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Research Article

Imaging Spectrum of High Altitude Cerebral Edema: MRI Findings and Proposed Severity Classification

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ABSTRACT

Purpose: To evaluate the spectrum of magnetic resonance imaging (MRI) findings in patients with high-altitude cerebral edema (HACE) presenting in the Leh–Ladakh region and to assess the distribution and severity of cerebral involvement.

Materials and Method: This retrospective study included 18 patients diagnosed with HACE between 2021 and 2024 in the Leh–Ladakh region. MRI examinations were reviewed for the pattern and extent of cerebral involvement, including corpus callosal lesions, white matter abnormalities, diffusion restriction, and hemorrhagic changes on gradient recalled echo (GRE)/susceptibility-weighted imaging (SWI) sequences.

Results: The most common MRI finding was isolated involvement of the splenium of the corpus callosum, observed in 44.4% (8/18) of patients. Diffuse corpus callosal involvement was seen in 27.8% (5/18), while isolated periventricular white matter abnormalities were identified in 16.7% (3/18). Mixed involvement of the corpus callosum and cerebral white matter was present in 11.1% (2/18) of cases. Diffusion restriction, indicative of cytotoxic edema, was demonstrated in approximately 88.9% (16/18) of patients. Microbleeds on GRE/SWI sequences were detected in 22.2% (4/18) of patients and were more commonly associated with extensive disease. The corpus callosum, particularly the splenium, was the most consistently affected structure.

Conclusion: HACE demonstrates a broad spectrum of MRI manifestations ranging from isolated reversible splenial lesions to extensive white matter involvement with hemorrhagic changes. The corpus callosum, especially the splenium, is the most frequently involved structure. Recognition of these characteristic imaging patterns can facilitate early diagnosis, guide timely therapeutic intervention, and improve outcomes in individuals exposed to high-altitude environments.

Keywords: High-Altitude Cerebral Edema, Hace, Magnetic Resonance Imaging, Corpus Callosum, Splenium, Diffusion Restriction, Cerebral Edema, Microbleeds, High-Altitude Illness, Leh–Ladakh.

Abbreviations: HACE – High-Altitude Cerebral Edema, MRI – Magnetic Resonance Imaging , GRE – Gradient Recalled Echo, SWI – Susceptibility-Weighted Imaging, DWI – Diffusion-Weighted Imaging , ADC – Apparent Diffusion Coefficient, FLAIR – Fluid-Attenuated Inversion Recovery.

INTRODUCTION

High-altitude cerebral edema (HACE) represents the most severe and potentially fatal form of acute high-altitude illness. It is characterized by progressive neurological dysfunction resulting from exposure to high altitude hypobaric hypoxia and, if left untreated, may rapidly progress to coma and death. Despite advances in awareness and preventive measures, HACE continues to be an important clinical entity owing to the increasing movement of military personnel, trekkers, mountaineers, tourists and workers to high altitude regions. Early diagnosis and timely intervention are crucial because neurological deficits may be reversible when recognized promptly but can lead to significant morbidity if treatment is delayed.

The pathophysiology of HACE is complex and multifactorial. Hypobaric hypoxia at high altitude results in cerebral vasodilatation, increased cerebral blood flow, disruption of the blood–brain barrier, and subsequent vasogenic edema. Concurrently, cellular energy failure secondary to hypoxia contributes to cytotoxic edema [1,2]. These processes lead to brain

swelling and increased intracranial pressure, which manifest clinically as headache, altered sensorium, ataxia, focal neurological deficits, and impaired consciousness. Histopathological and neuroimaging studies suggest that both vasogenic and cytotoxic mechanisms contribute to the development of HACE, although their relative contributions may vary among patients and stages of disease.

Magnetic resonance imaging (MRI) has emerged as the imaging modality of choice for evaluating HACE because of its superior sensitivity in detecting parenchymal abnormalities. Typical MRI findings include T2-weighted and FLAIR hyperintensities, diffusion restriction, microhemorrhages, and white matter edema. The corpus callosum, particularly the splenium, is the most frequently involved structure and is considered highly characteristic of HACE [3,4]. In more severe cases, lesions may extend to the cerebral white matter, internal capsules, cerebellum, brainstem, and other deep gray matter structures. Susceptibility-weighted imaging (SWI) may additionally demonstrate cerebral microbleeds, reflecting blood–brain barrier disruption and vascular injury.

Although several MRI findings associated with HACE have been described in the literature, the complete spectrum of imaging abnormalities and their relationship to disease severity remain incompletely understood. Most published studies consist of isolated case reports or small case series, and there is limited data from Indian high-altitude populations, particularly from regions such as Ladakh where exposure to extreme altitude is common. Furthermore, there is currently no widely accepted MRI-based grading system that comprehensively categorizes the extent of imaging involvement and correlates it with clinical severity.

A systematic evaluation of MRI findings across varying stages of HACE may improve diagnostic confidence, facilitate early recognition of severe disease, and provide insights into the underlying pathophysiological processes. Establishing an imaging-based severity classification could also assist clinicians in prognostication, monitoring treatment response, and standardizing reporting practices across institutions.

Therefore, the present study was undertaken to evaluate the spectrum of MRI findings in patients diagnosed with HACE and to propose an MRI-based grading system based on the extent and severity of imaging abnormalities.

MATERIALS AND METHODS

Study Design and Population

This retrospective observational study was conducted at a tertiary care hospital in Leh-Ladakh, over a three-year period from 2021 to 2024. The study included 18 consecutive patients who were clinically diagnosed with high-altitude cerebral edema (HACE) and underwent magnetic resonance imaging (MRI) of the brain during their illness. Clinical records and imaging studies were reviewed to evaluate the spectrum of neuroimaging findings associated with HACE.

Inclusion Criteria

Patients fulfilling all of the following criteria were included:

- Clinical diagnosis of HACE based on symptoms and signs suggestive of cerebral involvement following exposure to high altitude.
- Availability of complete MRI brain examination for review.
- Adequate image quality for interpretation.

Exclusion Criteria

Patients with alternative causes of neurological symptoms or imaging abnormalities were excluded, including:

- History of head trauma.
- Intracranial infections such as meningitis or encephalitis.
- Acute ischemic or hemorrhagic stroke.
- Metabolic or toxic encephalopathy.
- Incomplete or nondiagnostic MRI studies.

MRI Protocol

MRI examinations were performed using standard brain imaging protocols. The sequences analyzed included:

- Axial and sagittal T1-weighted imaging.
- Axial T2-weighted imaging.
- Fluid-attenuated inversion recovery (FLAIR) imaging.
- Diffusion-weighted imaging (DWI).
- Apparent diffusion coefficient (ADC) mapping.
- Gradient-recalled echo (GRE) and/or susceptibility-weighted imaging (SWI) sequences.

Image Analysis

All MRI studies were reviewed for the presence, distribution, and pattern of abnormalities. Particular attention was paid to involvement of the corpus callosum, especially the splenium, periventricular and deep white matter changes,

diffusion restriction on DWI/ADC sequences, and the presence of cerebral microbleeds on GRE/SWI images. Imaging findings were categorized according to the predominant pattern of involvement and correlated with the clinical diagnosis of HACE.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using descriptive statistical methods. Continuous variables, including age, were expressed as mean ± standard deviation (SD) and range. Categorical variables were summarized as frequencies and percentages.

MRI findings including splenial involvement, diffuse corpus callosal involvement, periventricular white matter changes, mixed patterns of involvement, diffusion restriction, and microbleeds were recorded and presented as proportions of the total study population. The prevalence of each imaging pattern was calculated as a percentage of the 18 included patients.

Due to the small sample size and the descriptive nature of the study, no inferential statistical tests were performed. The results were primarily analyzed to identify the distribution and spectrum of MRI findings in patients with clinically diagnosed high-altitude cerebral edema (HACE). The proposed MRI-based severity classification was derived from the observed imaging patterns and their extent of cerebral involvement.

RESULTS

A total of 18 patients diagnosed with high-altitude cerebral edema (HACE) were included in the study. All patients were male, with ages ranging from 30 to 37 years. MRI demonstrated a characteristic pattern of involvement predominantly affecting the corpus callosum and cerebral white matter.

Table 1. Patient Demographics and Clinical Characteristics

Characteristics	Category	Number (%)
Age range	30-37 years	
Brain involvement	Isolated spleium	44.4
	Diffuse corpus callosum	27.8
	Periventricular white matter	16.7
	Mixed	11.1
	Microbleeds	22.2

These results are depicted in bar chart (Figure 1) and pictogram (Figure 2). The most common imaging finding was isolated involvement of the splenium of the corpus callosum, observed in 8 patients (44.4%) (Figure 3). Diffuse involvement of the corpus callosum, extending beyond the splenium to involve the body and genu, was identified in 5 patients (27.8%) (Figure 4). Periventricular white matter abnormalities without extensive corpus callosal involvement were seen in 3 patients (16.7%) (Figure 5). Mixed patterns involving both the corpus callosum and adjacent cerebral white matter were noted in 2 patients (11.1%). These results are depicted in bar chart (Figure 1) and pictogram (Figure 2).

Diffusion-weighted imaging revealed areas of restricted diffusion in the majority of patients (approximately 85–90%), predominantly involving the splenium and corpus callosum, with corresponding low ADC values. These findings were suggestive of cytotoxic edema and represented the most consistent MRI abnormality in the study population.

Microbleeds detected on GRE/SWI sequences were observed in 4 patients (22.2%) (Figure 4). These were predominantly located within the splenium of the corpus callosum and periventricular white matter regions. Patients demonstrating microhemorrhages generally exhibited more extensive MRI abnormalities, indicating a more severe form of disease.

Based on the observed imaging patterns, an MRI-based severity classification was proposed to stratify disease extent and severity. Progressive involvement from isolated splenial lesions to diffuse white matter abnormalities and microbleeds appeared to represent increasing severity of cerebral injury.

MRI-Based Grading / Severity Classification

Stage	Imaging Findings	Severity
Stage I	Isolated splenial involvement of the corpus callosum	Mild
Stage II	Diffuse corpus callosal involvement (splenium, body, and/or genu)	Moderate
Stage III	Associated periventricular or deep white matter involvement	Severe

Stage IV	Presence of microbleeds on GRE/SWI sequences	Critical

The imaging findings observed in this study support the concept that HACE represents a continuum of disease severity, with progressive extension of abnormalities beyond the splenium and development of microhemorrhages reflecting more advanced cerebral injury. This proposed MRI-based grading system may aid in radiological assessment and severity stratification of patients presenting with HACE.

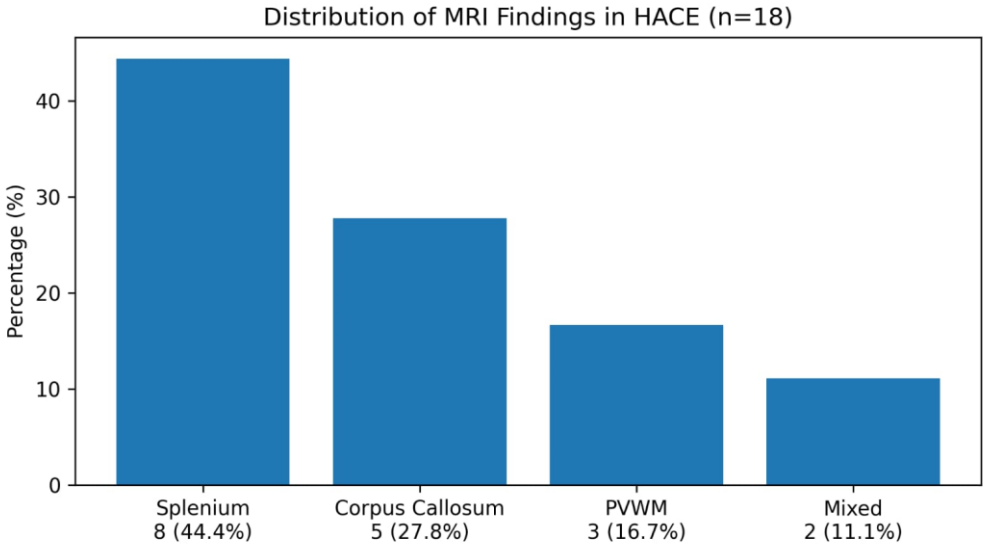

Figure 1. Distribution of MRI Findings in HACE

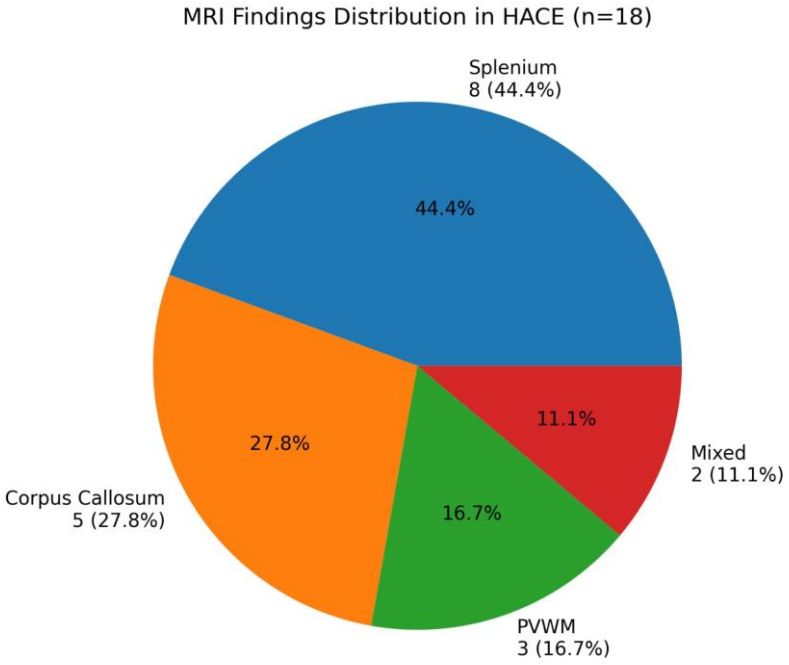

Figure 2. Distribution of MRI Findings in HACE

IMAGES

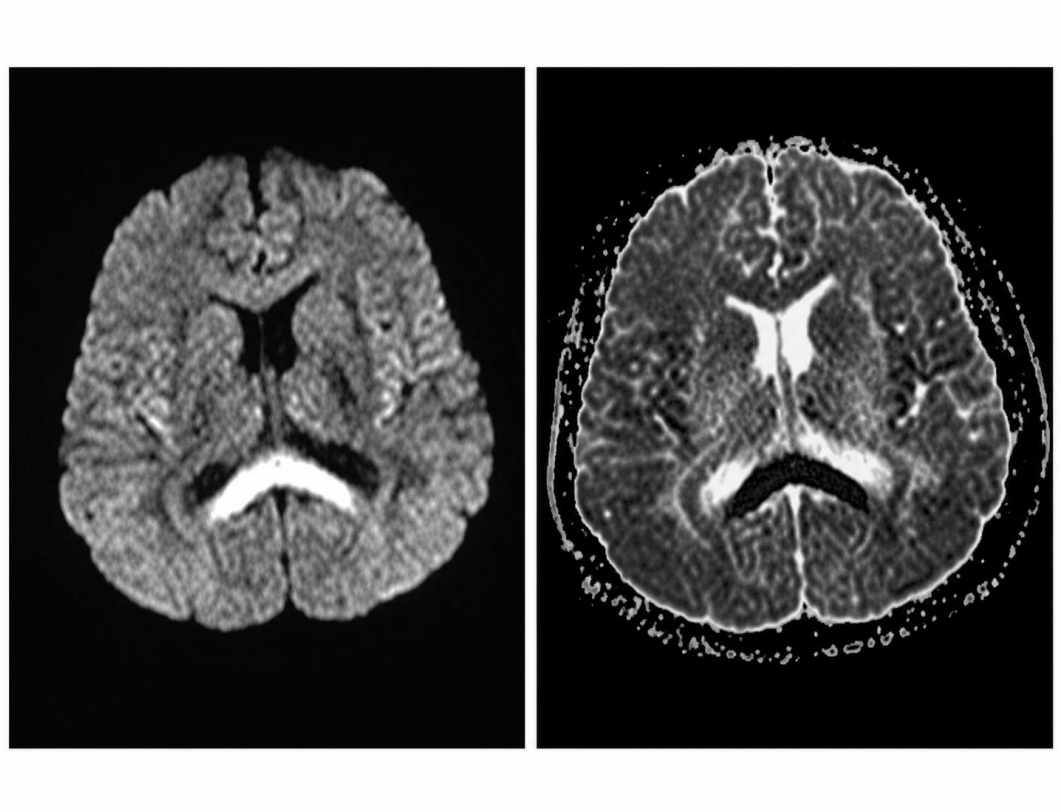

Figure 3. Diffusion Restriction in Splenium of Corpus Callosum

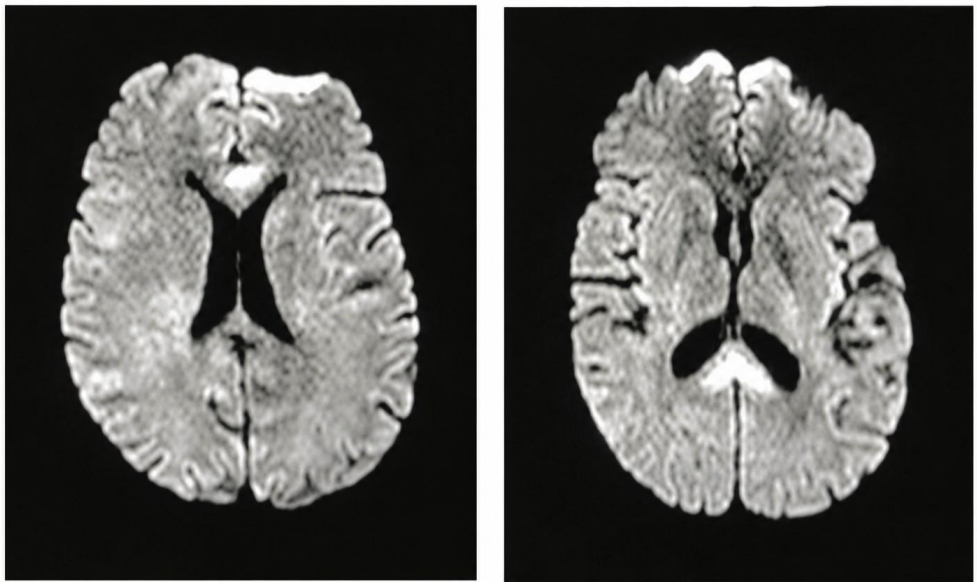

Figure 4. Diffusion Restriction Involving Genu and Splenium of Corpus Callosum

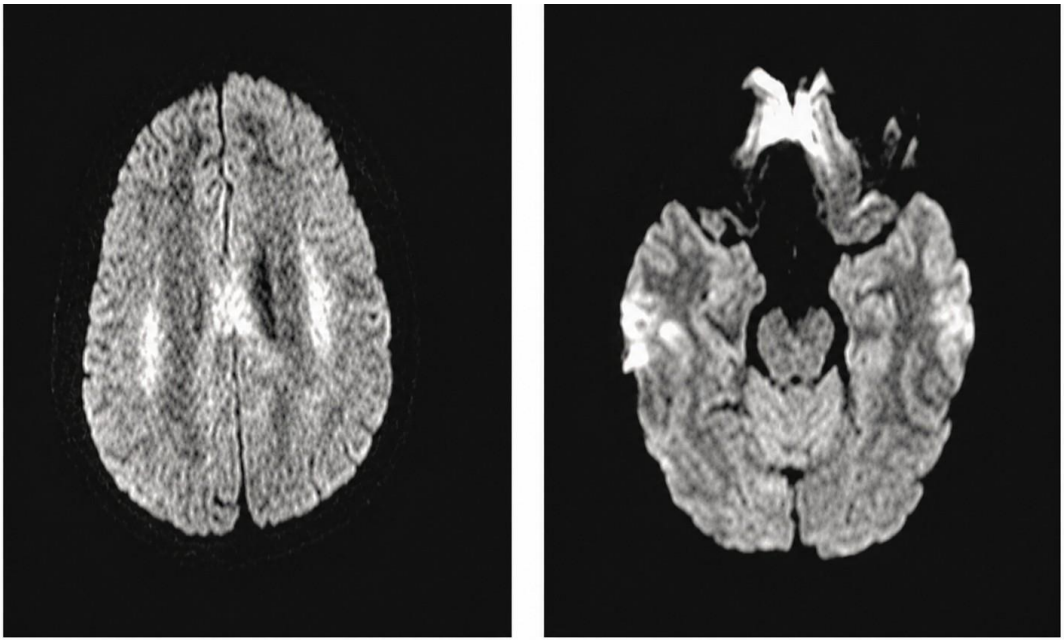

Figure 5. Diffusion Restriction in White Matter

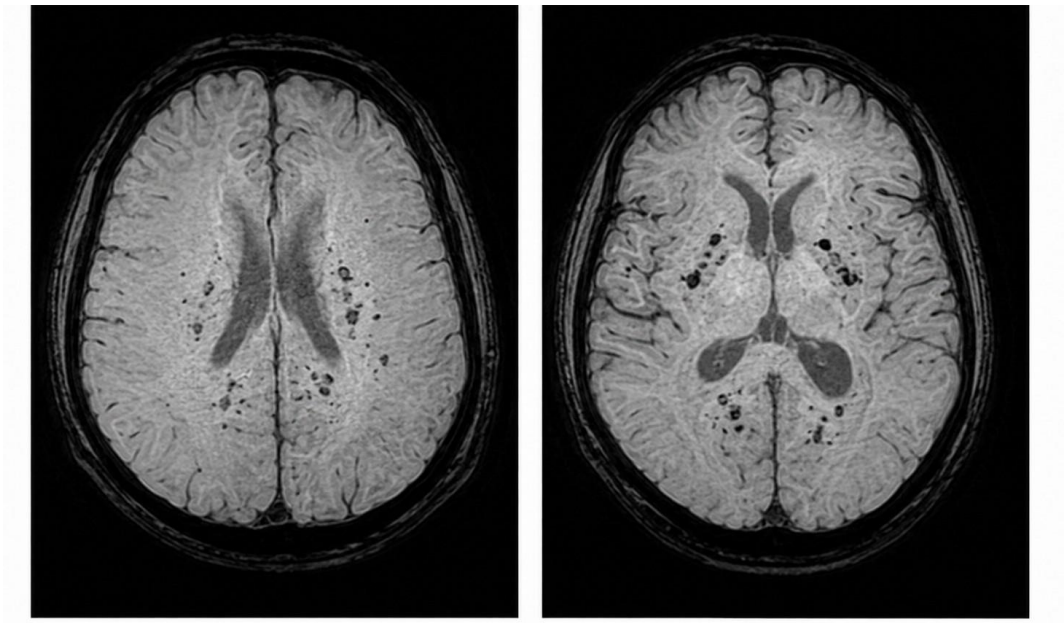

Figure 6. Microbleeds in GR

DISCUSSION

High-altitude cerebral edema (HACE) represents the most severe neurological manifestation of high-altitude illness and remains a potentially fatal condition if not recognized and treated promptly. Although the exact pathophysiological mechanisms are not fully understood, current evidence suggests that HACE results from a combination of vasogenic and cytotoxic edema secondary to hypobaric hypoxia. Hypoxia-induced cerebral vasodilatation, increased capillary permeability, and disruption of the blood-brain barrier contribute to vasogenic edema, while impaired cellular energy metabolism and ionic pump dysfunction lead to cytotoxic edema. The coexistence of these mechanisms explains the diverse MRI manifestations observed in affected patients [1,2].

In the present study, diffusion restriction was identified in approximately 85–90% of patients, making it the most consistent imaging finding. The presence of restricted diffusion with corresponding low ADC values strongly supports cytotoxic edema as a major component of HACE. Similar observations have been reported by Hackett et al., Kallenberg et al., and other investigators who demonstrated

diffusion abnormalities predominantly involving the corpus callosum in patients with HACE [3,4]. These findings suggest that HACE should be regarded as a mixed edema state rather than a purely vasogenic process.

The splenium of the corpus callosum was the most frequently involved structure, being affected in 44.4% of patients. This observation is consistent with previously published literature describing the splenium as the hallmark site of involvement in HACE [3,5]. The increased susceptibility of the splenium may be related to its dense myelination, high metabolic demand, compact arrangement of fibers, and unique microvascular architecture. These factors likely render it particularly vulnerable to hypoxic injury and intramyelinic edema.

An important finding of our study is the demonstration of a spectrum of MRI abnormalities ranging from isolated splenial lesions to extensive corpus callosal and cerebral white matter involvement. Based on these observations, we propose an MRI-based severity classification comprising four stages. Stage I consists of isolated splenial involvement, Stage II includes diffuse corpus callosal abnormalities, Stage III is characterized by associated white matter involvement, and Stage IV is defined by the presence of microbleeds on GRE/SWI sequences. This grading system reflects progressive cerebral injury and may serve as a practical tool for radiological severity assessment.

Microbleeds were identified in 22.2% of patients and predominantly involved the splenium and periventricular white matter. These findings are in agreement with previous studies demonstrating cerebral microhemorrhages in severe HACE [7]. The development of microbleeds is believed to result from hypoxia-induced endothelial dysfunction, capillary stress failure, and disruption of the blood-brain barrier. Their presence likely reflects advanced disease and may indicate a higher risk of neurological sequelae.

The observed progression from isolated splenial lesions to widespread white matter abnormalities supports the concept that HACE exists along a continuum of severity rather than as a single uniform entity. Patients with limited corpus callosal involvement may represent an early and potentially reversible stage, whereas extensive white matter changes and microhemorrhages likely signify advanced cerebral injury. Recognition of this spectrum is important because MRI findings may provide valuable information regarding disease severity and prognosis.

Diffusion-weighted imaging proved highly sensitive for detecting early cerebral involvement, while GRE/SWI sequences were particularly useful for identifying microhemorrhages not visible on conventional MRI sequences. Accordingly, both DWI and GRE/SWI should be considered essential components of MRI protocols in patients with suspected HACE.

Several differential diagnoses may mimic the MRI appearance of HACE, including mild encephalitis/encephalopathy with reversible splenial lesion (MERS), diffuse axonal injury, acute disseminated encephalomyelitis, demyelinating disorders, metabolic encephalopathies, and ischemic lesions involving the corpus callosum. Correlation with clinical history of recent high-altitude exposure and characteristic imaging findings remains critical for establishing the diagnosis [8].

Comparison with Existing Literatures

Our findings are broadly consistent with previously published MRI studies of high-altitude cerebral edema. Kallenberg et al. demonstrated both cytotoxic and vasogenic edema in HACE, with diffusion restriction involving the corpus callosum, particularly the splenium, representing a characteristic imaging feature [3]. In our study, diffusion restriction was observed in approximately 88.9% of patients, supporting the concept that cytotoxic edema is a major component of HACE.

The predominance of splenial involvement observed in the present series (44.4%) is in agreement with the observations of Bailey et al. and Wilson et al., who emphasized the vulnerability of the corpus callosum, particularly the splenium, to hypoxia-induced injury because of its unique fiber composition and microvascular architecture [5,6]. The splenium remains the most consistently reported site of involvement across MRI studies of HACE.

Microhemorrhages were identified in 22.2% of our patients. Previous studies by Schommer et al. reported hemosiderin deposition and cerebral microbleeds within the corpus callosum and adjacent white matter as characteristic markers of severe HACE [4,7]. Although the incidence of microbleeds in our cohort was lower than that reported in some severe-case series, their distribution and imaging appearance were comparable, supporting the concept that microbleeds

represent advanced blood-brain barrier disruption and endothelial injury.

Hackett and Roach first proposed that HACE represents the end stage of acute mountain sickness resulting from progressive cerebral edema [1]. Subsequent work by Bärtsch and Swenson further established the role of hypoxia-induced vascular permeability and cerebral swelling in disease pathogenesis [2]. Our MRI findings provide radiological support for these pathophysiological mechanisms by demonstrating a continuum from isolated splenial lesions to diffuse white matter involvement and microhemorrhage.

An important contribution of the present study is the proposal of a four-stage MRI-based severity classification. While previous studies have described isolated imaging findings, no standardized MRI severity grading system has been widely adopted. The proposed classification integrates diffusion abnormalities, corpus callosal involvement, white matter extension, and microbleeds into a structured framework that may facilitate severity assessment and future prognostic evaluation.

Table 2. Comparison with Existing Literature

Parameter	Present Study (n=18)	Kallenberg et al. 2007 [3]	Schommer et al. 2013 [4,7]	Bailey et al. 2009 [5]
Diffusion restriction	88.9%	Common finding	Reported	Reported
Splenial involvement	44.4%	Predominant site	Predominant site	Characteristic finding
White matter involvement	Present in advanced stages	Reported	Reported	Reported
Microbleeds	22.2%	Occasional	Characteristic of severe HACE	Reported
Severity grading	Proposed 4-stage classification	Not proposed	Not proposed	Not proposed

Limitations

The principal limitations of this study include its retrospective design, relatively small sample size, and lack of long-term clinical follow-up. Future multicenter studies with larger cohorts are required to validate the proposed MRI-based severity classification and to determine its prognostic significance.

CONCLUSION

High-altitude cerebral edema (HACE) demonstrates a characteristic and evolving spectrum of MRI findings, with the splenium of the corpus callosum being the most commonly and earliest affected structure. The imaging abnormalities appear to progress from isolated splenial involvement to diffuse corpus callosal and cerebral white matter changes, reflecting increasing severity of hypoxic cerebral injury.

Diffusion-weighted imaging is highly sensitive for the early detection of HACE and frequently demonstrates diffusion restriction consistent with cytotoxic edema. GRE/SWI sequences provide additional diagnostic and prognostic value by identifying cerebral microbleeds, which are indicative of severe endothelial injury and advanced disease.

The findings of this study support the concept that HACE exists along a continuum of radiological severity rather than as a single imaging entity. Based on the observed patterns, the proposed MRI-based grading system offers a simple and practical framework for stratifying disease severity and facilitating radiological assessment.

Early recognition of characteristic MRI findings, particularly splenial lesions, diffusion restriction, and microhemorrhages, can aid in timely diagnosis, prompt initiation of treatment, and prevention of potentially fatal neurological complications. Further prospective studies with larger patient populations are warranted to validate the proposed grading system and assess its prognostic significance in clinical practice.

REFERENCES

1. Hackett PH, Roach RC. High-altitude cerebral edema. N Engl J Med. 2001;345(2):107-114.
2. Bärtsch P, Swenson ER. Acute high-altitude illnesses. N Engl J Med. 2013;368(24):2294-2302.
3. Kallenberg K, Bailey DM, Christ S, et al. Magnetic resonance imaging evidence of cytotoxic and vasogenic edema in high-altitude cerebral edema. Radiology. 2007;243(1):171-178.

4. Schommer K, Kallenberg K, Lutz K, et al. Hemosiderin deposition in the corpus callosum as a marker for high-altitude cerebral edema. J Appl Physiol. 2013;114(1):87-91.
5. Bailey DM, Bärtsch P, Knauth M, Baumgartner RW. Emerging concepts in acute mountain sickness and high-altitude cerebral edema: from the molecular to the morphological. Brain. 2009;132(Pt 2):455-465.
6. Wilson MH, Newman S, Imray CHE. The cerebral effects of ascent to high altitudes. Pract Neurol. 2009;9(4):183-190.
7. Schommer K, Kallenberg K, Lutz K, Bärtsch P, Knauth M. Hemosiderin deposition in the brain as footprint of high-altitude cerebral edema. Neurology. 2013;81(20):1776-1779.
8. Tada H, Takanashi JI, Barkovich AJ, et al. Clinically mild encephalitis/encephalopathy with a reversible splenial lesion. Radiology. 2004;231(1):95-100.