Section: Infectious Diseases

Original Research Article

BEYOND THE BLOOD–BRAIN BARRIER: UNMASKING THE AETIOLOGICAL SPECTRUM AND BEDSIDE PREDICTORS OF OUTCOME IN CENTRAL NERVOUS SYSTEM INFECTIONS — A CROSS-SECTIONAL STUDY OF 50 HOSPITALISED ADULTS

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Received *: 25/01/2026*
Received in revised form *: 14/02/2026*
Accepted *: 01/03/2026*

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DOI: 10.70034/ijmedph.2026.3.329

Source of Support: Nil
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 2056-2061

ABSTRACT

Background: Central nervous system (CNS) infections remain a major cause of morbidity and mortality in tropical, resource-limited settings, where a broad spectrum of bacterial, tubercular, viral, fungal and parasitic pathogens must be distinguished on largely clinical and cerebrospinal fluid (CSF) grounds. This study describes the clinical profile, aetiological spectrum and predictors of short-term outcome among hospitalised adults with CNS infection.

Materials and Methods: This was a cross-sectional analysis of 50 adult patients with a clinico-radiologically and CSF-confirmed diagnosis of CNS infection, drawn as a representative sample from a larger institutional cohort of 200 patients. Demographic, clinical, haematological, CSF and radiological data were recorded, and outcome at discharge was classified using the modified Rankin Scale (mRS) and dichotomised into Good Outcome (mRS 0–2) and Poor Outcome (mRS 3–6). Continuous variables were compared between outcome groups using the Mann–Whitney U test, and categorical variables using the chi-square/Fisher's exact test; $p<0.05$ was considered significant.

Results: The mean age was 39.2 ± 14.0 years with a male preponderance (70%, M:F 2.3:1). Fever and altered sensorium were present in all patients (100%), headache in 72%, seizures in 46%, and neck stiffness in 36%. Tubercular CNS infections (32%) and viral CNS infections (32%) were the two leading aetiological categories, followed by bacterial (16%), fungal (8%), parasitic (4%), and other infectious/non-infectious encephalopathies (8%). A Poor Outcome was recorded in 70% of patients, including 18% in-hospital mortality (mRS 6). Lower admission Glasgow Coma Scale (GCS 9.9 ± 2.8 vs 13.3 ± 1.6, $p<0.001$), lower systolic (110 vs 124 mmHg, $p=0.045$) and diastolic blood pressure (75 vs 85 mmHg, $p=0.031$), and higher ESR (58.5 vs 24.3 mm/hr, $p<0.001$) were significantly associated with Poor Outcome. Aetiological category was also significantly associated with outcome ($p=0.027$), with tubercular meningitis contributing disproportionately to the poor-outcome group (14/16, 87.5%).

Conclusion: Tubercular and viral aetiologies dominate the spectrum of CNS infection in this cohort, and a substantial proportion of patients have unfavourable short-term outcomes. Depressed sensorium at admission (low GCS), haemodynamic compromise, and a raised ESR identify patients at high risk of poor outcome and may help triage patients for closer monitoring and earlier escalation of care.

Keywords: central nervous system infection; meningitis; encephalitis; tubercular meningitis; Glasgow Coma Scale; modified Rankin Scale; outcome; cerebrospinal fluid.

INTRODUCTION

Infections of the central nervous system (CNS) — meningitis, encephalitis, and their combined form meningoencephalitis — constitute a neurological emergency associated with substantial mortality and long-term disability if diagnosis and treatment are delayed. Unlike high-income settings where pyogenic and viral pathogens predominate, CNS infections in tropical and resource-limited regions such as India present a far wider aetiological spectrum encompassing tubercular, bacterial, viral, fungal, parasitic and rickettsial causes, each with overlapping clinical presentations but markedly different treatment and prognosis.

Tubercular meningitis (TBM) alone continues to contribute disproportionately to mortality among CNS infections in endemic regions, and depressed level of consciousness at presentation has repeatedly been identified as one of the strongest predictors of unfavourable outcome. Prior work using the Glasgow Coma Scale (GCS) and the British Medical Research Council (BMRC) staging system, as well as CSF parameters such as protein, glucose and cell count, has consistently shown that clinical severity at admission — more than the specific aetiological agent — drives short-term prognosis.

Given the diagnostic overlap between the different causes of CNS infection and the resource constraints that frequently limit access to advanced microbiological and molecular diagnostics, there remains a need for locally generated data describing the clinical profile, aetiological distribution, and bedside predictors of outcome that can be applied at the time of admission. This study was undertaken to describe the clinical, biochemical, and CSF profile of hospitalised adults with CNS infection at a tertiary care centre, to characterise the aetiological spectrum, and to identify clinical and laboratory parameters at admission that are associated with poor outcome.

MATERIALS AND METHODS

2.1 Study Design and Setting

This was a hospital-based, cross-sectional, observational study conducted in the Department of General Medicine of a tertiary care teaching hospital. [Study period, e.g. Month Year to Month Year, to be inserted by the author from the original thesis protocol.]

2.2 Study Population and Sample

The parent cohort comprised 200 consecutive adult patients admitted with a clinical suspicion of CNS infection who fulfilled diagnostic criteria based on clinical features, CSF analysis, CSF/blood culture, serological and molecular testing, and neuroimaging (CT/MRI brain). For the present analysis, a stratified random sample of 50 patients (25% of the parent cohort) was drawn, with sampling proportionate to the seven aetiological categories in the parent dataset (tubercular, viral, bacterial, fungal, parasitic, other infectious encephalopathies, and non-infectious/miscellaneous), so that the relative distribution of aetiologies in the sample approximated that of the full cohort. This sub-sample forms the basis of the descriptive and comparative analysis reported here; the parent cohort of 200 patients is available for a fully powered analysis in the primary thesis.

2.3 Data Collection

For each patient, the following were recorded at admission: age, sex, duration of symptoms, presenting clinical features (fever, altered sensorium, headache, seizures, neck stiffness), vital parameters (systolic and diastolic blood pressure, heart rate, body temperature), Glasgow Coma Scale, comorbidities (diabetes mellitus, hypertension), HIV (RVD) status, haemoglobin, total leucocyte count (TLC), platelet count, erythrocyte sedimentation rate (ESR), blood/urine culture, CSF findings (total cell count, differential count, protein, sugar, culture, and other CSF-specific investigations such as ADA, India ink, cryptococcal antigen, and viral/bacterial PCR panels), relevant serology, and neuroimaging findings. Final aetiological diagnosis was assigned based on the composite clinical, CSF, microbiological and radiological picture and grouped into seven broad categories: tubercular, viral, bacterial, fungal, parasitic, other infectious encephalopathies (e.g., cerebral malaria, scrub typhus, leptospirosis), and non-infectious/miscellaneous CNS syndromes.

Outcome at discharge was recorded using the modified Rankin Scale (mRS, 0 = no symptoms to 6 = death) and dichotomised for analysis into Good Outcome (mRS 0–2, no or slight disability) and Poor Outcome (mRS 3–6, moderate to severe disability or death), consistent with the outcome definition used in prior tubercular meningitis outcome literature.

2.4 Statistical Analysis

Data were analysed using Python (pandas, SciPy). Continuous variables are presented as mean ± standard deviation and were compared between outcome groups using the Mann–Whitney U test (given the modest sample size and non-normal distribution of several variables). Categorical variables are presented as frequencies and percentages and were compared using the chi-square test (Fisher's exact test where expected cell counts were <5). A two-tailed p-value <0.05 was considered statistically significant. Given the sample size of 50, the study should be regarded as hypothesis-generating; findings require confirmation in the full 200-patient cohort and in larger, adequately powered studies.

2.5 Ethical Considerations

The original data were collected as part of an institutionally approved postgraduate thesis protocol with Institutional Ethics Committee clearance and written informed consent from patients or their legal representatives. All personally identifying

information (patient names and identification numbers) was removed prior to this analysis; patients are not identifiable in this manuscript. [Insert IEC approval number and date, and consent statement, from the original thesis before submission.]

RESULTS

3.1 Demographic and Clinical Profile

Of the 50 patients studied, the mean age was 39.2 ± 14.0 years (median 39, range 18–72 years), with the largest proportion (30%) in the 21–30-year age group. There was a male preponderance, with 35 males and 15 females (M:F ratio 2.3:1). Fever and altered sensorium were universal presenting features (100%), followed by headache (72%), seizures (46%), and neck stiffness (36%). Diabetes mellitus and hypertension were present in 44% and 36% of patients respectively, and 14% were HIV (RVD)-positive. The median duration of symptoms prior to admission was in the 5–10-day category (56% of patients), 24% presented within 10–14 days, and 20% presented within 5 days of symptom onset. [Table 1]

Table 1: Demographic and clinical characteristics of the study population (n = 50)

Characteristic	n	%
Age, years (mean ± SD)	39.2 ± 14.0	
Age group ≤20 years	3	6.0
Age group 21–30 years	15	30.0
Age group 31–40 years	9	18.0
Age group 41–50 years	13	26.0
Age group 51–60 years	6	12.0
Age group 61–70 years	3	6.0
Age group >70 years	1	2.0
Sex — Male	35	70.0
Sex — Female	15	30.0
Fever	50	100.0
Altered sensorium	50	100.0
Headache	36	72.0
Seizures	23	46.0
Neck stiffness	18	36.0
Diabetes mellitus	22	44.0
Hypertension	18	36.0
HIV (RVD) positive	7	14.0

SD = standard deviation.

3.2 Aetiological Spectrum

Tubercular CNS infections (32%) and viral CNS infections (32%) were the two leading diagnostic categories, together accounting for nearly two-thirds of cases. Bacterial CNS infections accounted for 16%, fungal infections (predominantly cryptococcal meningitis) for 8%, and parasitic infections (neurocysticercosis and related conditions) for 4%. The remaining 8% comprised other infectious encephalopathies (cerebral malaria, scrub typhus/rickettsial disease, leptospirosis) and non-infectious/miscellaneous CNS syndromes (e.g., septic encephalopathy, PML) (Table 2). Within the tubercular category, tubercular meningitis was the single most common specific diagnosis (16/50, 32% of the entire cohort).

Table 2: Aetiological spectrum of CNS infection and its association with outcome (n = 50)

Aetiological category	Good Outcome	Poor Outcome	Total	%
Tubercular CNS infections	2	14	16	32.0
Viral CNS infections	4	12	16	32.0
Bacterial CNS infections	4	4	8	16.0
Fungal CNS infections	3	1	4	8.0
Parasitic CNS infections	0	2	2	4.0
Other infectious encephalopathies*	2	0	2	4.0
Non-infectious/miscellaneous†	0	2	2	4.0
Total	15	35	50	100.0

**Cerebral malaria, scrub typhus/rickettsial disease, leptospirosis. †Septic encephalopathy, progressive multifocal leukoencephalopathy and related non-infectious CNS syndromes. Chi-square test, χ^2 association between aetiological category and outcome: p = 0.027.*

3.3 Laboratory and CSF Findings

Median admission GCS was lower in patients with Poor Outcome than those with Good Outcome. CSF findings were heterogeneous across aetiological categories, as expected, with lymphocytic pleocytosis predominating in tubercular and viral infections and neutrophilic pleocytosis in bacterial infections. Table 3 summarises key continuous variables by outcome group.

Table 3: Comparison of clinical and laboratory parameters between outcome groups

Parameter	Good Outcome (n=15)	Poor Outcome (n=35)	p-value
Age, years	34.9 ± 14.1	41.1 ± 13.7	0.130
GCS (total score)	13.3 ± 1.6	9.9 ± 2.8	<0.001*
Systolic BP, mmHg	124.3 ± 16.5	110.4 ± 20.8	0.045*
Diastolic BP, mmHg	84.7 ± 11.7	75.3 ± 12.4	0.031*
Heart rate, /min	104.9 ± 9.9	104.6 ± 15.3	0.831
Body temperature, °C	37.2 ± 0.8	37.6 ± 0.8	0.140
Haemoglobin, g/dl	12.3 ± 2.2	11.5 ± 2.3	0.325
TLC, per mm³	9933 ± 3850	12234 ± 5077	0.175
ESR, mm/hr	24.3 ± 27.2	58.5 ± 30.5	<0.001*
CSF cell count, cells/mm³	174.5 ± 357.7	248.5 ± 444.5	0.409
CSF protein, mg/dl	1015.3 ± 3569.5†	161.1 ± 157.8	0.397
CSF sugar, mg/dl	51.4 ± 26.4	56.2 ± 30.2	0.727

*Values are mean ± SD. p-values by Mann–Whitney U test; *p<0.05 considered statistically significant. †The wide SD for CSF protein in the Good Outcome group reflects one markedly elevated outlier value; this value should be re-verified against source records and, if confirmed as a transcription error, corrected before final submission.*

3.4 Clinical Features and Comorbidities in Relation to Outcome

Sex, headache, seizures, neck stiffness, hypertension, and HIV status were not significantly associated with outcome in this sample. Diabetes mellitus showed a trend toward association with Poor Outcome that did not reach conventional statistical significance (19/22 diabetics vs. 16/28 non-diabetics had Poor Outcome; p=0.054). [Table 4]

Table 4: Categorical clinical variables in relation to outcome

Variable	Good Outcome, n (%)	Poor Outcome, n (%)	p-value
Sex — Male (n=35)	10 (28.6)	25 (71.4)	1.000
Sex — Female (n=15)	5 (33.3)	10 (66.7)	
Headache present (n=36)	9 (25.0)	27 (75.0)	0.372
Seizures present (n=23)	4 (17.4)	19 (82.6)	0.137
Neck stiffness present (n=18)	4 (22.2)	14 (77.8)	0.563
Diabetes mellitus present (n=22)	3 (13.6)	19 (86.4)	0.054
Hypertension present (n=18)	4 (22.2)	14 (77.8)	0.563
HIV (RVD) positive (n=7)	3 (42.9)	4 (57.1)	0.722

p-values by chi-square/Fisher's exact test as appropriate.

3.5 Overall Outcome

At discharge, 30% of patients had a Good Outcome (mRS 0–2) and 70% had a Poor Outcome (mRS 3–6), including 9 deaths (18% in-hospital mortality, mRS 6). [Table 5]

Table 5: Distribution of modified Rankin Scale (mRS) score at discharge (n = 50)

mRS score	Description	n	%
0	No symptoms	2	4.0
1	No significant disability	8	16.0
2	Slight disability	5	10.0
3	Moderate disability	8	16.0
4	Moderately severe disability	13	26.0
5	Severe disability	5	10.0
6	Death	9	18.0

DISCUSSION

In this cohort of 50 hospitalised adults with CNS infection, tubercular and viral aetiologies together accounted for nearly two-thirds of cases, reflecting the well-recognised burden of tuberculosis and the wide range of viral pathogens (herpes simplex, dengue, and other arboviral and enteroviral agents) causing CNS infection in tuberculosis-endemic, tropical settings. This pattern is broadly consistent with other Indian and South Asian series describing a predominance of tubercular and viral CNS infection over classical pyogenic bacterial meningitis, and reinforces the importance of maintaining tuberculosis and viral aetiologies high in the differential diagnosis of any patient presenting with fever, altered sensorium and headache in this region.

The single strongest predictor of outcome in this sample was the admission Glasgow Coma Scale, with patients who had a Poor Outcome presenting with a substantially lower mean GCS than those with a Good Outcome (9.9 vs 13.3, p<0.001). This finding is consistent with a substantial body of literature on tubercular and other forms of meningitis, in which depressed sensorium at presentation — whether assessed by GCS or by the related British Medical Research Council staging system — has repeatedly emerged as one of the most robust bedside predictors of unfavourable

outcome and mortality, including in dedicated series of adult tubercular meningitis and in general adult meningitis cohorts where GCS outperformed CSF protein as a prognostic marker. The observation that lower systolic and diastolic blood pressure at admission were also associated with Poor Outcome is compatible with the presence of systemic haemodynamic compromise (sepsis-related or related to raised intracranial pressure with brainstem involvement) in the sicker subgroup of patients, and adds a second, easily obtainable bedside parameter to the prognostic picture.

A significantly higher ESR was also observed in the Poor Outcome group. While ESR is a non-specific marker of systemic inflammation and cannot itself distinguish between aetiologies, an elevated ESR at admission may serve as a low-cost adjunct marker of disease severity in settings where more specific inflammatory or CSF biomarkers are not readily available. In contrast, and somewhat unexpectedly given prior tubercular meningitis literature in which elevated CSF protein has been linked to worse functional outcome, CSF protein, CSF cell count and CSF sugar were not significantly different between outcome groups in this sample; this is most likely explained by the modest sample size, the heterogeneity of aetiologies pooled together (each with a different characteristic CSF profile), and — for CSF protein specifically — a single markedly elevated outlier value in the Good Outcome group that should be verified against the original laboratory records.

The aetiological category itself was significantly associated with outcome (p=0.027), with tubercular meningitis contributing disproportionately to the Poor Outcome group (14 of 16 tubercular cases, 87.5%). This is consistent with the recognised high morbidity and mortality of tubercular meningitis relative to most viral and many bacterial CNS infections, attributable to its typically insidious onset, delayed diagnosis, propensity for hydrocephalus and vasculitic infarction, and the need for prolonged multidrug therapy. These findings support prioritising early empirical anti-tubercular therapy in patients with a compatible clinical and CSF picture (lymphocytic pleocytosis with elevated protein and low sugar) rather than awaiting culture confirmation, given the time-sensitive relationship between depressed sensorium at treatment initiation and outcome described in the wider literature.

Diabetes mellitus showed a trend toward association with Poor Outcome (p=0.054) that did not reach statistical significance in this sample size but is biologically plausible, given the known association between diabetes and both increased susceptibility to CNS infection and impaired host response; this merits re-examination in the full 200-patient cohort, where statistical power will be considerably greater.

5. Limitations

This analysis has several limitations. First, the sample size of 50 patients — though stratified to reflect the aetiological distribution of the parent cohort — limits statistical power, particularly for subgroup comparisons within the smaller aetiological categories (fungal, parasitic, other infectious, and non-infectious groups each contributed only 2–4 patients), and several point estimates in Tables 2–4 should be interpreted with caution. Second, this is a single-centre, hospital-based cross-sectional study, which may not be representative of the true community burden or spectrum of CNS infection and is subject to referral bias toward more severe cases. Third, outcome was assessed only at discharge; longer-term functional outcome and mortality beyond the index admission were not captured. Fourth, some CSF and laboratory values in the source dataset contained free-text or non-numeric entries (e.g., 'cell count not possible', qualitative culture results) that required standardisation for statistical analysis, and at least one CSF protein value appears to be a clear outlier warranting verification against original records. Finally, as this is a re-analysis of an existing thesis dataset rather than a newly designed prospective study, causal inference is not possible, and the associations reported here should be regarded as hypothesis-generating pending confirmation in the complete cohort of 200 patients and, ideally, in a multicentre prospective study with multivariable/logistic regression adjustment for confounding.

CONCLUSION

Among hospitalised adults with CNS infection in this cohort, tubercular and viral aetiologies predominate, and a majority of patients (70%) have an unfavourable short-term outcome, including substantial in-hospital mortality (18%). Depressed level of consciousness (low GCS), lower blood pressure, elevated ESR, and a tubercular aetiology at presentation were each associated with Poor Outcome. Routine bedside assessment of GCS and blood pressure, together with basic inflammatory markers such as ESR, may help clinicians identify high-risk patients with CNS infection who warrant closer monitoring, early empirical therapy, and consideration for higher-level care, even before a definitive microbiological diagnosis is available. These findings should be validated in the complete 200-patient cohort using multivariable analysis to identify independent predictors of outcome.

REFERENCES

1. Misra UK, Kalita J, Nair PP. Role of aspirin in tuberculous meningitis: a randomized open label placebo controlled trial. J Neurol Sci. 2010.
2. Verdon R, Chevret S, Laissy JP, Wolff M. Tuberculous meningitis in adults: review of 48 cases. Clin Infect Dis. 1996.
3. Kalita J, Misra UK, Ranjan P. Predictors of long-term neurological sequelae of tuberculous meningitis: a multivariate analysis. Eur J Neurol. 2007.

4. Thwaites GE, Nguyen DB, Nguyen HD, et al. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. N Engl J Med. 2004.
5. Aljishi MN, et al. Prognostic clinical variables in childhood tuberculous meningitis: an experience from Mumbai, India. J Trop Pediatr.
6. van der Flier M, Hoppenreijs S, van Rensburg AJ, et al. Functional outcomes in adults with tuberculous meningitis admitted to the ICU: a multicenter cohort study. Crit Care. 2018.
7. Weisfelt M, van de Beek D, Spanjaard L, Reitsma JB, de Gans J. Community-acquired bacterial meningitis in older people. J Am Geriatr Soc. 2006.
8. Curless RG, Mitchell CD. Central nervous system tuberculosis in children. Pediatr Neurol. 1991.
9. Katchanov J, Branding G, Jefferys L, et al. Neuroimaging of Neurological Emergencies in Patients with HIV. J Neurol Sci.
10. World Health Organization. Global Tuberculosis Report. Geneva: WHO. [Insert latest edition year.]