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Original Research Paper

Radio-Diagnosis

UTILITY OF MAGNETIC RESONANCE IMAGING IN THE EVALUATION AND CHARACTERIZATION OF DIFFUSE WHITE MATTER DISEASES USING ADVANCED IMAGING TECHNIQUES

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ABSTRACT

Background: White matter diseases of the central nervous system include demyelinating and dysmyelinating disorders, which often present with overlapping clinical and radiological features. Conventional imaging sequences such as T1- and T2-weighted MRI provide valuable information but have limitations in specificity and early lesion detection. Advanced techniques like fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) may enhance diagnostic accuracy. **Aim:** To evaluate the role of MRI, including advanced imaging sequences, in assessing and characterizing diffuse white matter diseases. **Methods:** This cross-sectional, hospital-based observational study was conducted at the Department of Radiodiagnosis, Sri Aurobindo Medical College & Postgraduate Institute, Indore, from June 2023 to November 2024. A total of 50 participants with suspected white matter disease on MRI were enrolled through convenience sampling. All underwent conventional (T1, T2, FLAIR) and advanced (DWI) MRI sequences. Imaging findings were recorded in a structured proforma and analyzed using descriptive and inferential statistics. **Results:** Of the 50 participants, 68% were male and 32% female, with the most common age group being 51–60 years (40%). Cognitive decline (32%), motor deficits (26%), and seizures (24%) were frequent clinical presentations. MRI revealed hypo-intense lesions in 50%, iso-intense in 30%, and hyperintense in 20%. FLAIR abnormalities were present in 84%, while DWI abnormalities were noted in 62%. Demyelinating lesions accounted for 70% and dysmyelinating for 30%. The most common diagnoses were multiple sclerosis (34%) and acute disseminated encephalomyelitis (22%), followed by metachromatic leukodystrophy (10%) and adrenoleukodystrophy (6%). Additional findings included corpus callosum involvement (50%), contrast enhancement (30%), ventricular enlargement (12%), and brainstem lesions (10%). **Conclusion:** MRI, particularly with the inclusion of FLAIR and DWI sequences, provides valuable insights into the diagnosis and classification of diffuse white matter diseases. These advanced techniques improve specificity, enable early lesion detection, and facilitate accurate differentiation between demyelinating and dysmyelinating conditions, reducing reliance on invasive procedures.

KEYWORDS : Diffuse white matter disease; Magnetic resonance imaging; Demyelination; Dysmyelination; Fluid-attenuated inversion recovery; Diffusion-weighted imaging; Multiple sclerosis; Leukodystrophies

INTRODUCTION

White matter diseases encompass a group of disorders that primarily affect the white matter of the central nervous system (CNS). White matter consists of myelinated axons, which facilitate the transmission of nerve impulses between different regions of the brain and spinal cord(1). Disorders of white matter can be broadly categorized into two groups: demyelinating diseases and dysmyelinating diseases(1).

MRI has become the gold standard for diagnosing white matter diseases due to its ability to provide detailed anatomical and pathological information. MRI enables early detection of white matter lesions, often before clinical symptoms manifest(2). This is crucial for diseases like multiple sclerosis, where early intervention can delay progression. It can differentiate between demyelinating, dysmyelinating, and other pathologies based on lesion appearance, size, and distribution(3). MRI allows for longitudinal assessment of white matter diseases, helping clinicians track disease activity, progression, and response to therapy(2). Techniques like contrast-enhanced imaging can highlight areas of active inflammation, aiding in treatment planning. MRI has facilitated breakthroughs in understanding the pathophysiology of white matter diseases, including the role of immune and genetic factors(4,5).

The evaluation of diffuse white matter diseases presents significant challenges, primarily due to the limitations of conventional imaging techniques and the complexity of these conditions. While modalities like computed tomography (CT) provide structural details, they lack the sensitivity needed to identify subtle or early white matter changes(6,7). Conventional MRI sequences, such as T1- and T2-weighted imaging, although effective for detecting lesions, often lack the specificity to differentiate between various pathological processes such as demyelination, dysmyelination, ischemia, or toxic encephalopathy(8). Many white matter diseases exhibit overlapping imaging characteristics, leading to diagnostic ambiguity. Advanced MRI techniques such as diffusion-weighted imaging (DWI) and magnetic resonance spectroscopy (MRS) have shown potential for improved characterization of white matter lesions(7). However, their application in routine clinical practice remains underexplored, particularly in terms of their diagnostic accuracy and reliability. There is a need for standardized protocols and criteria to classify and interpret findings from advanced MRI sequences to enhance diagnostic precision(7). This study is designed to address these gaps by utilizing advanced MRI techniques to improve the evaluation and characterization of these conditions.

AIM:

To evaluate the utility of Magnetic Resonance Imaging (MRI) in assessing and characterizing diffuse white matter diseases using advanced imaging techniques.

MATERIAL AND METHODS

- **Study Design:** A single centre, hospital-based, cross-sectional, observational study to evaluate and characterize diffuse white matter diseases using Magnetic Resonance Imaging (MRI).

- **Study Settings:** The study was conducted in the Department of Radiodiagnosis at Sri Aurobindo Medical College & Postgraduate Institute, Indore, Madhya Pradesh.

- **Ethical Clearance:** Ethical clearance for the study was

obtained after a rigorous review process. The research protocol, including the study design, data collection form, and informed consent document, was thoroughly scrutinized by the Institutional Ethical Committee. The study adhered to the ethical principles outlined in the Declaration of Helsinki, ensuring the safety, confidentiality, and informed participation of all study subjects.

- **Study Duration:** The total duration of the present study was 18 months, from June 2023 to November 2024.

- **Study Participants:** The participants for the present study were individuals undergoing MRI evaluations at the study institute who exhibited imaging findings suggestive of diffuse white matter diseases. Eligible participants included individuals of both genders across all age groups who fulfilled the inclusion criteria and consented to participate in the study.

Inclusion Criteria:

1. Patients with MRI showing lesions located predominantly within the white matter of the brain or brainstem.
2. Individuals of all genders, aged up to 60 years, to exclude arteriosclerotic or vascular lesions associated with aging.
3. Participants providing written informed consent.

Exclusion Criteria:

1. Patients unwilling to provide consent for the study.
2. Individuals with contraindications to MRI, such as claustrophobia, metallic implants, or cardiac pacemakers.
3. Cases with insufficient clinical data or imaging quality for evaluation.

Sample Size: All eligible participants coming to the study institute during the recruitment period and providing written informed consent were enrolled in the study. Following this approach, a total of 50 participants were included in the present study.

Sampling Methodology: The present study employed a non-probability convenience sampling methodology.

Adverse Event Monitoring: Participants were informed to report any discomfort during MRI scanning. MRI scans were performed under the supervision of experienced radiologists, ensuring participant safety throughout the procedure.

Data Collection Procedure: The data collection for this study was conducted in a systematic and meticulous manner to ensure the accuracy and reliability of the findings. The entire process was carried out in a temporal sequence as outlined below:

1. Obtaining Informed Consent: Before initiating any data collection, eligible participants were approached, and the purpose of the study, along with its procedures, potential benefits, and risks, was explained in detail. A bilingual consent form (Hindi and English) was provided to participants, and they were encouraged to ask questions to clarify their doubts. Written informed consent was obtained from participants who voluntarily agreed to participate.

2. Screening for Eligibility: Participants were assessed for eligibility based on the predefined inclusion and exclusion criteria. MRI findings showing diffuse white matter lesions predominantly in the brain or brainstem. Detailed demographic and clinical information, including age, gender, and medical history, was collected during this screening phase.

3. Clinical History and Physical Examination: A comprehensive clinical history was obtained, focusing on:
o Presenting symptoms such as cognitive decline, seizures, or motor deficits.
o Duration and progression of symptoms.
o Relevant medical history, including prior treatments and co-existing conditions.
o A general physical and neurological examination was conducted, except for unconscious or non-responsive participants.

4. Conducting MRI Evaluations: Participants underwent MRI scans using a 1.5 Tesla scanner (Somatom, Siemens, Germany) equipped with CP array head coils. The following sequences were performed for each participant:
o Conventional Sequences: T1-weighted, T2-weighted, and fluid-attenuated inversion recovery (FLAIR) imaging.
o Advanced Sequences: Diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) mapping for evaluating microstructural changes. Imaging parameters such as repetition time (TR), echo time (TE), section thickness, and field of view were standardized across scans to ensure consistency.

5. Data Recording from MRI: MRI findings were analyzed by an experienced radiologist and recorded systematically using a pre-structured proforma. Key imaging characteristics were noted, including:
o Lesion size, location, and intensity.
o Signal abnormalities on conventional and advanced sequences.
o Specific patterns such as periventricular hyperintensities or restricted diffusion.
o In cases where additional clinical or imaging data were required, participants were scheduled for follow-up imaging or laboratory tests.

9. Post-Study Communication Participants were informed of their MRI findings and advised to follow up with their respective physicians for further evaluation and treatment as needed.

- **Statistical Analysis:** Descriptive statistics, including mean and standard deviation for continuous variables and frequency and percentage for categorical variables, were calculated to summarize the dataset. The association between imaging findings and clinical presentations was tested using the Chi-square test for categorical data. Statistical significance was determined at a p-value of <0.05. All statistical and graphical analyses for this study were conducted using Stata software version 17.0.

- Funding: There was no external funding for this study.

- Conflict of Interest: The authors declare no conflict of interest in the design, implementation, or interpretation of the findings of this study.

RESULTS:

The study included 50 participants who fulfilled the inclusion criteria. The findings from each table are presented below. The majority of participants were in the age group of 51–60 years (40%), followed by 31–40 years (28%) and 41–50 years (14%). Only a small proportion were infants (2%) or children aged 1–10 years (2%). Males predominated (68%), while females constituted 32% of the study population. The most common presenting complaint was cognitive decline (32%), followed by motor deficits (26%) and seizures (24%). Other miscellaneous complaints were reported in 18% of participants (Table 1).

Table 1: Characteristics of Participant (years)

Age of participant (years)	Freq.	Percent
<1 Year (Infant)	1	2.00
1-10 (Child)	1	2.00
21-30	3	6.00
31-40	14	28.00
41-50	7	14.00
51-60	20	40.00
61-70	4	8.00

Gender		
Female	16	32.00
Male	34	68.00
Presenting Complaints		
Presence of Cognitive Decline	16	32.0
Seizures	12	24.00
Motor Deficits	13	26.00
Other	9	18.0

Half of the participants (50%) demonstrated hypo-intense lesions, 30% showed iso-intense lesions, and 20% had hyperintense lesions. FLAIR abnormalities were present in a large proportion (84%) of cases, while 16% showed no such changes. Diffusion-weighted imaging (DWI) abnormalities were observed in 62% of participants, whereas 38% had normal DWI findings. Based on MRI lesion classification, 70% of cases were demyelinating, while 30% were dysmyelinating (Table 2).

Table 2: Lesion Characteristics on MRI

Lesion Intensity on MRI	Freq.	Percent
Hypo-Intense	25	50.00
Iso-Intense	15	30.00
Hyperintense	10	20.00
FLAIR Abnormality Present		
No	8	16.00
Yes	42	84.00
DWI Abnormality Present		
No	19	38.00
Yes	31	62.00
MRI Based Lesion Classification		
Demyelinating	35	70.00
Dysmyelinating	15	30.00

Multiple sclerosis was the most frequent diagnosis, observed in 34% of participants, followed by acute disseminated encephalomyelitis (22%). Among dysmyelinating disorders, metachromatic leukodystrophy was most common (10%), followed by adrenoleukodystrophy (6%). Other diagnoses included Alexander's disease (4%), toxic demyelination (6%), and rare conditions such as globoid leukodystrophy, Pelizaeus–Merzbacher disease, mitochondrial disorders, Canavan's disease, and Van der Knaap disease (each 2%). Single cases (2%) of HIV encephalopathy, progressive multifocal leukoencephalopathy (PML), central pontine myelinolysis (CPM), and periventricular leukomalacia (PVL) were also documented (Table 3).

Table 3: MRI Diagnosis

Diagnosis	Freq.	Percent
Multiple Sclerosis (MS)	17	34.00
Acute Disseminated Encephalomyelitis (ADEM)	11	22.00
Toxic Demyelination	3	6.00
HIV Encephalopathy	1	2.00
Progressive Multifocal Leukoencephalopathy (PML)	1	2.00
Central Pontine Myelinolysis (CPM)	1	2.00
Periventricular Leukomalacia (PVL)	1	2.00
Metachromatic Leukodystrophy (MLD)	5	10.00
Adrenoleukodystrophy (ALD)	3	6.00
Alexander's Disease	2	4.00
Globoid Leukodystrophy (GLD)	1	2.00
Pelizaeus-Merzbacher Disease (PMD)	1	2.00
Mitochondrial Disorders	1	2.00
Canavan's Disease	1	2.00
Van der Knaap Disease	1	2.00
Total	50	100.00

Corpus callosum involvement was the most frequent additional finding, seen in 50% of participants. Contrast enhancement was present in 30%, while ventricular enlargement and brainstem lesions were detected in 12% and 10% of cases, respectively. Edema was noted in 16% of participants (Table 4).

Table 4: Additional MRI Findings

Additional MRI Findings	Freq.	Percent
Ventricular Enlargement	6	12.00
Corpus Callosum Involvement	25	50.00
Brainstem Lesion Present	5	10.00
Contrast Enhancement on MRI	15	30.00
Edema on MRI	8	16.00

DISCUSSION:

In the present study, 50% of lesions appeared hypo-intense on MRI, followed by iso-intense lesions in 30% and hyperintense lesions in 20% of participants. These signal characteristics reflect the typical MRI appearance of various white matter diseases, where T1-weighted hypo-intensity and T2-weighted hyperintensity are common in demyelinating and dysmyelinating conditions. Ahsan et al., (2008) observed that all patients with multiple sclerosis showed lesions that were hypo-intense on T1-weighted images and hyperintense on T2-weighted images, with at least three or more lesions per case(10). Kamireddy et al., (2017) also noted similar intensity patterns, reporting that T2-weighted and FLAIR images were more sensitive in detecting the extent of demyelination, while T1 hypo-intensity helped assess chronicity(11). Rana et al., (2018) reported comparable findings, with T2 and FLAIR sequences demonstrating bright signal changes in affected white matter regions, particularly in demyelinating conditions(12).

In the present study, FLAIR abnormalities were observed in 84% of participants, while 16% showed no such findings. This highlights the value of FLAIR sequences in detecting subtle changes in white matter, particularly in demyelinating conditions. FLAIR helps suppress CSF signals, making periventricular and subcortical lesions more visible. Similar results were reported by Rana et al., (2018), who noted that FLAIR sequences were more sensitive than conventional T2-weighted images in identifying demyelinating lesions(12). Their study emphasised the importance of FLAIR in detecting periventricular white matter involvement, especially in multiple sclerosis. Kamireddy et al., (2017) also supported this observation, stating that FLAIR sequences provided better lesion contrast and were essential in identifying white matter changes in both MS and ADEM(11).

In the present study, diffusion-weighted imaging (DWI) abnormalities were seen in 62% of participants, while 38% showed no abnormality on DWI. This suggests that a significant proportion of diffuse white matter diseases may present with restricted diffusion, indicating active demyelination, cytotoxic oedema, or metabolic changes depending on the disease type. Sashikanth et al., (2021) also highlighted the role of DWI in identifying restricted diffusion in demyelinating and toxic-metabolic conditions, noting that DWI abnormalities were more frequent in acute or early disease stages(13).

In the present study, demyelinating lesions were more common, seen in 70% of cases, while dysmyelinating lesions accounted for 30%. This pattern reflects the predominance of acquired white matter diseases, such as multiple sclerosis and ADEM, in the studied population. It also indicates that MRI features can reliably help distinguish between these two major categories based on lesion distribution, intensity, and clinical correlation. Sashikanth et al., (2021) reported a similar predominance of demyelinating lesions in their study, where ADEM and MS together constituted the majority of cases. Kamireddy et al., (2017) found that demyelinating conditions made up 64% of their sample, supporting the current study's findings. Rana et al., (2018) also identified demyelinating lesions as the most frequent, with multiple

sclerosis being the leading diagnosis. In contrast, Gowdar et al., (2015) studied paediatric leukodystrophies, resulting in a higher proportion of dysmyelinating conditions. Their cohort was younger, with a mean age of 5.8 years, and the most common diagnoses were metachromatic leukodystrophy (38.4%) and adrenoleukodystrophy (23.1%). This difference highlights the influence of age and population characteristics on the observed lesion type.

In the present study, multiple sclerosis (MS) was the most common diagnosis, seen in 34% of patients. MRI findings in these cases typically showed multiple, small lesions in the periventricular and pericallosal regions, consistent with typical demyelinating patterns. This high frequency reflects the global pattern of MS as the most prevalent acquired white matter disease in adults. Ahsan et al., (2008) reported a similar finding, with MS accounting for 48% of white matter diseases in their cohort. Their patients showed classic hypo-intense lesions on T1 and hyperintense lesions on T2-weighted images, with at least three or more periventricular plaques in most cases. Kamireddy et al., (2017) also found MS to be the most common demyelinating disorder, making up 36% of their cases, and described similar imaging features involving the corpus callosum and periventricular white matter. Rana et al., (2018) confirmed this trend, noting MS as the predominant demyelinating diagnosis in adults, with lesion distribution similar to the current study.

Acute disseminated encephalomyelitis (ADEM) was the second most common diagnosis, found in 22% of participants. These patients showed widespread, asymmetric lesions involving the subcortical white matter, basal ganglia, and cerebellum. ADEM usually presents after infection or vaccination and is monophasic in nature. Sashikanth et al., (2021) reported ADEM in 28% of their cohort, with imaging features closely resembling those seen in this study(13). Ahsan et al., (2008) also included ADEM among the white matter diseases they studied, describing T2 and FLAIR hyperintensities in subcortical and cerebellar regions with patchy enhancement, which matches the present findings(10). Metachromatic leukodystrophy (MLD), a dysmyelinating disorder, was diagnosed in 10% of patients. Lesions were bilateral and symmetrical, typically involving the periventricular white matter with a frontal predominance. Gowdar et al., (2015) found MLD to be the most common leukodystrophy in their paediatric sample, accounting for 38.4% of cases. Their imaging findings showed symmetrical periventricular T2 hyperintensities, matching those observed in the present study(14). Ahsan et al., (2008) also reported three cases of MLD, with similar age distribution and MRI findings in the frontal and peritrigonal white matter(10).

Central Pontine Myelinolysis (CPM) (2%) CPM was seen in one case (2%) and showed classical T2 and FLAIR hyperintensity confined to the central pons, with no mass effect or contrast enhancement. This imaging pattern is characteristic of osmotic demyelination. Kamireddy et al., (2017) reported similar findings in CPM, where the lesion was restricted to the central pons with no peripheral extension(11). Sashikanth et al., (2021) included CPM among their differentials for central white matter diseases and described similar imaging localisation and signal characteristics(13).

Periventricular Leukomalacia (PVL) (2%) One patient (2%) had PVL, with MRI showing periventricular white matter volume loss and T2 hyperintensities adjacent to the lateral ventricles. This condition is more common in preterm infants and reflects perinatal hypoxic injury. Nowell et al., (2024) described PVL in their series of children with developmental delay, where MRI demonstrated periventricular high signal and white matter thinning. These imaging patterns matched the present case and supported a diagnosis of chronic white matter injury(15).

Alexander's Disease (4%) Two patients (4%) had MRI findings suggestive of Alexander's disease, with frontal dominant white matter changes and periventricular signal alterations. Ahsan et al., (2008) reported similar findings in two patients with Alexander's disease, showing cerebellar and frontal white matter changes. Nowell et al., (2024) also identified Alexander's disease, noting peritrigonal and cerebellar involvement. The imaging matched the classical frontal-predominant dysmyelination pattern described in both studies(15).

Canavan's Disease (2%) One patient (2%) was diagnosed with Canavan's disease. MRI showed bilateral, diffuse T2 hyperintensity in the white matter and involvement of the basal ganglia. Ahsan et al., (2008) reported one case of Canavan's disease, describing similar findings with extensive symmetric signal changes involving both white matter and basal ganglia. Nowell et al., (2024) also identified Canavan's disease, where MRI showed widespread involvement of subcortical white matter and thalamus(15).

Van der Knaap Disease (2%) One patient (2%) had findings consistent with Van der Knaap disease, with extensive subcortical cystic white matter changes and sparing of the central white matter. Ahsan et al., (2008) included one such case and described characteristic subcortical cysts, frontal sparing, and mildly affected central white matter. Their imaging closely matched the present case, confirming the diagnosis(10).

CONCLUSION

This study highlights the critical role of magnetic resonance imaging (MRI) in the evaluation and characterization of diffuse white matter diseases. Conventional sequences such as T1- and T2-weighted imaging remain useful for detecting lesions, but advanced techniques like fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) significantly enhance diagnostic accuracy. In this cohort, demyelinating disorders, particularly multiple sclerosis and acute disseminated encephalomyelitis, were more common than dysmyelinating conditions. FLAIR abnormalities and DWI changes were frequently observed, underscoring their value in identifying subtle and early lesions. Additional findings such as corpus callosum involvement, contrast enhancement, and ventricular changes provided further diagnostic clues.

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