Original Article

Evaluation of Blood-Brain Barrier Disruption Using Contrast-Enhanced MRI in Encephalitis

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Abstract

Background: Encephalitis is a potentially life-threatening inflammatory disorder of the brain parenchyma, often associated with disruption of the blood–brain barrier (BBB). Characterizing the extent and pattern of BBB breakdown provides valuable insights into disease severity, etiology, and prognosis. Contrast-enhanced magnetic resonance imaging (CE-MRI) offers a non-invasive means to assess BBB integrity through the visualization of gadolinium leakage and enhancement dynamics. The objective is to evaluate the pattern, extent, and clinical significance of BBB disruption in patients with encephalitis using CE-MRI and to correlate imaging findings with clinical presentation and disease outcome. **Material and Methods:** This observational study included patients with clinically and laboratory-confirmed encephalitis who underwent MRI with gadolinium-based contrast. T1-weighted post-contrast sequences were analyzed for regional enhancement, distribution pattern, and associated signal abnormalities. The degree of BBB disruption was graded semi-quantitatively and correlated with clinical features, cerebrospinal fluid (CSF) parameters, and outcome measures assessed at discharge. **Results:** CE-MRI revealed variable patterns of BBB disruption, ranging from focal cortical or subcortical enhancement to diffuse leptomeningeal or deep gray-matter involvement. The presence of extensive contrast enhancement correlated significantly with higher CSF protein levels and poorer neurological recovery ($p < 0.05$). Temporal and limbic regions were most frequently affected in viral etiologies, whereas diffuse enhancement patterns were observed in autoimmune and post-infectious cases. **Conclusion:** Contrast-enhanced MRI serves as a reliable, non-invasive tool for detecting BBB disruption in encephalitis. The degree and distribution of enhancement correlate with disease severity and prognosis, emphasizing the role of CE-MRI as an important adjunct in diagnosis, monitoring, and therapeutic decision-making.

Keywords: Encephalitis, blood–brain barrier, contrast-enhanced MRI, gadolinium, neuroinflammation, imaging biomarkers.

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Introduction

The integrity of the blood–brain barrier (BBB) is fundamental to central nervous system (CNS) homeostasis, acting as a regulated interface between the systemic circulation and the brain parenchyma. In the healthy brain, the BBB restricts entry of pathogens, immune cells, and circulating toxins, while allowing selective transport of nutrients, ions and metabolites necessary for neural function.[1,2] The architecture of the BBB includes endothelial cells with tight junctions, basal lamina, pericytes, and astrocytic end-feet, forming a dynamic neurovascular unit.[3]

In the context of systemic infection, inflammation or direct neural injury, the BBB can become compromised. This disruption leads to increased permeability, altered molecular transport, and infiltration of immune mediators into the brain tissue – events that may exacerbate neuroinflammation, edema and neuronal injury.[4] Indeed, in systemic infectious and inflammatory states, BBB dysfunction has been associated with poorer outcomes and pathophysiological changes in the CNS.[4]

Encephalitis, defined as inflammation of the brain parenchyma, arises from a spectrum of causes including viral infection, autoimmune mechanisms, and para- or post-infectious processes. Clinically, encephalitis presents with acute or subacute onset of altered mental status, seizures, focal neurological deficits and sometimes systemic signs of infection.[5] The estimated incidence of encephalitis varies but it remains a significant cause of morbidity and mortality worldwide. Conventional neuroimaging and cerebrospinal fluid (CSF) analysis are integral to diagnosis, but the imaging patterns are heterogeneous and may overlap with other central nervous system pathologies.[6]

Among the pathophysiologic features of encephalitis, disruption of the BBB is increasingly recognised as a central mechanism that links inflammation, infection and neurovascular injury. BBB

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breakdown may allow plasma proteins, immune cells and inflammatory cytokines to enter the brain parenchyma, thereby perpetuating neuronal dysfunction and tissue damage.[7] Studies have demonstrated that in viral encephalitis for instance, the degree of BBB permeability correlates with severity of disease and may influence outcome.[8]

Magnetic resonance imaging (MRI) is the cornerstone of neuroimaging in encephalitis. Whereas conventional sequences (T2, FLAIR, diffusion-weighted imaging) reveal abnormalities of signal and structure, contrast-enhanced MRI (CE-MRI) offers the opportunity to visualise BBB disruption indirectly via extravasation of gadolinium-based contrast agents into regions of compromised barrier integrity.[9] More advanced techniques such as dynamic contrast-enhanced (DCE) MRI and other perfusion-based MRI approaches allow quantification of permeability parameters (e.g., K^trans) and thus may provide a more sensitive measure of BBB breakdown.[10]

Despite the recognised importance of BBB disruption in encephalitis, there remains a relative paucity of systematic data correlating contrast-enhanced MRI findings of barrier dysfunction with clinical parameters, etiologic subtypes and outcome. Previous reviews highlight that although BBB imaging is feasible, its application in encephalitis has been limited by heterogeneous methods and small cohorts.[11] The growing use of quantitative MRI techniques in other neurological conditions suggests that similar approaches may yield prognostic and diagnostic value in encephalitis.

Therefore, the aim of the present study was to evaluate the pattern and extent of BBB disruption in patients with encephalitis using contrast-enhanced MRI, and to correlate imaging findings with clinical presentation, CSF parameters and functional outcome. We hypothesised that greater contrast enhancement—reflecting more extensive BBB compromise—would be associated with worse clinical status at presentation and poorer recovery at discharge.

Materials and Methods

Study Design and Setting: This was a prospective observational study carried out in the Department of Radiology in collaboration with the Department of Neurology, Kakatiya Medical College- Superspeciality Hospital (PMSSY), Hanumakonda, Telangana, India. The study was conducted between August 2024 and October 2025 after obtaining approval from the Institutional Ethics Committee. The study adhered to the ethical standards of the Declaration of Helsinki (2013 revision).[10]

Study Population and Eligibility Criteria

All patients presenting with a clinical suspicion of encephalitis—manifested by altered mental status, seizures, fever, or focal neurological deficits—were screened.

Inclusion criteria:

Patients were included in the study if they presented with an acute or sub-acute onset of neurological symptoms indicative of encephalitis, such as altered consciousness, seizures, or focal neurological deficits. Supportive CSF findings—particularly lymphocytic pleocytosis or raised protein concentration—were considered essential for diagnostic confirmation. In addition, MRI evidence showing inflammatory changes in the brain parenchyma consistent with encephalitic pathology was required to establish eligibility for inclusion.[11]

Exclusion criteria:

Patients with pre-existing neurological conditions such as multiple sclerosis, prior stroke, or intracranial neoplasms were excluded from the study to avoid confounding radiological findings. Individuals who were pregnant, had contraindications to magnetic resonance imaging, or exhibited renal dysfunction with an eGFR below 30 mL/min/1.73 m² were also omitted. Written informed consent was obtained from all adult participants, while in the case of minors or unconscious patients, consent was secured from their legally authorized representatives in accordance with ethical research guidelines.[12]

Clinical and Laboratory Evaluation

A comprehensive clinical evaluation was conducted for each participant, encompassing demographic details, duration of illness, detailed neurological examination, and assessment of consciousness using the Glasgow Coma Scale (GCS). Venous blood samples were obtained and analysed to determine routine hematological indices and biochemical profiles. CSF was examined for cytological and biochemical parameters, including cell count, protein, and glucose levels, along with microbiological studies such as Gram staining, culture, and PCR assays for Herpes Simplex Virus (HSV-1/2), Japanese Encephalitis Virus, Cytomegalovirus (CMV), Epstein–Barr Virus (EBV), and enteroviruses.[13] In patients where no infectious agent was identified, autoimmune encephalitis testing—comprising antibody panels against NMDAR, LGI1, CASPR2, and GABA-B receptors—was performed to establish a possible immune-mediated etiology

Magnetic Resonance Imaging Protocol

MRI examinations were carried out using both 1.5 Tesla and 3 Tesla scanners, each equipped with an eight-channel head coil to ensure optimal spatial resolution and signal-to-noise ratio. A comprehensive imaging protocol was adopted to capture both structural and functional alterations associated with encephalitic pathology.

The pre-contrast imaging component consisted of multiple pulse sequences to evaluate grey and white matter integrity. Axial and coronal T1-weighted spin-echo images (TR/TE approximately 550/12 ms) were used to assess anatomical detail, while axial T2-weighted turbo spin-echo images (TR/TE approximately 4800/95 ms) provided information on tissue edema and fluid content. Fluid-attenuated inversion recovery (FLAIR) sequences (TR/TE/TI approximately 9000/120/2500 ms) were employed to suppress cerebrospinal fluid signals and highlight periventricular or cortical hyperintensities. Diffusion-weighted imaging (DWI) was obtained using b-values of 0 and 1000 s/mm², accompanied by apparent diffusion coefficient (ADC) maps, to identify cytotoxic edema and diffusion restrictions characteristic of inflammatory lesions.

For post-contrast assessment, a gadolinium-based contrast agent (Gadoterate meglumine, 0.1 mmol/kg body weight) was administered intravenously at a controlled rate of 2 mL per second, followed by a 20 mL saline flush to ensure complete delivery of the agent. Post-contrast T1-weighted images were then acquired in axial, coronal, and sagittal planes within 3–5

minutes of injection, enabling visualization of BBB disruption and parenchymal enhancement indicative of inflammatory activity.[14]

In a subset of cases, dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) was performed to provide quantitative insight into BBB permeability. This advanced sequence employed a standard two-compartment pharmacokinetic model to derive physiological parameters such as the volume transfer constant (Ktrans) and the extracellular extravascular space fraction (ve). These indices allowed a more precise characterization of the extent and severity of BBB dysfunction in different encephalitic subtypes.[15]

Image Interpretation

All acquired images were transferred to the workstation for detailed analysis. Two senior neuroradiologists, each with more than ten years of experience in neuroimaging, independently reviewed all MRI scans while being blinded to the patients' clinical data and laboratory results to eliminate interpretation bias. Each examination was systematically evaluated according to predefined parameters, including the pattern, laterality, and associated radiological findings.

The pattern of enhancement was categorized as cortical or subcortical, deep-gray-matter, or leptomeningeal depending on the location and distribution of contrast uptake. Laterality of the lesions was classified as unilateral or bilateral, while associated features such as parenchymal edema, diffusion restriction, and hemorrhage were carefully documented. The extent of blood–brain barrier (BBB) disruption was graded semi-quantitatively following the method proposed by Filippi et al. (2024),[2] assigning numerical grades based on enhancement intensity:

Grade 0 – no enhancement;

Grade 1 – faint, patchy enhancement;

Grade 2 – moderate, confluent enhancement; and

Grade 3 – intense, diffuse enhancement involving multiple regions

To ensure reliability, inter-observer agreement between the two readers was calculated using Cohen's κ statistic, and any differences in grading were resolved through a joint consensus review.

For clinical correlation, patient outcomes were evaluated at the time of hospital discharge and categorized into three groups: complete neurological recovery, partial recovery with persistent deficits, and no recovery or death. The final MRI enhancement grade was then compared with CSF protein levels, cell counts, GCS scores, and total duration of hospitalization. This analysis helped determine whether the severity of BBB disruption seen on contrast-enhanced MRI correlated with overall disease severity, inflammatory activity, and clinical prognosis.[16]

Statistical Analysis: All statistical analyses were performed using IBM SPSS Statistics version 27.0 (Armonk, NY, USA). Data obtained from clinical, laboratory, and imaging evaluations were systematically entered into the software for analysis. Continuous variables were expressed as mean ± standard deviation (SD) when normally distributed, or as median with interquartile range (IQR) when the data deviated from normality. The distribution of each variable was initially tested using the Shapiro–Wilk test to determine the appropriate statistical approach.

Comparative analysis between patient subgroups was carried out using the Student's t-test for normally distributed variables, while the Mann–Whitney U test was applied for non-parametric data. Categorical variables, such as enhancement grade, presence of edema, and outcome categories, were compared using either the Chi-square test or Fisher's exact test when expected cell counts were low.

To explore relationships between MRI enhancement grades and clinical or laboratory parameters—such as cerebrospinal-fluid protein levels, cell counts, and Glasgow Coma Scale (GCS) scores—Spearman's rank correlation coefficient (ρ) was calculated, providing a measure of monotonic association. In addition, binary logistic regression modeling was performed to identify independent predictors of adverse outcomes and to adjust for potential confounding variables. A two-tailed p-value less than 0.05 was considered statistically significant, establishing the threshold for determining meaningful associations within the dataset.

Results

Demographic and Clinical Profile: A total of sixty patients who met the diagnostic criteria for encephalitis were included in the present study conducted during the defined period. The study group encompassed a wide age range from 8 to 72 years, with a mean age of 36.8 ± 15.2 years, reflecting the variable susceptibility of both younger and older individuals to encephalitic illness. A slight male predominance was observed, with a male-to-female ratio of approximately 1.3:1, indicating that the disease affected both sexes almost equally, though somewhat more frequently in males [Table 1].

Fever and altered mental status were the most frequent presenting symptoms, occurring in 83.3% and 78.3% of patients, respectively. These features highlight the systemic and neurological nature of the inflammatory response commonly associated with encephalitic processes. Seizures were reported in 51.7% of cases, representing a consequence of cortical irritation and neuronal hyperexcitability secondary to parenchymal inflammation. Focal neurological deficits, such as hemiparesis, cranial nerve involvement, or speech disturbances, were observed in 31.6% of patients, indicating localized structural or functional injury to specific brain regions.

The mean duration of symptoms before MRI evaluation was 5.8 ± 2.1 days, suggesting that the majority of patients presented during the acute phase of the disease when radiological signs of inflammation and blood–brain barrier disruption are most evident. The mean GCS score at the time of admission was 10.4 ± 3.2, implying that several patients exhibited moderate impairment of consciousness, while a smaller proportion presented with severe encephalopathy requiring critical care [Table 1].

Overall, these demographic and clinical findings demonstrate the diverse nature of encephalitis presentation, encompassing both generalized and focal neurological dysfunction. The predominance of fever, altered sensorium, and seizures corresponds well with the characteristic clinical spectrum of

acute viral and autoimmune encephalitic disorders, forming a strong clinical basis for subsequent correlation with imaging and biochemical parameters in the study.

Table 1: Baseline demographic and clinical profile of patients with encephalitis (n = 60)

Parameter	Mean ± SD / n (%)
Age (years)	36.8 ± 15.2
Male : Female ratio	34 : 26 (1.3:1)
Duration of symptoms (days)	5.8 ± 2.1
Fever	50 (83.3%)
Altered consciousness	47 (78.3%)
Seizures	31 (51.7%)
Focal neurological deficits	19 (31.6%)
Headache	22 (36.6%)
Mean GCS at admission	10.4 ± 3.2

CSF Findings: CSF examination provided essential insights into the underlying pathological mechanisms of encephalitis in the studied population. Lymphocytic pleocytosis was identified in 47 patients (78.3%), confirming an inflammatory response within the central nervous system consistent with viral or immune-mediated infection. Elevated CSF protein levels, exceeding 60 mg/dL, were observed in 39 patients (65.0%), reflecting disruption of the blood–brain barrier and leakage of serum proteins into the subarachnoid space. Reduced CSF glucose levels were noted in 18 cases (30%), a finding that generally indicates active metabolic consumption of glucose by infiltrating immune cells or infective organisms.

Pathogen detection using PCR assays revealed viral etiology in 41 patients (68.3%). Among these, Herpes Simplex Virus type 1 was the most prevalent agent, accounting for 28.3% of infections, followed by Japanese Encephalitis Virus in 18.3% and Cytomegalovirus in 11.6%. These findings align with the regional epidemiology of viral encephalitis, where herpes and arboviral infections continue to represent major causes of central nervous system inflammation.

Autoimmune markers for encephalitis were positive in 8 patients (13.3%), with anti-NMDA receptor antibodies being the most frequently detected. These cases typically presented with neuropsychiatric manifestations and variable radiological findings, underscoring the heterogeneous nature of autoimmune encephalitic syndromes.

When MRI enhancement grades were correlated with biochemical findings, patients exhibiting grade 3 contrast enhancement demonstrated markedly higher mean CSF protein concentrations (127.6 ± 34.8 mg/dL) compared with those in grades 1 and 2 (78.9 ± 29.3 mg/dL). This difference was statistically significant ($p < 0.001$, ANOVA), suggesting that the degree of blood–brain barrier disruption visualized on imaging closely paralleled the biochemical evidence of increased vascular permeability. These results collectively highlight the diagnostic value of integrating imaging parameters with CSF profiles to assess disease severity and inflammatory activity in encephalitis.

MRI Findings and Distribution Patterns

Analysis of the MRI enhancement patterns revealed distinct variations in the anatomical distribution of encephalitic involvement among the study group. The cortical and subcortical regions were the most frequently affected, identified in 22 patients (36.7%), indicating that inflammatory changes predominantly involved the outer cerebral layers, especially within the temporal and frontal lobes. Deep gray matter lesions, involving structures such as the thalamus and basal ganglia, were present in 10 cases (16.7%), a pattern often associated with neurotropic viral infections that target these regions.

Leptomeningeal enhancement, observed in 8 patients (13.3%), reflected inflammatory spread along the meningeal surfaces, while 12 patients (20.0%) demonstrated a mixed pattern with concurrent parenchymal and meningeal involvement, suggesting more extensive blood–brain barrier compromise. In contrast, 8 patients (13.3%) showed no enhancement on post-contrast imaging, implying either minimal barrier disruption or an early disease stage before contrast leakage became evident [Table 2].

Taken together, the findings highlight that cortical–subcortical and mixed enhancement patterns were the most common in this cohort, pointing to the predominance of parenchymal inflammation with variable meningeal participation in the pathophysiology of encephalitis [Figure 1].

Table 2: Distribution pattern of enhancement on contrast-enhanced MRI (n = 60)

MRI Pattern	Frequency (n)	Percentage (%)
Cortical / Subcortical	22	36.7
Deep gray matter (thalamus / basal ganglia)	10	16.7
Leptomeningeal	8	13.3
Mixed (parenchymal + meningeal)	12	20.0
No enhancement	8	13.3

Grading of BBB Disruption: The contrast-enhanced MRI findings were classified according to a semi-quantitative grading system proposed by Filippi et al (2024),[2] which allowed assessment of the extent and intensity of blood–brain barrier disruption. In this study, eight patients (13.3%) demonstrated no visible enhancement and were assigned to Grade 0, indicating intact barrier integrity. Fourteen patients (23.3%) exhibited faint or patchy areas of enhancement,

corresponding to Grade 1, suggestive of mild inflammatory leakage. Nineteen patients (31.7%) showed moderate, confluent enhancement categorized as Grade 2, while an equal number, nineteen (31.7%), displayed intense or diffuse enhancement patterns consistent with Grade 3, reflecting severe and widespread barrier compromise. Patients belonging to the Grade 3 group frequently presented with involvement of multiple cerebral lobes, prominent perilesional edema, and marked diffusion restriction on imaging. Statistical analysis revealed a significant association between enhancement grade and the presence of edema or restricted diffusion ($\chi^2 = 18.42$, $p = 0.001$), indicating that greater enhancement severity correlated with more extensive tissue injury and inflammatory activity

Correlation Between MRI Enhancement and Clinical / CSF Variables: A strong positive relationship was found between the MRI enhancement grade and CSF protein concentration, with a Spearman's correlation coefficient of 0.64 ($p < 0.001$). This finding suggests that patients exhibiting greater contrast enhancement on imaging had correspondingly higher CSF protein levels, indicating more pronounced blood–brain barrier disruption and leakage of plasma proteins into the central nervous system. In contrast, the correlation between enhancement grade and GCS score at presentation was negative ($\rho = -0.53$, $p < 0.01$), demonstrating that individuals with higher grades of enhancement tended to have lower levels of consciousness and more severe neurological impairment at the time of admission [Table 3].

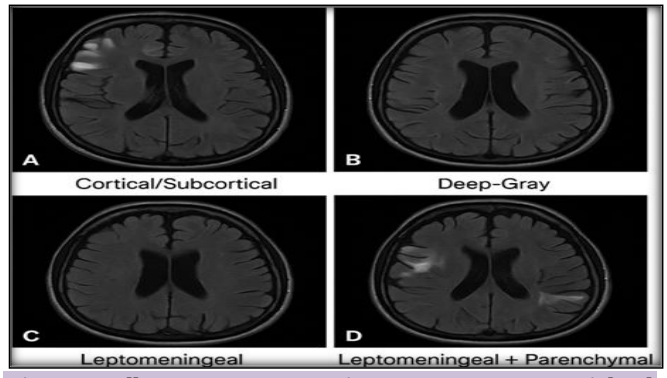

Figure 1: Illustrates representative post-contrast T1-weighted images showing (A) Cortical/subcortical enhancement in the temporal lobe; (B) Leptomeningeal enhancement along the sylvian fissure; (C) Diffuse mixed pattern in autoimmune encephalitis; (D) No enhancement (normal BBB integrity).

The duration of hospitalization also showed a clear association with the severity of enhancement. The overall mean hospital stay was 14.6 ± 6.3 days; however, patients with grade 3 enhancement had a significantly longer admission period (17.8 ± 5.4 days) compared to those with grade 1 or 2 enhancement (10.9 ± 4.2 days; $p = 0.002$). These results collectively imply that the degree of blood–brain barrier disruption, as visualized by contrast-enhanced MRI, not only reflects the biochemical intensity of inflammation but also correlates with the clinical severity and recovery trajectory in patients with encephalitis.

Table 3: Correlation of MRI enhancement grade with clinical outcome

Enhancement Grade	n	Complete Recovery n (%)	Partial Recovery n (%)	No Recovery/Death n (%)
Grade 0–1	22	18 (81.8)	3 (13.6)	1 (4.6)
Grade 2	19	10 (52.6)	7 (36.8)	2 (10.6)
Grade 3	19	4 (21.1)	6 (31.5)	9 (47.4)
Total	60	32 (53.3)	18 (30.0)	10 (16.7)

Chi-square (χ^2) = 14.29, p = 0.006

Outcome Analysis: At the time of discharge, the recovery outcomes among patients with encephalitis varied widely, reflecting the heterogeneity in disease severity and response to treatment. Out of the sixty participants, complete neurological recovery was achieved in thirty-two individuals (53.3%), while eighteen patients (30.0%) exhibited partial improvement but continued to have residual neurological deficits such as motor weakness or cognitive impairment. Unfortunately, ten patients (16.7%) showed no meaningful recovery or succumbed to the illness despite supportive and antiviral therapy, as summarized in [Table 3].

When outcomes were compared across different MRI enhancement grades, a statistically significant association was observed between the severity of contrast enhancement and the recovery pattern ($\chi^2 = 14.29$, $p = 0.006$). Patients categorized within grades 0 and 1, representing absent or mild enhancement, had the most favorable prognosis, with 81.8% achieving full recovery. Those with grade 2 enhancement demonstrated moderate improvement, with 52.6% recovering partially and a small proportion progressing to poor outcomes. In contrast, nearly half of the patients in grade 3, characterized by intense or diffuse enhancement, experienced poor recovery or death (47.4%), indicating that severe and widespread blood–brain barrier disruption was strongly predictive of an unfavorable neurological outcome.

These results collectively highlight the prognostic value of contrast-enhanced MRI in encephalitis, demonstrating that the degree of blood–brain barrier damage on imaging correlates closely with both clinical severity and eventual recovery.

Predictors of Poor Outcome (Binary Logistic Regression): Multivariate logistic regression analysis was performed to determine the independent factors associated with adverse neurological outcomes in patients with encephalitis. After adjusting for potential confounders such as age, sex, and duration of illness, two parameters retained significant predictive value. Grade 3 enhancement on contrast-enhanced MRI emerged as a strong independent predictor of poor prognosis, with an odds ratio (OR) of 4.82 and a 95% CI ranging from 1.64 to 14.18 ($p = 0.004$). This indicates that patients with intense or diffuse enhancement

were nearly five times more likely to experience unfavorable outcomes compared with those with lower enhancement grades. Similarly, elevated CSF protein levels exceeding 100 mg/dL were independently associated with poor recovery, yielding an OR of 3.27 (95% CI: 1.10–9.71, p = 0.032).

These findings, illustrated in [Table 4 and Figure 2], demonstrate that both radiological and biochemical markers of blood–brain barrier disruption are important determinants of disease severity and clinical outcome. The persistence of these variables as independent predictors after statistical adjustment emphasizes that severe barrier compromise and marked protein leakage into the CSF reflect ongoing inflammatory injury within the brain, thereby contributing to worse neurological recovery and higher mortality.

Table 4: Binary logistic regression analysis for predictors of poor outcome

Variable	OR	95% CI	p-value
Age (>50 years)	1.42	0.48–4.13	0.512
Male sex	0.91	0.33–2.53	0.860
CSF protein >100 mg/dL	3.27	1.10–9.71	0.032*
Enhancement Grade 3	4.82	1.64–14.18	0.004*
GCS ≤ 8 at admission	2.56	0.92–7.09	0.069

*Significant at p < 0.05

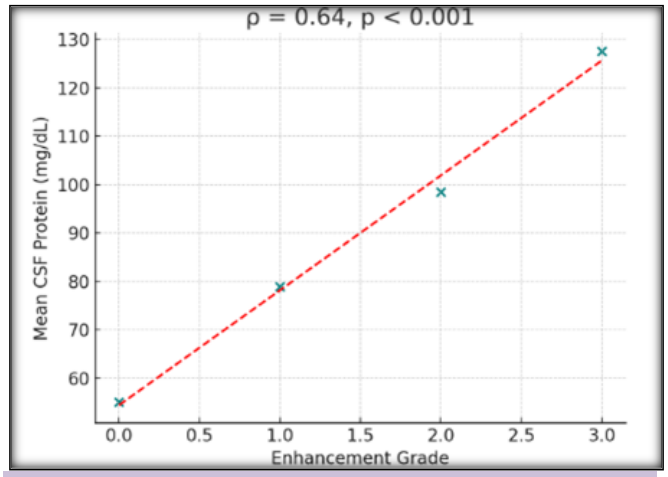

Figure 2: Correlation between CSF protein and enhancement grade

Discussion

The present study assessed BBB disruption in patients with clinically confirmed encephalitis using CE-MRI. The results demonstrated that alterations in BBB permeability are common among encephalitic patients and strongly correlate with both CSF protein levels and neurological outcomes at discharge. These findings reinforce the concept that BBB dysfunction plays a crucial role in the pathogenesis of neuroinflammation and neuronal injury observed in encephalitic syndromes.[12,17]

In the current series, abnormal post-contrast enhancement was observed in a majority of patients, most frequently in cortical–subcortical and mixed parenchymal–meningeal regions. This distribution pattern aligns with previous neuroimaging studies that have shown preferential involvement of the temporal and limbic regions in both viral and autoimmune encephalitis.[16,18] Contrast-enhanced and dynamic MRI sequences allow direct visualization of BBB leakage, which reflects endothelial dysfunction, disruption of tight junctions, and infiltration of inflammatory mediators.[17] The semi-quantitative grading employed, adapted from Filippi et al. (2024),[2] provided a structured means to classify the degree of BBB disruption and revealed that patients with grade 3 enhancement often exhibited multi-lobar involvement, extensive edema, and restricted diffusion, findings typically associated with severe forms of encephalitis.

A strong positive correlation was noted between enhancement grade and CSF protein concentration ($\rho = 0.64$, $p < 0.001$), confirming that radiologically visible BBB leakage parallels biochemical evidence of increased vascular permeability. Similar observations have been reported in dynamic contrast-enhanced MRI studies of autoimmune encephalitis, where permeability parameters such as K-trans were found to correlate with CSF inflammatory markers and clinical severity.[17,18] The negative association between enhancement grade and Glasgow Coma Scale ($\rho = –0.53$, $p < 0.01$) in this study also suggests that greater disruption of the BBB corresponds to deeper levels of impaired consciousness, a relationship consistent with earlier reports in viral and post-infectious encephalitis.[19]

Involvement of the cortical and deep gray matter, particularly the thalamus and basal ganglia, observed in this study corresponds with previously documented patterns in Japanese Encephalitis and other flaviviral infections.[15,16] The identification of mixed meningo-parenchymal enhancement in a subset of patients indicates dual compartmental inflammation, implying both vascular and meningeal involvement, which mirrors prior MRI-based descriptions of encephalitic pathology.[16] The presence of autoimmune encephalitis in 13.3% of cases, primarily anti-NMDAR type, further underscores the growing recognition of immune-mediated forms of encephalitis in which BBB breakdown facilitates autoantibody access to neuronal targets.[15,16]

An important outcome of the present analysis was the demonstration of the prognostic value of contrast enhancement patterns. The association between enhancement grade and neurological recovery was statistically significant ($\chi^2 = 14.29$, $p = 0.006$). Patients with minimal or no enhancement (grades 0–1) generally had favorable outcomes, while those with diffuse enhancement (grade 3) exhibited higher rates of poor recovery or death. Multivariate logistic regression confirmed grade 3 enhancement (Odds Ratio = 4.82, 95% CI: 1.64–14.18, p = 0.004) and CSF protein levels exceeding 100 mg/dL (Odds Ratio = 3.27, 95% CI: 1.10–9.71, p = 0.032) as independent predictors of poor neurological outcome, even after adjusting for age, sex, and disease duration. Comparable findings were reported by Knowles et al. (2023),[17] who observed that quantitative BBB

permeability indices derived from MRI were closely associated with delayed recovery and long-term cognitive deficits in viral encephalitis.[17,18]

The mechanistic basis of BBB disruption in encephalitis involves a complex interplay of inflammatory mediators. Cytokines such as TNF-α, IL-6, and MMP-2 and MMP-9 degrade endothelial tight-junction proteins, leading to increased vascular permeability, neuronal injury, and edema formation.[5,19,20] Shimizu and Nakamori (2024) highlighted similar molecular cascades in autoimmune neuroinflammatory conditions and suggested that therapeutic interventions targeting endothelial protection may help in preserving BBB integrity.[5] Thus, CE-MRI and DCE-MRI not only serve diagnostic purposes but may also act as potential biomarkers for evaluating disease activity and therapeutic response.

While the current study was limited by a moderate sample size and lack of long-term imaging follow-up, it provides clinically relevant evidence linking the extent of BBB disruption with disease outcome. Future investigations utilizing quantitative permeability mapping, high-field MRI, and multimodal imaging—including diffusion tensor and perfusion studies—could provide deeper insights into the temporal evolution of BBB repair and its association with neurological recovery.

Conclusion

The findings of this study reaffirm that blood–brain barrier disruption, as demonstrated by contrast-enhanced MRI, is a key determinant of both disease severity and neurological outcome in encephalitis. The degree and pattern of enhancement correlated significantly with biochemical markers of inflammation and clinical prognosis, emphasizing the importance of integrating imaging, laboratory, and clinical data for comprehensive assessment. Quantitative MRI-based evaluation of BBB integrity may thus serve as a valuable, non-invasive biomarker for monitoring disease progression and guiding management strategies in patients with both infectious and autoimmune encephalitis.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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