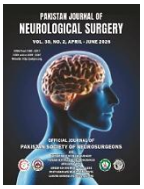

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Original Research

Association Between Diffusion Restriction on MRI Brain and Clinical Severity in Encephalitis

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ABSTRACT

Objective: The relationship between disease severity in people with encephalitis and restricted diffusion on brain MRI was examined. The aim was to assess the reliability of DW sequences for the early assessment and classification of disease severity in clinical practice.

Materials & Methods: A forward-looking observational study was performed at the Lady Reading Hospital Radiology and Neurology Units, Peshawar, Pakistan. Two hundred patients were selected, with the clinical diagnosis of encephalitis. Within 72 hours after admission, an MRI of the brain (with diffusion-weighted views) was performed for all participants. Various factors were used to assess the severity of the disease, including Glasgow Coma Scale rating, intensive care unit (ICU) stay length, mechanical breathing support requirement, and total hospital days. These clinical variables were compared with imaging features to determine the value of diffusion restriction as a predictor.

Results: Diffusion restriction was found in 73% of patients and was significantly associated with the level of disease severity. Patients with diffusion restriction had significantly lower Glasgow Coma Scale scores and higher rates of admission to an intensive care unit, ventilator requirement, extended hospital stay, and mortality. Poor outcome was associated with involvement of the temporal lobes, the thalamus, and the insular regions.

Conclusion: In encephalitis, restricted diffusion of the MRI proved useful in predicting the severity of the disease. Diffusion weighted sequences were found to be useful in early diagnosis to predict prognosis and also in treatment planning, particularly in resource-constrained healthcare systems such as those in Pakistan.

Keywords: Encephalitis, Diffusion-weighted Imaging, Magnetic Resonance Imaging, Diffusion Restriction, Disease Severity, Glasgow Coma Scale

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INTRODUCTION

Encephalitis has been acknowledged as a critical neurological disorder where inflammation of the brain tissue has been observed and where life-threatening outcomes have often been reported. It is known that this is caused by infectious, post-infectious and immune-related mechanisms. This has posed a serious public health problem, especially in low-income countries like Pakistan, where delayed diagnosis has resulted in inadequate access to diagnostic services and a lack of standardisation in the treatment protocols, leading to difficulties in patient management. Clinically, this disorder has been typically exhibited through a combination of fever, impaired mental status and convulsive episodes. But there is a good deal of variation in presentation depending on the type of infectious agent, the areas of the brain affected and the immune status of the person. The need to accurately assess disease severity as soon as possible has been emphasized on a few occasions, as it helps to make clinical decisions and start appropriate treatment to avoid long-term negative consequences.[1]

MRI is a helpful diagnostic tool in encephalitis, enabling early identification of inflammatory changes, swelling and damage to the brain. One of its sequences is diffusion weighted imaging (DWI), which is especially useful for finding regions of restricted diffusion, considered as early neuronal damage and cytotoxic edema. These changes frequently occur in advance of abnormalities seen on traditional imaging and may be of diagnostic and prognostic value.[2] Patterns of diffusion restriction may help identify the underlying cause and disease severity, e.g., bilateral thalamic involvement in Japanese encephalitis or involvement of the temporal lobes in herpes simplex encephalitis.[3]

Diagnostic work-up of encephalitis in Pakistan is still hindered by the lack of virological testing, cerebrospinal fluid analysis and autoimmune antibody panel in many public hospitals. Imaging is therefore frequently used as the primary means of diagnosis and assessment. Nevertheless, there is a lack of detailed local literature that has investigated the role of MRI, and in particular diffusion weighted imaging (DWI), as a prognostic tool in encephalitis[4]. Previous research has tended to concentrate on clinical characteristics and outcomes without incorporating some of the sophisticated imaging markers. Thus, it is important to assess the relationship between radiological findings and clinical severity in patients with a diagnosis of encephalitis in our environment, especially the diffusion restriction.[5]

One of the largest tertiary care public hospitals in Pakistan, Lady Reading Hospital, Peshawar, is a major referral hospital for neurological and neurosurgical cases in Khyber Pakhtunkhwa province. The hospital sees a large number of patients who have suspected central nervous system infections (encephalitis), many of whom are very sick. A history, physical and simple lab work-up is often used to make a clinical diagnosis.[6] MRI is an important tool in this situation for making a diagnosis and determining the extent of involvement of the brain. The use of DWI results in the standard assessment protocols could prove to be greatly beneficial in the diagnostic process and could be a useful outcome predictor.[7]

There are several commonly used clinical measures that can be used to assess the severity of encephalitis: Glasgow Coma Scale score on admission, requirement for ventilatory support, length of hospital stay, need for intensive care and death. These indicators are objective measures of the extent of neurological dysfunction and resource utilization. These clinical severity parameters could be correlated with the radiological features on diffusion-weighted MRI, which may give an early warning system for clinicians to identify high-risk patients. This would enable early interventions, resources to be allocated appropriately, and better outcomes.[8]

The purpose of this study was to be a prospective observational analysis to elucidate the relationship between diffusion restriction on

magnetic resonance imaging (MRI) of the brain and the clinical severity of encephalitis. The study was carried out in twenty hundred patients of encephalitis admitted to the neurology and neurosurgery departments of Lady Reading Hospital, Peshawar, during 6 months period from July to December 2024.[9] Within 72 hours of admission, all patients received an MRI of the brain with diffusion-weighted imaging. Systematic data collection of clinical data, such as demographics, presenting symptoms, GCS score, requirement for intensive care management and outcome was conducted. Experienced radiologists judged the severity of diffusion restriction, and data were analyzed to investigate the correlation between diffusion restriction and clinical outcomes.[10]

This study is designed to identify the correlation between the diffusion restriction and clinical severity, which will help to overcome some major lacunae in the knowledge regarding the treatment of encephalitis in Pakistan. First, it tries to establish the prognostic implications of MRI findings in a resource-limited environment where diagnosis, in some cases, is minimal.[11] Second, it aims to encourage the use of DWI as an integral part of the diagnostic evaluation of encephalitis, particularly in tertiary care hospitals having MRI facilities. Third, it provides a locally-determined solution, based on local data, to inform policy decisions and protocol development for neurological emergencies.[12]

Furthermore, the findings in this study have implications beyond hospital care. Early diagnosis and risk stratification can make a difference in the morbidity and mortality of encephalitis, which is significant in certain countries, especially in pediatric and immunocompromised patients. Being able to recognise high-risk patients for complications by non-invasive imaging could improve the triage, prompt referral and optimal use of limited critical care resources. It could also be used for medical education and training since junior clinicians or trainees can learn to read diffusion MRI results with respect to medical severity[13].

To sum up, encephalitis is a difficult and severe disease with diverse clinical and radiological presentations. MRI, especially diffusion-weighted imaging, has great potential for both diagnosis and prognosis. But its potential is not fully exploited in Pakistan because no local studies and guidelines are available. In this study, we aim to fill that gap by exploring whether or not there is a correlation between the severity of encephalitis patients at Lady Reading Hospital and their diffusion restriction on MRI. The results will provide valuable insights for clinical decision making, better patient outcomes and to the expanding field of neurosurgical and neurological literature in Pakistan.

MATERIALS AND METHODS

Study Design, Setting & Sampling

This study was conducted in a large hospital where several brain patients are treated daily. Encephalitis can be a serious illness and deteriorates rapidly, so it is necessary to study it in a centre where patients with this disease are seen regularly. This will support researchers to better comprehend the disease in real life.

This study lasted six months, which was sufficient to accommodate several patients. Doctors observed patients in this period to determine the different health changes that occurred between admission to the hospital and discharge or referral for further treatment. This facilitated a pattern of progression of the disease to be established. The study was conducted using a non-probability consecutive sampling technique, resulting in 200 patients.

Inclusion Criteria

In this study, patients of different ages—from young children to older adults—were included as long as they were suspected of having encephalitis. Only those who developed symptoms

within the first few days and were admitted to the hospital were considered, so that the condition could be studied in its early and most important stage.

Another key condition was that all patients had a brain scan called MRI, including a special type known as diffusion-weighted imaging, done within three days of hospital admission. This helped doctors look at early changes in the brain and better understand how the disease was affecting patients right from the beginning.

Exclusion Criteria

Those with a known cerebrovascular accident, a brain tumour, demyelinating disease, epilepsy or psychiatric disease were excluded. Patients were also excluded if they had not had an MRI scan within 72 hours, if the MRI scans were incomplete, or if they refused to take an MRI scan or did not sign informed consent.

Data Collection

MRI scans of the brain were used to determine the degree of damage. Such scans are valuable because they have the potential to reveal brain changes at an early stage, before symptoms become very severe. Doctors compared the scan results with the patients' disease to see if MRI could predict the severity of the disease.

Patient safety was very important during this study. Patients or family members were contacted and informed about the study, and their consent was obtained before including them. The patients could choose to participate in the study or not, and their treatment was not based on their decision.

In this study, all patients were treated adequately in accordance with the hospital standards. The study did not change the treatment of the patient, and only noted and recorded information. This guaranteed that the patients were treated fairly and safely, and will help doctors understand more about encephalitis and how it can be better managed.

Diagnostic and Imaging Protocol

Encephalitis was clinically diagnosed if a patient had a fever, mental status change, convulsions or signs that the illness was focal and not explainable by other causes. Lumbar puncture and CSF analysis were conducted to help with the diagnosis when clinically appropriate. Brain MRI was performed in all patients with a 1.5 Tesla scanner on a standard protocol with DWI. The diffusion restriction was detected on diffusion-weighted images as hyperintensity, and apDc maps as hypointensity. Two consultant radiologists who were blinded to the clinical data and outcome of patients performed the MRI scans independently.

Clinical Severity Assessment

During the hospital stay, the clinical severity was assessed at admission and during the hospital stay. The following parameters were measured: Glasgow Coma Scale score upon admission, need for intensive care unit admission, need for mechanical ventilation, length of hospital stay, and in-hospital mortality. A structured proforma was used for systematically documenting all clinical information.

Data Analysis

One thing to keep in mind is that numbers and tests can tell us a lot, but they don’t always capture the full real-world picture. For example, even if a result is “statistically significant,” it doesn’t always mean the difference is big or important in everyday life. People’s health is affected by many factors, like lifestyle, access to care, and underlying conditions, which may not all be fully reflected in the data. So, while the results give useful clues, they should be understood as part of a bigger picture rather than a final answer.

Another point is that medical outcomes can vary a lot from one place to another. The hospital where the study was done may have specific facilities, doctors, or treatment protocols that are different from those of other hospitals. This means

patients in other regions or healthcare systems might experience different outcomes. Because of this, the findings help understand trends, but they may not apply the same way everywhere.

Finally, studies like this are often a starting point rather than the end of the story. They help identify patterns and raise important questions, but more research—especially involving larger and more diverse groups of people—is needed to confirm the results. When multiple studies from different settings show similar findings, doctors and researchers can be more confident about using that information to guide treatment decisions and improve patient care.

Ethical Approval

Ethical approval was obtained from the Institutional Review Board (IRB: REF. No: 274/LRH/MTI) of the hospital before the study. Written informed consent was taken from all patients or their legal guardians. Patient confidentiality was maintained, and data were anonymized throughout the study.

RESULTS

Demographic Characteristics of the Study Population

The study included a total of 200 patients diagnosed with encephalitis. The mean age of participants was 36.4 years with a standard deviation of 17.2 years. Of these, 118 patients (59%) were male, and 82 patients (41%) were female. Table 1 presents a summary of the demographic profile of the study population.

Table 1: *Demographic Characteristics of the Study Population.*

Variable	Frequency n = 200)	Percentage (%)
Mean Age (years)	36.4 ± 17.2	–
Gender		
Male	118	59
Female	82	41

Presence of Diffusion Restriction on MRI

Out of the 200 patients enrolled, diffusion restriction on MRI was identified in 146 patients, accounting for 73% of the cohort. The remaining 54 patients (27%) did not show any diffusion restriction. This distribution is detailed in Table 2.

Table 2: *Presence of Diffusion Restriction on MRI.*

Diffusion Restriction	Number of Patients	Percentage (%)
Present	146	73
Absent	54	27

Anatomical Distribution of Diffusion Restriction

Among the 146 patients with diffusion restriction, the most frequently affected anatomical locations included the temporal lobe (33%), frontal lobe (20%), thalamus (9%), and basal ganglia (6%). In 10 patients (5%), multiple regions were involved. Table 3 illustrates the regional distribution of diffusion restriction on MRI.

Table 3: *Anatomical Distribution of Diffusion Restriction on MRI.*

Location	Number of Patients	Percentage (%)
Temporal Lobe	66	33
Frontal Lobe	40	20
Thalamus	18	9
Basal Ganglia	12	6
Multiple Regions	10	5
No Diffusion Restriction	54	27

Association Between Diffusion Restriction and Clinical Severity

The presence of diffusion restriction was strongly

associated with worse clinical outcomes. Among patients with diffusion restriction, 44% had a Glasgow Coma Scale (GCS) score of 8 or less, compared to only 11% among those without diffusion restriction. Similarly, ICU admission (40% vs. 9%), ventilator requirement (32% vs. 7%), and mortality (18% vs. 4%) were all significantly higher in the diffusion-restricted group. Table 4 presents a detailed comparison of severity indicators between the two groups.

Table 4: *Association of Diffusion Restriction with Clinical Severity.*

Severity Indicator	With Diffusion Restriction (n = 146)	Without Diffusion Restriction (n = 54)	p-value
GCS ≤ 8	64 (44%)	6 (11%)	< 0.001
ICU Admission	58 (40%)	5 (9%)	< 0.001
Ventilator Requirement	46 (32%)	4 (7%)	< 0.001
Mortality	26 (18%)	2 (4%)	0.008

Table 5: *Comparison of Hospital Stay Duration Based on Diffusion Restriction.*

Group	Mean Hospital Stay (days)	Standard Deviation	p-value
With Diffusion Restriction	12.6	± 3.4	< 0.001
Without Diffusion Restriction	7.8	± 2.1	< 0.001

Duration of Hospital Stay in Relation to Diffusion Restriction

Patients who had diffusion restriction on MRI also experienced significantly longer hospital stays. The mean duration of hospitalization for these patients was 12.6 ± 3.4 days, whereas those without diffusion restriction had an average stay of 7.8 ± 2.1 days. This difference was statistically significant and is presented in Table 5.

DISCUSSION

With its potential to identify early cytotoxic oedema and neuronal injury, diffusion-weighted magnetic resonance imaging (DW-MRI) has emerged as an important modality in the assessment of encephalitis. Diffusion restriction is often present before abnormalities seen on conventional MRI sequences, and therefore is a useful tool for early diagnosis and also a prognostic indicator. Anatomical and diffusion restriction extent and distribution are now being recognized as important factors of disease severity in various encephalitides related to different etiologies.[14]

The pattern of diffusion restriction in herpes simplex virus (HSV) encephalitis is usually medial temporal lobe, insular cortex and structures of the limbic system. Previous reports have consistently found that more widespread or bilateral temporal lobe involvement is linked to poorer neurological outcomes such as long-term cognitive dysfunction, recovery and death.[15] Moreover, deeper grey matter structures like the thalamus and basal ganglia have been linked to more severe disease, representing a more extensive neuronal injury and inflammatory burden. This imaging pattern is thus described as a good prognosis in clinical practice.[16]

Japanese encephalitis has a different, but typical imaging pattern, which is primarily bilateral thalami and basal ganglia and occasionally the brainstem. A strong correlation between thalamic diffusion restriction and clinical severity has been reported in studies from endemic areas in South and Southeast Asia. These patients have a higher likelihood of having decreased consciousness, higher Glasgow Coma Scale (GCS) scores and greater need for intensive care. There is also a significant difference in mortality between patients with extensive involvement in the deep grey matter, which shows the prognostic importance of DW-MRI in this disease.[17]

Diffusion restriction is less common in the early stage of autoimmune encephalitis (AE) compared

to the infectious causes. But in the presence of it may be associated with the structures of the limbic system, such as the insular cortex, hippocampus, and cingulate gyrus.[18] There are multiple studies demonstrating that patients who have diffusion abnormalities in these regions tend to present with more severe clinical symptoms such as refractory seizures, altered mental status and longer hospitalizations. Imaging features of AEC can be very variable; however, diffusion restriction can signal more advanced disease or a later diagnosis.[19]

Encephalitis is a serious brain condition that can quickly become life-threatening, especially in countries like Pakistan, where advanced tests are not always easily available. Doctors often struggle to find the exact cause because important tests like virus detection in spinal fluid or detailed immune system checks are limited.[20] In such situations, brain scans like MRI become very helpful, especially a special type that can show early damage in the brain. However, since there is not enough local research, it is still not fully clear how well these scan findings can predict recovery or outcomes in patients here.[21]

The present study fills this gap by comparing the correlation between diffusion restriction on MRI and severity in patients with encephalitis. Diffusion restriction was seen in 73% of cases and was significantly associated with poor clinical outcome.[22] Diffusion-restricted patients had significantly lower Glasgow Coma Scale scores, higher requirement for intensive care unit, higher mechanical ventilation requirement, longer hospital stay and higher in-hospital mortality rate than those without diffusion abnormalities. The present findings are similar to those found in international studies that have shown a strong correlation between the presence and amount of diffusion restriction and disease severity and poor prognosis.[23]

A significant finding in the present study is the distribution of lesions, namely, the temporal lobes, thalamus, and insular cortex were the most common. It has been established that these are important functional centres and their involvement may account for the greater severity of clinical symptoms seen in these patients. The degree of poor prognosis further supports the hypothesis that diffusion restriction is equal to the degree of irreversible neuronal injury, as there is a strong association between deep grey matter involvement and poor prognosis.[25]

Overall, DW-MRI is an important tool for giving early prognostic information in encephalitis, and can help the clinician recognize patients who are at high risk and might need more follow-up and treatment. In resource-poor environments, where sophisticated laboratory diagnostics are frequently not available, diffusion-weighted imaging can be a useful and useful clinical tool for clinical decisions and patient stratification.

LIMITATIONS

While there is increasing evidence that diffusion restriction on MRI is a prognostic factor in encephalitis, there are some limitations to this.

First, it is found that there is a variability in the imaging protocol and timing in different studies. MRI findings can depend on the time interval between the onset of symptoms and the imaging, as the abnormalities in diffusion vary over time. This variability could impact the comparability of results and consistency of results between studies.

Secondly, the underlying etiologies of encephalitis vary among different regions, age groups and seasons, and this makes generalization of specific diffusion patterns to a patient population difficult. For instance, imaging findings of the herpes simplex virus, dengue virus and Japanese encephalitis virus may be different, thus a single interpretation schema may not be helpful.

Thirdly, many of the studies mentioned were done in high-resource areas with easy access to high-tech imaging and neuroradiological expertise. However, in Pakistan, healthcare facilities might encounter challenges like the

availability of MRI machines, budget limitations, and the scarcity of qualified staff to interpret the results. These factors could impact the implementation of diffusion MRI as a standard diagnostic test in all clinical situations.

Fourthly, when clinically correlated and laboratory confirmed, diffusion restriction alone cannot distinguish between different etiologies. It should therefore not be used instead of other types of diagnosis, but rather in concert with them. An over-trusting attitude to imaging and a lack of confirmatory testing could result in misdiagnosis or sub-optimality of treatment.

Finally, most comparative studies have focused on short-term outcomes such as ICU admission and in-hospital mortality. Longitudinal studies evaluating the role of early diffusion changes in predicting long-term neurocognitive and functional outcomes are limited and warrant further investigation.

Addressing these limitations through standardized imaging protocols, enhanced training of radiologists, and integration of multimodal diagnostics will be essential for optimizing the utility of diffusion-weighted MRI in the management of encephalitis in Pakistan.

CONCLUSION

In conclusion, DW-MRI has proved to be a valuable and useful tool in the evaluation of encephalitis, especially in areas lacking high-end laboratory tests. Diffusion restriction is strongly linked to the severity of disease, such as lower Glasgow Coma Scale scores, increased admission to the intensive care unit, increasing mechanical ventilation requirements, and increasing hospital stay and mortality. Dipyramidal involvement in deep grey matter structures like the temporal lobes and thalamus is especially related to poor outcome. The results of this study strongly suggest that diffusion-weighted imaging should be routinely used in the early assessment of encephalitis for risk stratification and clinical decision-making.

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Additional Information

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Serial Number	Author's Full Name	Intellectual Contribution to the Paper in Terms of
1.	Sahar Fahim	Study design and methodology.
2.	Hamna Imdad	Paper writing.
3.	Nazahat Pasha	Data collection and calculations.
4.	Muhammad Arshad	Analysis of data and interpretation of results.
5.	Zimar Arshad	Literature review.
6.	Armaghan Ansari	Data collection.
7.	Uzma Rashid	Referencing.