and clinical presentation

A total of 342 children were enrolled. The mean age was 2.8 years, with 75% being under 5 years old. Over half (54.5%) were from rural areas, and 20.1% were malnourished (Table 1). Fever was the most common symptom (92.1%), followed by neck stiffness (53.8%) and seizures (38%). Notably, 21.1% of children presented with coma at admission (Table 2).

Table 1
Socio-demographic and Clinical Baseline of Children with Bacterial Meningitis (n = 342)

Variable	Category	Frequency (n)	Percentage (%)
Age Group	< 1 year	98	28.7
	1–5 years	162	47.4
	6–10 years	52	15.2
	11–14 years	30	8.7
Sex	Male	198	58.0
	Female	144	42.0
Residence	Urban	156	45.5
	Rural	186	54.5
Nutritional Status	Malnourished (WAZ < -2 SD)	69	20.1
	Well-nourished	273	79.9
Vaccination Status	Fully Vaccinated	259	75.7
	Incomplete/Unvaccinated	83	24.3
Presence of Comorbidity	Yes (e.g., Pneumonia, Otitis)	141	41.3
	No	201	58.7

Table 2
Clinical Presentation and Cerebrospinal Fluid (CSF) Profiles

Parameter	Category	Frequency (n)	Percentage (%)
Symptoms at Admission	Fever	315	92.1
	Neck Stiffness	184	53.8
	Seizures	130	38.0
	Coma	72	21.1
Admission Timing	Delayed (> 48 hrs)	184	53.8
	Early (< 48 hrs)	158	46.2
CSF Appearance	Turbid/Cloudy	289	84.5
	Yellow/Xanthochromic	14	4.1
	Clear	39	11.4
CSF Biochemistry	Elevated Protein	257	75.1
	Low Glucose	238	69.6
	High WBC Count (Pleocytosis)	301	88.0
Microbiology	Positive CSF Culture	25	7.2

Laboratory findings

CSF pleocytosis was observed in 88% of cases. Elevated protein and low glucose were found in 75.1% and 69.6%, respectively. Bacterial cultures were positive in 25 cases (7.2%) (Table 2).

Predictors of poor outcomes

Overall, 71.6% of patients achieved good clinical outcomes, whereas 28.4% experienced poor outcomes. Multivariable logistic regression analysis identified four independent predictors significantly associated with poor outcomes (Table 3).

Distribution of Composite Poor Clinical Endpoints

Among the 342 children followed prospectively, a composite poor clinical outcome was observed in 28.4% (n = 97) of the cohort, while 71.6% (n = 245) achieved a favorable discharge status. Within the sub-group experiencing poor outcomes, the endpoints were not mutually exclusive. In-hospital mortality occurred in 9.4% (n = 32) of the total study population. Acute neurological complications at the time of discharge primarily persistent seizures, severe hypertonia, or cranial nerve palsies were documented in 11.1% (n = 38) of survivors. Additionally, prolonged hospitalization exceeding 14 days due to delayed clinical recovery or secondary systemic infections was noted in 14.9% (n = 51) of cases.

Table 3. Bivariable and multivariable logistic regression analysis of factors associated with poor clinical outcomes among children with bacterial meningitis (n = 342)

Variable	Poor Outcome n (%)	Good Outcome n (%)	COR (95% CI)	AOR (95% CI)	p-value
Admission Delay (>48h)	72 (39.1)	112 (60.9)	3.4 (2.0–5.7)	3.1 (1.9–5.2)	<0.001
Coma at Presentation	48 (66.7)	24 (33.3)	9.0 (5.0–16.1)	4.6 (2.6–8.1)	<0.001
Malnutrition	35 (50.7)	34 (49.3)	3.5 (2.0–6.1)	2.8 (1.5–4.9)	0.002
Positive CSF Culture	15 (60.0)	10 (40.0)	4.3 (1.9–9.9)	2.5 (1.1–5.8)	0.028
Age <1 year	30 (30.6)	68 (69.4)	1.2 (0.7–2.0)	1.4 (0.8–2.5)	0.180
Rural Residence	58 (31.2)	128 (68.8)	1.4 (0.8–2.2)	1.2 (0.7–1.9)	0.320

Abbreviations: COR = Crude Odds Ratio; AOR = Adjusted Odds Ratio; CI = Confidence Interval; CSF = Cerebrospinal Fluid.

Reference categories: Admission ≤48 hours; No coma at presentation; Well-nourished; Negative CSF culture; Age ≥1 year; Urban residence.

Discussion

In this prospective multicenter cohort, nearly one in three children (28.4%) experienced poor discharge outcomes, underscoring that pediatric bacterial meningitis remains a major cause of mortality and neurological morbidity in Northwest Ethiopia. In the present study, three-quarters of children with bacterial meningitis were younger than five years of age, and more than half originated from rural areas. This finding is consistent with reports from Ethiopia and other sub-Saharan African countries, where bacterial meningitis predominantly affects young children because of their immature immune systems and increased susceptibility to invasive bacterial infections (16, 17). The predominance of rural residents observed in this study may reflect disparities in healthcare access, transportation difficulties, and delayed care-seeking behavior. Similar observations have been reported in Ethiopian studies (13, 16).

Approximately one-fifth of the study participants were malnourished. Malnutrition compromises both innate and adaptive immune responses, thereby increasing vulnerability to severe infections and poor recovery. Similar findings have been documented in Ethiopia and other low- and middle-income countries (13, 18, 19).

Regarding clinical presentation, fever was the most common symptom, followed by neck stiffness, seizures, and coma. These findings agree with studies conducted in Ethiopia, Nigeria, Sudan, and India, where fever was the predominant presenting symptom among children with bacterial meningitis (13, 20). Fever reflects systemic inflammatory responses induced by bacterial invasion. Furthermore, seizures and coma indicate severe central nervous system involvement and have been reported frequently in previous African studies (16, 17).

More than half of the children arrived at the hospital after 48 hours of symptom onset. Similar findings have been reported in Ethiopian and African studies (13, 16, 18). Delayed presentation may be attributed to poor health-seeking behavior, transportation difficulties, referral delays, financial constraints, and inadequate awareness among caregivers. Since bacterial meningitis is a medical emergency, delayed initiation of treatment may substantially worsen outcomes.

The cerebrospinal fluid findings observed in the present study were characteristic of bacterial meningitis. Pleocytosis was detected in most patients, while elevated protein concentration and reduced glucose levels were also common. Similar laboratory profiles have been reported previously (20). Increased protein concentration results from disruption of the blood-brain barrier and inflammatory exudation, whereas low glucose levels occur because of glucose consumption by bacteria and inflammatory cells. Pleocytosis reflects leukocyte migration into the cerebrospinal fluid in response to infection.

The culture positivity rate in the present study was relatively low (7.2%). Comparable low yields have been reported in Ethiopia (19), although higher positivity rates have been documented in developed countries (21). The low culture recovery observed in this study could be explained by prior antibiotic exposure before lumbar puncture, delayed specimen processing, low bacterial load, inadequate laboratory capacity, and the presence of fastidious organisms. This low microbiological yield highlights an important diagnostic challenge and supports the need for expanded molecular diagnostic capacity in similar settings.

Overall, 71.6% of children had favorable outcomes, whereas 28.4% experienced poor outcomes. Although the majority recovered, the proportion of unfavorable outcomes remains considerable and demonstrates the continuing burden of bacterial meningitis in Ethiopia. Similar findings have been reported in southwestern and eastern Ethiopia (13, 18) and other African countries (19).

Multivariable analysis revealed that delayed hospital presentation was independently associated with poor outcomes. Children presenting after 48 hours had approximately three times higher odds of unfavorable outcomes compared with those presenting earlier. Similar associations have been reported in Ethiopia and other African countries (13, 16, 18). Delayed treatment permits progression of inflammation, cerebral edema, and irreversible neurological injury.

Coma at admission was another independent predictor of poor outcomes. Children presenting with coma had more than fourfold increased odds of unfavorable outcomes. This finding agrees with previous studies that identified altered consciousness as an indicator of severe disease and poor

prognosis (16). Coma may reflect increased intracranial pressure, extensive cerebral inflammation, and advanced disease severity.

Malnutrition was also significantly associated with poor outcomes. Malnourished children had nearly threefold increased odds of unfavorable outcomes compared with well-nourished children. Similar observations have been reported in Ethiopia and other developing countries (13, 19). Impaired immune function among malnourished children may hinder bacterial clearance and prolong recovery.

In addition, positive CSF culture was independently associated with poor outcomes. Culture-positive children had significantly higher odds of unfavorable outcomes than culture-negative patients. This may indicate higher bacterial burden or infection with more virulent pathogens. Similar findings have been described in previous studies (13), although some reports have shown no significant association.

Strengths of the Study

This study's strengths include its prospective cohort design, multicenter implementation, standardized WHO-aligned diagnostic framework, and direct clinical follow-up from admission to discharge, enhancing internal validity and regional applicability.

Study Limitations

This study has several limitations. First, molecular diagnostic methods such as PCR were unavailable, which may have underestimated pathogen confirmation. Second, prior antibiotic exposure before lumbar puncture may have reduced CSF culture positivity. Third, follow-up was limited to hospital discharge; therefore, long-term neurological sequelae such as hearing impairment and cognitive deficits were not assessed. Fourth, because probable cases were included, some degree of diagnostic misclassification may have occurred despite the use of standardized WHO-compatible criteria. Finally, the study was conducted in two tertiary hospitals, which may limit the generalizability of the findings to lower-level health facilities.

Conclusion

Nearly one-third of children with bacterial meningitis experienced unfavorable discharge outcomes. Delayed hospital presentation, coma at admission, malnutrition, and positive CSF culture were independently associated with poor prognosis. Early recognition of high-risk patients and improvements in referral systems, nutritional support, and diagnostic capacity may help improve outcomes among children with bacterial meningitis in resource-limited settings.

Abbreviations

PBM
Pediatric Bacterial Meningitis
CSF

Cerebrospinal Fluid
AOR
Adjusted Odds Ratio
COR
Crude Odds Ratio
WAZ
Weight–for–Age Z–score
WHO
World Health Organization

Declarations

Clinical trial number

Not applicable.

Ethical approval and consent to participate

Ethical clearance was obtained from the Institutional Review Board of the College of Medicine and Health Sciences, Bahir Dar University (Ref: CMHS 1039/2024). Because the study involved children aged 0–14 years, written informed consent was obtained from the parents or legal guardians of all participating children prior to enrollment. In addition, assent was obtained from children when appropriate, according to their age and level of understanding. Participant confidentiality was maintained using coded data. The study was conducted in accordance with the Declaration of Helsinki.

Competing interest: The authors declare that they have no competing interest.

Funding: This study received no external funding.

Data availability: All data generated or analyzed during this study are included in this published article.

Author contributions

Tadese Sisay: designed this study, collected and analyzed data, interpreted results, and drafted the manuscript; Ayenew Berhan: participated in data management and analyzed data; Kefiyalew Mihrete and Eyoel Hunie participated in the design, data collection, and analysis, interpretation of the results, supervising the overall work of this study, review and approval of the manuscript; Abel Temeche, Yohannis Tenagne and Alemie Fentie: prepared the manuscript, data analysis and data collection. All authors read the manuscript and approve it for submission.

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ACKNOWLEDGMENTS

The authors would like to thank Bahir Dar University, College of Medicine and Health Sciences, Department of Medical laboratory Science for the opportunity to conduct this study. Our sincere gratitude also goes to the Amhara Public Health Institute, TGTH, and FHCSH microbiology laboratory staff and pediatricians for their cooperation and support with sample access, laboratory materials, kind assistance and study participants.

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Figures

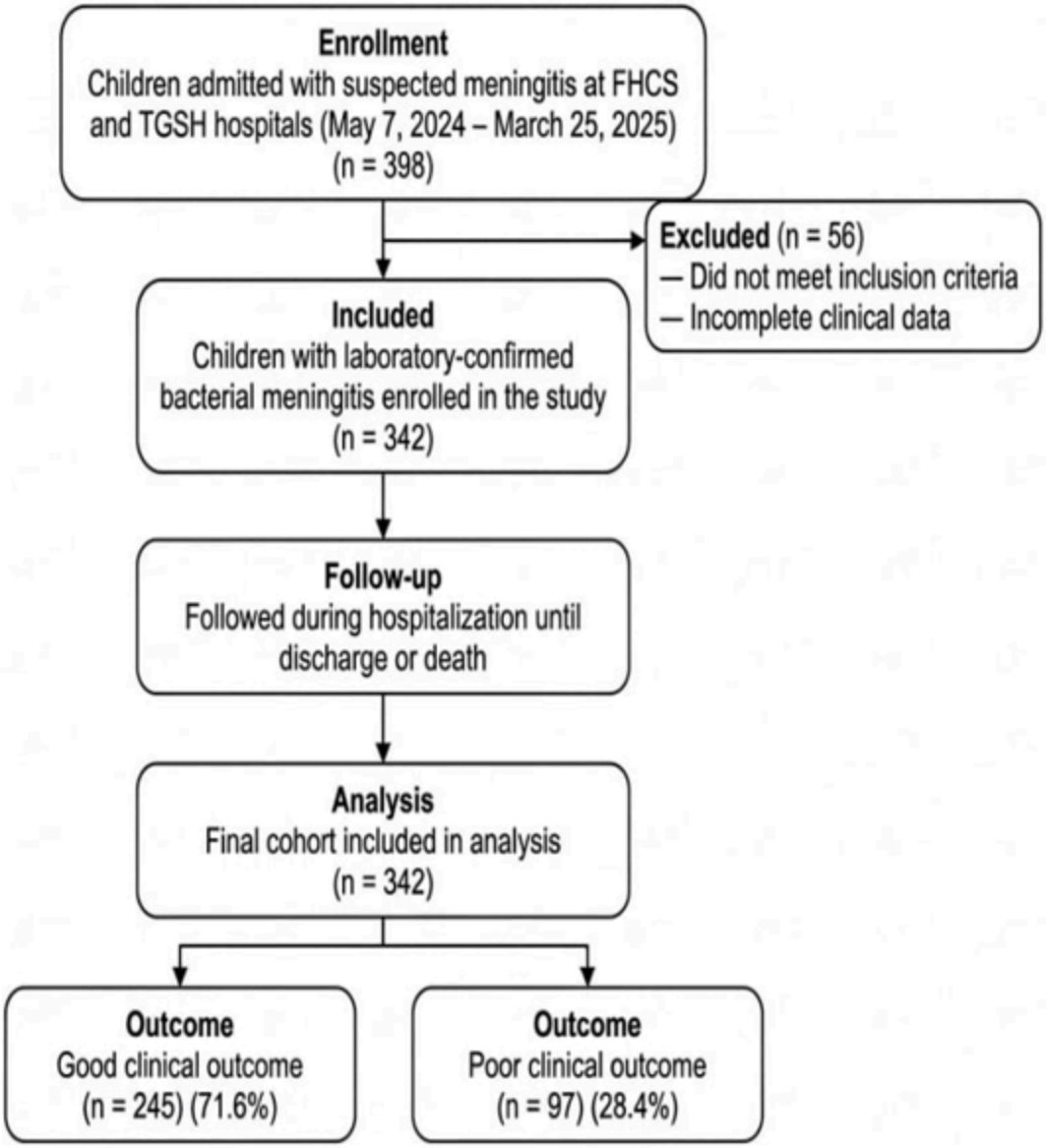


Figure 1

STROBE flow diagram showing the selection and follow-up of study participants.