

ORIGINAL ARTICLE

MRI Patterns and Functional Outcomes in Patients with Viral Encephalitis

TABASSUM BEGUM¹, MUHAMMAD SADIQ¹, ZUBAIR JANAN ORAKZAI¹, LAILA KHAN¹, HINA BAIG¹, SUMAIRA NOUREEN¹¹Department of Radiology, Mardan Medical Complex, MardanCorrespondence to: Dr. Muhammad Sadiq, Email: mskhan14142@gmail.com

ABSTRACT

Objective: To determine magnetic resonance imaging patterns in patients with viral encephalitis and assess their association with functional outcomes at hospital discharge.**Material and Methods:** This prospective observational study included 89 patients with viral encephalitis treated at Mardan Medical Complex Mardan from 15 January 2023 to 15 September 2023. Clinical findings laboratory results and magnetic resonance imaging characteristics were recorded. Functional outcome was assessed at discharge through the modified Rankin Scale. Scores from 0 to 2 were classified as favorable while scores from 3 to 6 were classified as unfavorable. Associations were assessed through chi square testing and multivariable logistic regression.**Results:** Temporal limbic involvement was the most frequent magnetic resonance imaging pattern and was observed in 26 patients. Deep gray matter involvement was found in 18 patients while diffuse cortical involvement was present in 15 patients. Diffusion restriction was identified in 54 patients and extensive involvement was found in 34 patients. Favorable outcome was recorded in 51 patients while 38 patients had an unfavorable outcome. Extensive magnetic resonance imaging involvement was independently associated with unfavorable outcome. A Glasgow Coma Scale score of 8 or below and brainstem involvement were also significant predictors of poor recovery.**Conclusion**

Magnetic resonance imaging patterns were associated with early functional outcome in viral encephalitis. Extensive involvement and brainstem disease were linked with greater disability. Combined clinical and imaging assessment may support early prognostic evaluation.

Keywords: Encephalitis Viral, Magnetic Resonance Imaging, Treatment Outcome, Prognosis, Seizures. Brain Diseases

INTRODUCTION

Viral encephalitis is recognized as a severe inflammatory disorder of the brain that is caused by viral invasion of neural tissue or by an immune mediated response after infection. A wide clinical spectrum can be produced. Mild confusion may be observed in some patients while coma seizures and profound neurological disability may be produced in others. Significant mortality and long term dependence are still reported despite improvements in antiviral therapy and critical care. Early recognition is therefore required so that treatment can be started before irreversible injury is established. Diagnosis is usually supported by clinical findings cerebrospinal fluid analysis electroencephalography and neuroimaging. Among these methods magnetic resonance imaging has been accepted as the most sensitive technique for the demonstration of brain involvement in viral encephalitis.¹

Characteristic magnetic resonance imaging patterns can be produced by different viral agents. Temporal and inferior frontal lobe involvement is commonly associated with herpes simplex encephalitis. Thalamic basal ganglia brainstem and cerebellar changes may be demonstrated in several arboviral infections. Diffuse cortical or subcortical abnormalities may also be observed when the causative virus cannot be confirmed. These patterns are important because etiological suspicion may be strengthened before laboratory confirmation is received. A prompt diagnosis may therefore be supported and targeted treatment may be initiated. However overlap between imaging appearances is frequently encountered. Similar signal abnormalities can be caused by metabolic disease autoimmune encephalitis hypoxic injury and postictal change. Careful interpretation is therefore required so that misleading conclusions are avoided.²

Magnetic resonance imaging changes in viral encephalitis are usually demonstrated as areas of high signal intensity on T2 weighted and fluid attenuated inversion recovery sequences. Restricted diffusion may be identified during the early phase because cytotoxic edema is produced by cellular injury. Swelling of the affected cortex may be seen and loss of normal sulcal definition may be produced. Hemorrhagic components may be detected on susceptibility sensitive sequences. Contrast enhancement may be absent at first and may appear later as

disruption of the blood brain barrier progresses. These findings can evolve during the disease course. For this reason the timing of imaging is important. A normal early examination does not fully exclude encephalitis and repeat imaging may be required when clinical suspicion remains high.³

The anatomical distribution of abnormalities is believed to reflect viral neurotropism and the pathway through which the central nervous system is reached. Hematogenous spread may be used by some viruses while neural pathways may be followed by others. Selective vulnerability of specific neurons and regional immune responses may also influence the final appearance. In herpes simplex infection the limbic system is often affected. In Japanese encephalitis the thalamic and basal ganglia are frequently involved. In enteroviral infection the brainstem and spinal cord may be targeted. In varicella zoster infection vascular complications may be produced and infarcts may be demonstrated. Although these associations are well known they are not absolute and atypical distributions can be shown in routine practice.⁴

Functional outcome after viral encephalitis is determined by several interacting factors. Age immune status level of consciousness seizure burden viral type and delay in treatment can influence recovery. The extent and location of structural brain injury are also expected to be important. Damage involving memory networks may result in persistent cognitive impairment. Motor pathway involvement may be followed by weakness and dependence in daily activities. Brainstem disease may be associated with respiratory failure and severe disability. Diffuse cortical injury may lead to prolonged unconsciousness and poor rehabilitation potential. Even after survival has been achieved subtle deficits in attention behavior speech and executive function may remain. These deficits may not be recognized during early hospitalization but can seriously affect social and occupational reintegration.⁵

MRI may provide information that is relevant to prognosis because the burden of tissue injury can be visualized. Extensive bilateral abnormalities may indicate widespread disease. Deep gray matter involvement may be associated with impaired consciousness and movement disorders. Brainstem involvement may be linked with greater clinical severity. Hemorrhage necrosis or marked diffusion restriction may suggest aggressive tissue destruction. In contrast limited unilateral abnormalities may be associated with a more favorable course when treatment is started early. Yet these relationships have not been consistently

Received on 28-11-2023

Accepted on 25-12-2023

demonstrated across published studies. Different viral causes and different outcome scales have been used. Imaging has often been performed at variable times. As a result the prognostic meaning of individual MRI patterns has remained uncertain.⁶

Clinical outcome is commonly measured through scales that assess disability and independence. The modified Rankin Scale is frequently used because global functional status can be graded in a simple and reproducible manner. The Glasgow Outcome Scale may also be used. Cognitive and behavioral consequences may require additional assessment because they may not be fully represented by broad disability scales. A patient may be able to walk independently while important memory or personality changes remain. Therefore interpretation of outcome should be performed with awareness of the limitations of each instrument. In resource limited settings simple functional scales are often preferred because detailed neuropsychological testing may not be available. This practical approach allows recovery to be compared with imaging findings during admission and follow up.⁷

Seizures are frequently produced during viral encephalitis and may complicate the interpretation of MRI. Cortical diffusion restriction and swelling can be caused by prolonged seizures even when direct viral injury is limited. Distinction between postictal change and encephalitic involvement may therefore be difficult. Electroencephalographic correlation may be required. Serial imaging may also be helpful because seizure related changes can resolve while areas of permanent injury may evolve into gliosis or atrophy. Status epilepticus is itself associated with worse outcome and can increase neuronal damage. When MRI findings and clinical course are assessed together a more accurate understanding may be achieved. However this combined assessment has not been performed consistently in many available studies.⁸

Laboratory confirmation of a specific virus is not always achieved. Polymerase chain reaction testing can be limited by timing prior treatment or low viral load. Some viral panels may not be available in every hospital. A probable diagnosis may therefore be made through clinical presentation cerebrospinal fluid findings and imaging patterns. This uncertainty can affect research because heterogeneous cases may be grouped together. It can also reduce the ability to compare outcomes between specific etiologies. In developing health systems delayed presentation and restricted access to advanced tests may further complicate diagnosis. Under these conditions MRI becomes especially valuable because an early objective assessment of brain injury can be provided even when virological confirmation is incomplete.⁹

Most previous investigations have focused on the diagnostic appearance of a single viral infection or on the sensitivity of MRI for encephalitis. Fewer studies have directly linked the distribution and extent of MRI abnormalities with functional outcome at discharge or follow up. Sample sizes have often been small. Pediatric and adult populations have sometimes been combined. Definitions of favorable and unfavorable outcome have varied. Imaging protocols have also differed between centers. These limitations have prevented a clear prognostic model from being established. A particular gap is present in regional data from South Asian tertiary care hospitals where delayed referral severe disease and limited laboratory facilities are frequently encountered. Local evidence is needed because disease patterns and health care access may differ from those reported in high income settings.¹⁰

A clearer understanding of MRI patterns may improve clinical decision making. Patients with imaging features associated with severe disability could be identified early and may be considered for closer monitoring intensive rehabilitation and detailed counseling of families. Imaging could also be used to support discussions about expected recovery when laboratory results are delayed. At the same time prognosis should not be based on a single scan because neurological recovery can continue for months and early abnormalities may partially resolve. MRI findings should therefore be interpreted with clinical severity treatment timing and complications. A structured comparison

between imaging patterns and measured functional outcomes is required so that useful associations can be recognized without overstating certainty.

The present study was designed to address this gap by evaluating the magnetic resonance imaging patterns observed in patients with viral encephalitis and by determining their relationship with functional outcomes. The distribution of lesions the involved brain regions the presence of diffusion restriction hemorrhage enhancement and the extent of disease were planned to be assessed. Functional status was planned to be measured through a standardized outcome scale. The objective of the study was to determine whether specific MRI patterns were associated with favorable or unfavorable functional outcomes in patients with viral encephalitis.

MATERIALS AND METHODS

Study Design: This prospective observational study evaluated magnetic resonance imaging patterns and their association with functional outcomes in patients with viral encephalitis. No treatment was assigned by the investigators. All patients were managed according to routine clinical protocols.

Study Setting: The study was conducted at Mardan Medical Complex Mardan. This tertiary care teaching hospital provides neurological radiological laboratory and critical care services.

Study Duration: The study was carried out from 15 January 2023 to 15 September 2023. Eligible patients were recruited throughout this period until the required sample size was completed.

Study Population: Patients admitted with suspected or confirmed viral encephalitis were considered. Diagnosis was based on acute fever altered mental status seizures behavioral change focal neurological deficit or reduced consciousness with supportive cerebrospinal fluid laboratory electroencephalographic or MRI findings.

Sample Size and Sampling Technique: A total of 89 patients were included. Consecutive nonprobability sampling was used. Every eligible patient was enrolled until the required number was achieved.

Inclusion Criteria: Patients of either sex and any age with clinical features consistent with acute viral encephalitis were included. MRI brain during the acute admission was required. Cases with supportive cerebrospinal fluid findings or positive viral polymerase chain reaction results were included when available. Probable cases were accepted after bacterial fungal tuberculous metabolic autoimmune and structural causes had been excluded. Written consent was obtained from patients or legal guardians.

Exclusion Criteria: Patients with bacterial meningitis tuberculous meningitis fungal infection autoimmune encephalitis brain tumor recent major head trauma acute stroke intracranial hemorrhage severe metabolic encephalopathy or hypoxic brain injury were excluded. Patients with a chronic neurological disorder that could independently affect functional status were also excluded. Cases with incomplete records unavailable MRI images severe motion artifact or undocumented discharge outcome were removed from analysis.

Clinical Assessment: A detailed history was obtained from the patient or attendant. Age sex duration of illness fever seizures headache vomiting behavioral symptoms focal weakness and level of consciousness were recorded. Neurological examination included mental status cranial nerves motor power tone reflexes sensation and meningeal signs. Glasgow Coma Scale score was documented at admission. Status epilepticus intensive care admission mechanical ventilation and major complications were also recorded.

Laboratory and Ancillary Evaluation: Routine investigations included complete blood count serum electrolytes renal function liver function blood glucose and inflammatory markers. Cerebrospinal fluid analysis was performed when clinically appropriate. Cell count protein glucose and viral polymerase chain reaction results were recorded when available.

Electroencephalography findings were reviewed in patients who underwent the test.

MRI Acquisition Protocol: MRI brain was performed according to the departmental encephalitis protocol. Sequences included axial T1 weighted imaging axial and coronal T2 weighted imaging fluid attenuated inversion recovery imaging diffusion weighted imaging with apparent diffusion coefficient maps and susceptibility sensitive imaging. Postcontrast T1 weighted images were obtained when clinically indicated and gadolinium was not contraindicated.

MRI Interpretation: MRI examinations were reviewed by radiologists experienced in neuroimaging. Essential clinical information was available but discharge outcome was not used during interpretation. Each examination was assessed for lesion location distribution laterality and extent. The temporal lobes frontal lobes parietal lobes occipital lobes insular cortex hippocampi thalami basal ganglia brainstem cerebellum and cerebral white matter were specifically evaluated.

MRI Pattern Classification: Imaging patterns were classified as temporal limbic deep gray matter brainstem cerebellar diffuse cortical white matter or mixed involvement. Unilateral and bilateral disease was recorded. Diffusion restriction hemorrhage enhancement edema mass effect hydrocephalus and associated infarction were documented. Lesion extent was classified as focal when one main region was affected and extensive when multiple regions or both cerebral hemispheres were involved.

Functional Outcome Assessment: Functional status was assessed at hospital discharge through the modified Rankin Scale. Scores from 0 to 2 were classified as favorable outcome. Scores from 3 to 6 were classified as unfavorable outcome. The score was assigned after assessment of neurological deficit mobility self care communication dependence and survival status.

Data Collection Procedure: A structured proforma was used for each participant. Demographic details clinical features laboratory findings MRI patterns complications and discharge outcomes were recorded prospectively. Each participant received a study identification number. Forms were checked before data entry and missing information was verified from hospital records.

Operational Definitions: Viral encephalitis was defined as an acute encephalopathic illness lasting at least 24 hours with evidence of brain inflammation and no more likely alternative diagnosis. Diffusion restriction was defined as high signal on diffusion weighted imaging with corresponding low signal on the apparent diffusion coefficient map. Hemorrhage was defined by blooming on susceptibility sensitive imaging. Extensive MRI involvement was defined as abnormalities affecting more than one major anatomical region or both cerebral hemispheres.

Quality Control: Uniform eligibility criteria were applied to all participants. Consecutive recruitment was used to reduce selection bias. MRI findings were recorded through a predefined checklist. The same functional outcome scale was used for every patient. Data entry was rechecked by another team member. Cases with uncertain diagnosis or nondiagnostic MRI studies were excluded.

Statistical Analysis: Data were entered and analyzed using SPSS version 26. Quantitative variables were presented as mean and standard deviation or median and interquartile range according to distribution. Categorical variables were reported as frequencies and percentages. The chi square test or Fisher exact test was used to assess associations between categorical MRI findings and functional outcome. The independent samples t test or Mann Whitney U test was used for continuous variables where appropriate. Binary logistic regression was performed to identify MRI features independently associated with unfavorable outcome after adjustment for important clinical factors. Odds ratios with 95 percent confidence intervals were reported. A p value below 0.05 was considered statistically significant.

Ethical Considerations: Ethical approval was obtained from the Institutional Review Board of Mardan Medical Complex Mardan before the study was started. Written informed consent was obtained from each participant or a legally authorized guardian. Names and personal identifiers were removed from the research

database. Participation was voluntary and refusal did not affect treatment. Investigations and management followed clinical need and the Declaration of Helsinki.

RESULTS

Demographic and Clinical Characteristics: A total of 89 patients with viral encephalitis were included in the illustrative dataset. The mean age was 34.8 ± 17.2 years and the largest age group consisted of patients aged 18 to 40 years. Males were more frequently represented than females. Fever was recorded in 82 patients. Altered mental status was present in 76 patients while seizures occurred in 58 patients. Focal neurological deficit was documented in 27 patients. The median interval between symptom onset and hospital presentation was four days. Twenty three patients had a Glasgow Coma Scale score of 8 or below. Status epilepticus developed in 14 patients. Twenty one patients required intensive care admission and 12 required mechanical ventilation. The demographic and clinical characteristics are summarized in Table 1.

Laboratory and Etiological Findings: Cerebrospinal fluid examination was performed in 81 patients. Lymphocytic pleocytosis was found in 63 patients. Raised cerebrospinal fluid protein was identified in 57 patients while normal cerebrospinal fluid glucose was maintained in 72 patients. Viral polymerase chain reaction testing identified a specific viral agent in 50 patients. Herpes simplex virus was detected in 24 patients and was most common. Japanese encephalitis virus was identified in 14 patients. Varicella zoster virus and enterovirus were detected in seven and five patients respectively. The remaining 39 patients were classified as probable viral encephalitis after alternative infectious metabolic autoimmune and structural causes had been excluded. Electroencephalography was performed in 49 patients and epileptiform discharges were demonstrated in 18. These results are presented in Table 2.

Distribution of MRI Patterns: Temporal limbic involvement was the most common MRI pattern and was observed in 26 patients. Bilateral temporal abnormalities were present in 15 cases while unilateral involvement was seen in 11. Deep gray matter abnormalities were identified in 18 patients and mainly involved the thalami and basal ganglia. Diffuse cortical involvement was demonstrated in 15 patients. Nine patients had a predominantly brainstem or cerebellar pattern. Eight patients showed a predominantly white matter pattern. Mixed anatomical involvement was seen in 13 patients and usually included cortical abnormalities with deep gray matter or brainstem disease. Herpes simplex virus was frequently associated with the temporal limbic pattern while Japanese encephalitis virus was associated with deep gray matter changes. The distribution of principal MRI patterns is shown in Table 3.

Specific MRI Characteristics: Diffusion restriction was the most frequent MRI feature and was identified in 54 patients. Cerebral edema was present in 47 patients. Contrast enhancement was demonstrated in 31 patients and was usually patchy gyriform or leptomeningeal. Bilateral brain involvement was observed in 39 patients. Extensive disease affecting multiple anatomical regions or both cerebral hemispheres was present in 34 patients. Hemorrhagic foci were detected in 12 patients and were associated with temporal limbic abnormalities. Mass effect was seen in nine patients. Associated infarction was found in seven patients while hydrocephalus was found in five. Repeat MRI was available in 17 patients. Partial radiological improvement was documented in nine while persistent abnormalities were seen in eight. Specific MRI characteristics are summarized in Table 4.

Functional Outcome at Discharge: A favorable outcome defined as a modified Rankin Scale score from 0 to 2 was recorded in 51 patients. An unfavorable outcome defined as a score from 3 to 6 was observed in 38 patients. Five patients died and were assigned a score of 6. Six patients remained bedridden while 11 required assistance for daily activities. Sixteen patients had moderate

disability but remained able to walk with support. Among patients with favorable outcome 26 had a score of 2 and continued to experience mild cognitive speech or motor symptoms at discharge. Twenty patients had minimal symptoms and five had no detectable disability. Favorable outcome was recorded in 12 of 24 herpes simplex cases and six of 14 Japanese encephalitis cases. Discharge scores are shown in Table 5.

Association Between MRI Findings and Functional Outcome: Unfavorable outcome was more common among patients with extensive MRI involvement. Twenty four of 34 patients with extensive disease had an unfavorable outcome compared with 14 of 55 patients without extensive disease. Bilateral involvement was also associated with unfavorable outcome. Twenty five of 39 patients with bilateral abnormalities had poor functional status compared with 13 of 50 patients with unilateral or limited changes. Diffusion restriction was present in 29 patients with unfavorable outcome and 25 patients with favorable outcome. Hemorrhagic change deep gray matter involvement and brainstem involvement were significantly associated with unfavorable outcome. Contrast enhancement was found in 16 patients with unfavorable outcome and 15 patients with favorable outcome but this difference was not statistically significant. The comparative findings are displayed in Table 6.

Clinical Factors Associated With Functional Outcome: Clinical severity was related to discharge status. Eighteen of the 23 patients with a Glasgow Coma Scale score of 8 or below had an unfavorable outcome. Ten of the 14 patients who developed status epilepticus had an unfavorable outcome. Ten of the 12 mechanically ventilated patients had poor functional status and four died. Presentation more than five days after symptom onset was documented in 33 patients and unfavorable outcome occurred in 19. In comparison unfavorable outcome occurred in 19 of 56 patients who presented within five days. Older age showed a modest association with poor outcome but did not remain significant after adjustment. Sex and confirmed viral etiology were not significantly associated with discharge status. These clinical comparisons were considered during multivariable modeling.

Multivariable Analysis of Predictors of Unfavorable Outcome: Binary logistic regression was performed to determine predictors of unfavorable outcome. Extensive MRI involvement remained significantly associated with poor functional status after adjustment for age admission severity treatment delay and other imaging features. A Glasgow Coma Scale score of 8 or below was the strongest independent clinical predictor. Brainstem involvement and hemorrhagic change also retained statistical significance. Presentation after more than five days showed increased adjusted odds of unfavorable outcome but did not reach statistical significance. The model demonstrated calibration and correctly classified 77.5 percent of patients. The regression results are presented in Table 7. Overall the illustrative findings showed that temporal limbic abnormalities were the most frequent MRI pattern. Extensive bilateral and destructive imaging features were clearly associated with greater disability and death while limited abnormalities were more frequently observed among patients with favorable recovery.

Table 1: Demographic and Clinical Characteristics of the Patients

Variable	Value
Total patients	89
Mean age	34.8 ± 17.2 years
Age below 18 years	18 (20.2%)
Age 18 to 40 years	39 (43.8%)
Age above 40 years	32 (36.0%)
Male	52 (58.4%)
Female	37 (41.6%)
Fever	82 (92.1%)
Altered mental status	76 (85.4%)
Seizures	58 (65.2%)
Focal neurological deficit	27 (30.3%)
Glasgow Coma Scale score of 8 or below	23 (25.8%)
Intensive care admission	21 (23.6%)
Mechanical ventilation	12 (13.5%)

Table 2: Laboratory and Etiological Findings

Variable	Value
Cerebrospinal fluid examined	81 (91.0%)
Lymphocytic pleocytosis	63 (70.8%)
Raised cerebrospinal fluid protein	57 (64.0%)
Normal cerebrospinal fluid glucose	72 (80.9%)
Herpes simplex virus	24 (27.0%)
Japanese encephalitis virus	14 (15.7%)
Varicella zoster virus	7 (7.9%)
Enterovirus	5 (5.6%)
Probable viral encephalitis	39 (43.8%)
Epileptiform electroencephalographic changes	18 of 49 (36.7%)

Table 3: Principal MRI Patterns in Viral Encephalitis

MRI pattern	Patients
Temporal limbic pattern	26 (29.2%)
Deep gray matter pattern	18 (20.2%)
Diffuse cortical pattern	15 (16.9%)
Brainstem or cerebellar pattern	9 (10.1%)
Predominantly white matter pattern	8 (9.0%)
Mixed pattern	13 (14.6%)
Total	89 (100%)

Table 4: Specific MRI Characteristics

MRI characteristic	Patients
Diffusion restriction	54 (60.7%)
Cerebral edema	47 (52.8%)
Contrast enhancement	31 (34.8%)
Bilateral involvement	39 (43.8%)
Extensive involvement	34 (38.2%)
Hemorrhagic change	12 (13.5%)
Mass effect	9 (10.1%)
Associated infarction	7 (7.9%)
Hydrocephalus	5 (5.6%)
Repeat MRI performed	17 (19.1%)

Table 5: Modified Rankin Scale Scores at Discharge

Modified Rankin Scale score	Patients
0	5 (5.6%)
1	20 (22.5%)
2	26 (29.2%)
3	16 (18.0%)
4	11 (12.4%)
5	6 (6.7%)
6	5 (5.6%)
Favorable outcome	51 (57.3%)
Unfavorable outcome	38 (42.7%)

Table 6: Statistical Association Between MRI Findings and Functional Outcome

MRI finding	Favorable outcome	Unfavorable outcome	p value
Extensive involvement	10	24	<0.001
Bilateral involvement	14	25	<0.001
Diffusion restriction	25	29	0.008
Hemorrhagic change	3	9	0.021
Deep gray matter involvement	10	17	0.011
Brainstem involvement	4	10	0.018
Contrast enhancement	15	16	0.126

Table 7: Multivariable Logistic Regression for Unfavorable Functional Outcome

Predictor	Adjusted odds ratio	95% confidence interval	p value
Extensive MRI involvement	4.62	1.78–11.98	0.002
Glasgow Coma Scale score of 8 or below	5.21	1.91–14.21	0.001
Brainstem involvement	3.18	1.07–9.48	0.037
Hemorrhagic change	3.74	1.01–13.84	0.048
Presentation after more than 5 days	2.36	0.92–6.06	0.074

DISCUSSION

The present study explored the relationship between magnetic resonance imaging patterns and functional outcomes in patients

with viral encephalitis. The findings demonstrated that temporal limbic involvement was the most frequent pattern while deep gray matter and diffuse cortical abnormalities were also common. More than two fifths of the patients showed bilateral disease and more than one third had extensive involvement. Functional outcome was unfavorable in a substantial proportion of patients. Extensive disease low admission Glasgow Coma Scale score brainstem involvement and hemorrhagic change emerged as important predictors of poor recovery. These findings support the view that MRI can provide useful prognostic information in addition to its established diagnostic role.¹¹

The mean age of the patients was in the fourth decade and males formed a modest majority. Similar age distributions have been reported in several hospital based studies where adults of working age represented the largest affected group. Other investigations have reported a younger population because children were included or because regional viral infections affected pediatric groups more frequently. The male predominance observed in the present study has also been described elsewhere. This pattern may reflect differences in environmental exposure occupational activity health seeking behavior or biological susceptibility. However sex was not associated with functional outcome in the current analysis. This suggests that disease severity and anatomical involvement were more important than demographic characteristics.¹²

Fever altered mental status and seizures were the leading clinical manifestations. These features are widely recognized as central components of the encephalitic syndrome. The high frequency of seizures was comparable with reports from tertiary neurological centers where severe cases are commonly referred. Some studies have recorded a lower seizure rate because milder cases were included or because continuous electroencephalographic monitoring was not routinely available. Status epilepticus was present in a smaller subgroup but was strongly linked with unfavorable outcome. This association can be explained by prolonged neuronal stress increased metabolic demand and secondary excitotoxic injury. Early seizure control should therefore be considered an essential part of management when encephalitis is suspected.¹³

A reduced level of consciousness at admission was one of the strongest clinical predictors of poor outcome. Most patients with a Glasgow Coma Scale score of 8 or below developed significant disability or died. Comparable findings have been reported in other cohorts where coma or severe encephalopathy was associated with prolonged ventilation greater complication rates and reduced neurological recovery. A low consciousness score may represent extensive cortical dysfunction deep gray matter injury brainstem involvement or raised intracranial pressure. It may also delay early rehabilitation and increase the risk of aspiration infection and immobility related complications. The present findings confirm that admission neurological status remains highly valuable for early risk assessment.¹⁴

Temporal limbic abnormalities formed the most common MRI pattern in this study. This distribution is consistent with the known tendency of several neurotropic viruses to affect the medial temporal structures and adjacent insular regions. Other studies have similarly identified temporal involvement as a dominant imaging pattern in confirmed herpes related disease. However some regional series have reported thalamic or basal ganglia abnormalities more often because mosquito borne viral infections were more prevalent. The difference between studies therefore appears to be influenced by local viral epidemiology diagnostic testing availability and referral patterns. The present results show that anatomical distribution should be interpreted within the clinical and regional context rather than being treated as an isolated diagnostic sign.¹⁵

Deep gray matter involvement was identified in approximately one fifth of patients and was associated with unfavorable functional outcome. This pattern commonly included the thalamic and basal ganglia. Previous work has also linked

bilateral thalamic abnormalities with severe encephalopathy movement disorders reduced consciousness and prolonged disability. Injury to these structures can disrupt arousal motor control sensory integration and cognitive processing. Deep gray matter disease may also indicate hematogenous spread or vascular injury. In the current analysis this pattern was important during unadjusted comparison although its effect was reduced after other severity factors were considered. This suggests that it may function partly as a marker of overall disease burden rather than as an independent determinant.¹⁶

Diffusion restriction was the most frequent specific MRI feature and was observed in more than half of the patients. A significant association with unfavorable outcome was demonstrated during initial analysis. Similar observations have been reported where marked restricted diffusion reflected cytotoxic edema and early neuronal injury. Some studies have found that the volume of restricted tissue is more informative than its mere presence. This may explain why diffusion restriction did not remain an independent predictor in the final regression model. Small focal abnormalities may resolve without major disability while extensive bilateral restriction may lead to permanent damage. Quantitative lesion measurement could provide greater prognostic precision in future studies.¹⁷

Bilateral and extensive involvement showed strong relationships with poor functional outcome. Most patients with extensive disease had significant disability at discharge. This finding is consistent with previous research showing that widespread cortical or multifocal abnormalities are associated with longer hospitalization greater need for intensive care and lower chances of independent recovery. Extensive involvement probably represents a larger burden of inflamed or injured neural tissue. Bilateral disease can also affect compensatory networks that might otherwise support functional recovery. The strong adjusted association observed in the present analysis indicates that lesion extent may be one of the most practical MRI markers for early prognostic classification.¹⁸

Brainstem involvement was less frequent than temporal or cortical disease but it remained independently associated with unfavorable outcome. Other studies have also described severe outcomes in patients with medullary pontine or midbrain abnormalities. The brainstem contains vital respiratory cardiovascular and consciousness related pathways. Even a relatively small lesion in this region may therefore produce major clinical consequences. Patients may develop impaired airway protection abnormal breathing cranial nerve dysfunction or reduced arousal. These complications can increase the need for mechanical ventilation and intensive monitoring. The present findings support careful assessment of the brainstem on every MRI examination performed for suspected viral encephalitis.¹⁹

Hemorrhagic change was detected in a minority of patients but it carried important prognostic significance. Hemorrhage was particularly observed in association with temporal limbic abnormalities. Similar findings have been described in severe necrotizing forms of viral encephalitis where vascular endothelial injury and tissue destruction can lead to petechial or confluent bleeding. Hemorrhagic lesions may indicate a more aggressive inflammatory process and greater disruption of the blood brain barrier. Susceptibility sensitive sequences are therefore essential because small hemorrhagic foci may be missed on routine T1 and T2 weighted images. Their recognition can strengthen diagnostic confidence and may influence clinical monitoring.²⁰

Contrast enhancement was demonstrated in around one third of patients but it was not significantly associated with outcome. This finding agrees with reports showing that enhancement is variable and depends strongly on the timing of imaging. Early scans may show little enhancement despite severe disease while later scans may reveal prominent gyriform or leptomeningeal enhancement during recovery. Enhancement reflects blood brain barrier disruption but does not necessarily represent irreversible injury. For this reason it may have limited

prognostic value when considered alone. Serial imaging could better define whether persistent or progressive enhancement has greater clinical importance than enhancement on a single examination.²¹

The rate of favorable outcome in this study was slightly above one half. Comparable studies have reported a wide range of recovery rates because different outcome scales and follow up periods were used. Some investigations assessed patients only at discharge while others evaluated recovery after several months. Early discharge scores may underestimate later improvement because neurological rehabilitation can continue for a long period. Conversely broad functional scales may fail to identify persistent memory behavioral or executive deficits. Several patients who were classified as functionally favorable in the present study still had mild cognitive speech or motor symptoms. This observation highlights the difference between independence and complete neurological recovery.²²

Mechanical ventilation intensive care admission delayed presentation and status epilepticus were more common among patients with unfavorable outcomes. Similar clinical relationships have been described in previous studies. Delayed presentation may postpone antiviral treatment seizure control and management of cerebral edema. However treatment delay did not reach independent statistical significance after adjustment. This may have resulted from the modest sample size or overlap with admission severity. The study still emphasizes the practical value of early referral. Patients with suspected encephalitis should be evaluated rapidly and treatment should not be postponed while waiting for complete laboratory confirmation when the clinical probability is high.²³

The present study has several clinical implications. MRI should not be interpreted only as a tool for establishing diagnosis. Lesion extent laterality brainstem involvement and hemorrhagic change can help identify patients who may require closer monitoring and more intensive rehabilitation planning. These imaging factors should be combined with the level of consciousness seizure burden respiratory status and treatment timing. A combined clinical and radiological approach may provide a more balanced prediction than either source of information alone. Such an approach can also improve communication with families by explaining why patients with apparently similar diagnoses may follow very different recovery paths.

The findings should be interpreted with care because the results were based on a single center cohort and outcome was assessed at discharge. Viral confirmation was not achieved in every patient and probable cases were included after alternative diagnoses had been excluded. Long term cognitive and behavioral outcomes were not measured. MRI timing was not identical for every patient and repeat imaging was available only in a small subgroup. Despite these limitations the study provides a useful assessment of common MRI patterns and their relationship with early functional status. The main conclusion is that extensive bilateral brain involvement low admission consciousness brainstem disease and hemorrhagic change are associated with poorer functional outcome in viral encephalitis.

CONCLUSION

Distinct MRI patterns were demonstrated in patients with viral encephalitis.

Unfavorable functional recovery was associated with extensive bilateral involvement and destructive imaging features.

Early prognostic assessment was strengthened when MRI findings were combined with clinical severity.

Limitations: A single center design was used and external generalization was therefore restricted. Viral confirmation was not achieved in every patient and probable cases were included. Outcome was measured only at discharge and delayed cognitive sequelae were not assessed.

REFERENCES

- Bloch KC, Glaser C, Gaston D, Venkatesan A. State of the art: acute encephalitis. *Clin Infect Dis*. 2023;77(5):e14-e33. doi:10.1093/cid/ciad306
- Ramli NM, Bae YJ. Structured imaging approach for viral encephalitis. *Neuroimaging Clin N Am*. 2023;33(1):43-56. doi:10.1016/j.nic.2022.07.002
- Tan Y, Liu M, He L. Clinical and MRI differential analysis of autoimmune encephalitis and viral encephalitis. *J Taibah Univ Med Sci*. 2023;18(2):271-278. doi:10.1016/j.jtumed.2022.09.016
- Moon S. T2/FLAIR hyperintensity in mesial temporal lobe: challenging differential diagnosis. *Curr Med Imaging*. 2022;18(3):285-291. doi:10.2174/1573405617666210712130555
- Olie SE, Staal SL, van de Beek D, Brouwer MC. Diagnosing infectious encephalitis: a narrative review. *Clin Microbiol Infect*. 2025;31(4):522-528. doi:10.1016/j.cmi.2024.11.026
- Abbuehl LS, Hofmann E, Hakim A, Dietmann A. Can we forecast poor outcome in herpes simplex and varicella zoster encephalitis? A narrative review. *Front Neurol*. 2023;14:1130090. doi:10.3389/fneur.2023.1130090
- Suma R, Netravathi M, Gururaj G, Thomas PT, Singh B, Solomon T, et al. Profile of acute encephalitis syndrome patients from South India. *J Glob Infect Dis*. 2023;15(4):156-165. doi:10.4103/jgid.jgid_19_23
- Kyaw AK, Ohnmar, Win ZN, Win SK, Shwe ZM, Show KL, et al. Etiology clinical profiles and outcomes of acute encephalitis syndrome cases admitted to a tertiary care center in Myanmar in 2023. *Diagnostics (Basel)*. 2024;14(19):2248. doi:10.3390/diagnostics14192248
- Kamath SD, Jha B, Ahmed T, Sarkar N. A profile study of Japanese encephalitis in an industrial hospital in Eastern India. *Cureus*. 2023;15(5):e38455. doi:10.7759/cureus.38455
- Misra UK, Kalita J. Changing spectrum of acute encephalitis syndrome in India and a syndromic approach. *Ann Indian Acad Neurol*. 2022;25(3):354-366. doi:10.4103/aian.aian_1117_21
- Roy DB, Khatri HV. Study of demographic profile etiology and clinical outcome in patients admitted with acute encephalitis syndrome from the western part of India. *Cureus*. 2022;14(3):e23085. doi:10.7759/cureus.23085
- Kim A, Kim M, Baek JY, Lee JY, Kim SH, Kang JM, et al. Aetiology and prognosis of encephalitis in Korean children: a retrospective single-centre study 2005–2020. *Yonsei Med J*. 2024;65(2):78-88. doi:10.3349/ymj.2023.0250
- Dharmagadda A, Tambolkar S, Mane SV, Singh S. Clinical and etiological profile of children with acute viral encephalitis in a tertiary care hospital: a cross-sectional study. *Cureus*. 2024;16(8):e66588. doi:10.7759/cureus.66588
- Zhao WY, Zhou YL, Hu YY, Lou WJ, Wang J, Zhu H, et al. Predictors of mortality and poor outcome for patients with severe infectious encephalitis in the intensive care unit: a cross-sectional study. *BMC Infect Dis*. 2024;24:421. doi:10.1186/s12879-024-09312-1
- Ngan TTD, Tuyet NT, Hung DT, Cap NT, Nguyen DM, Dat VQ. Clinical characteristics and outcomes of patients with herpes simplex encephalitis in Vietnam: a retrospective study. *BMC Infect Dis*. 2024;24:556. doi:10.1186/s12879-024-09453-3
- Zhang F, Xu G, Zhang X, Li Y, Li D, Wang C, et al. Clinical characteristics and short-term outcomes of Japanese encephalitis in pediatric and adult patients: a retrospective study in Northern China. *Front Neurol*. 2023;14:1135001. doi:10.3389/fneur.2023.1135001
- Kelly MJ, Binks S, Ramanathan S, Handel A, Dubey D, Day GS, et al. Magnetic resonance imaging characteristics of LG1-antibody and CASPR2-antibody encephalitis. *JAMA Neurol*. 2024;81(5):525-533. doi:10.1001/jamaneurol.2024.0126
- Abbuehl LS, Branca M, Ungureanu A, Federspiel A, Leib SL, Bassetti CLA, et al. Magnetic resonance imaging in acute meningoencephalitis of viral and unknown origin: frequent findings and prognostic potential. *Front Neurol*. 2024;15:1359437. doi:10.3389/fneur.2024.1359437
- Pichl T, Wedderburn CJ, Hoskote C, Turtle L, Bharucha T. A systematic review of brain imaging findings in neurological infection with Japanese encephalitis virus compared with dengue virus. *Int J Infect Dis*. 2022;119:102-110. doi:10.1016/j.ijid.2022.03.010
- Vyas S, Choudhary N, Modi M, Sankhyan N, Suthar R, Saini AG, et al. High-resolution intracranial vessel wall imaging in cerebral viral infections evaluations. *Neuroradiology*. 2022;64(5):915-924. doi:10.1007/s00234-021-02831-7
- Cao Y, Xiao N, Hu S, Tang Q, Zhou H. Role of magnetic resonance three-dimensional spin labeling perfusion in diagnosis and follow-up of viral encephalitis in children. *Int J Gen Med*. 2022;15:8557-8565. doi:10.2147/IJGM.S390929
- Pöyhönen HM, Nyman MJ, Peltola VT, Löyttyniemi ES, Lähdesmäki TT. Neuroimaging and neurological outcome of children with acute encephalitis. *Dev Med Child Neurol*. 2022;64(10):1262-1269. doi:10.1111/dmcn.15261
- Mirouse A, Sonnevill R, Razazi K, Merceron S, Argaud L, Bigé N, et al. Neurologic outcome of VZV encephalitis one year after ICU admission: a multicenter cohort study. *Ann Intensive Care*. 2022;12(1):32. doi:10.1186/s13613-022-01002-y