Original Article

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Radiology Section

Diffusion Weighted Imaging versus Contrast-enhanced T1-weighted Imaging Sequences in Inflammatory Demyelinating Diseases of Brain: A Cross-sectional Study

KR MANOHAR KUMAR[1], RUPI JAMWAL[2], MOHAN KUMAR[3]

ABSTRACT

Introduction: Based on the literature, Contrast-enhanced T1-Weighted (CE T1WI) imaging sequence is considered as the gold standard radiological marker of active inflammatory demyelinating diseases of brain. However, administration of gadolinium based contrast agents is not always possible due to various comorbidities that the patient may suffer from, such as chronic kidney disease or contrast allergy. Diffusion Weighted Imaging (DWI) may potentially play a role in identifying disease activity in such cases without the need for intravenous administration of contrast.

Aim: To compare signal intensity of lesions in inflammatory demyelinating diseases of brain on DWI with the status of enhancement on CE T1WI.

Materials and Methods: This was a cross-sectional study conducted for two years from June 2015 to June 2017 among patients in the age group of two to 50 years presenting with clinicoradiological features of inflammatory demyelinating diseases in the Department of Radiodiagnosis in collaboration with Department of Neurology, Vardhman Mahavir Medical College (VMMC) and Safdarjung Hospital, New Delhi, India. Magnetic Resonance Imaging (MRI) of brain was done using different imaging sequences such as T1-Weighted Imaging (T1WI), T2-Weighted Imaging (T2WI), Fluid Attenuated Inversion Recovery (FLAIR), DWI, CE T1WI and were analysed for the lesions of demyelinating diseases. The signal intensity of demyelinating lesions on DWI were assessed against Contrast Enhancement on CE T1W1 imaging. Validity measures were estimated using appropriate formulae. Data was entered into Microsoft Excel software and qualitative variables were assessed for significance using Fisher's-exact test. Sensitivity, specificity, negative predictive value, positive predictive value and accuracy were assessed. Data analysis was done using Statistical Package for the Social Sciences (SPSS) software version 18.0.

Results: There were a total of 73 contrast enhancement lesions. DWI hyperintensity showed 100% sensitivity, 60.9% specificity, positive predictive value of 84.7% and negative predictive value of 100% with accuracy of 87.7% whereas diffusion restriction showed 100% specificity, 12% sensitivity, positive predictive value of 100% and negative predictive value of 34.3% with accuracy of 39.7%.

Conclusion: Hence, hyperintense lesions in DWI can be considered as a better screening tool and diffusion restriction can be considered as a diagnostic tool in active phase of inflammatory demyelinating diseases of brain, when compared to CE T1WI sequence.

Keywords: Acute disseminated encephalomyelitis, Diffusion restriction, Gadolinium, Multiple sclerosis, Neuromyelitis optica

INTRODUCTION

Demyelinating disorders of the Central Nervous System (CNS) affecting the young adults occur as a result of inflammation and selective destruction of myelin. The most common inflammatory demyelinating disorders of the CNS include Multiple Sclerosis (MS), Acute Disseminated Encephalomyelitis (ADEM) and Neuromyelitis Optica (NMO) which represent an important cause of neurological disability [1,2]. Among Indians, prevalence of MS was noted to be 8.3 per 1,00,000 and that of Neuromyelitis Optica Spectrum Disorders (NMOSD) to be 2.7 per 1,00,000 [3].

The spatial and temporal distributions of demyelinating plaques in the brain and spinal cord in multiple sclerosis can be well appreciated in MRI [4]. The advanced techniques of MRI can differentiate MS from other inflammatory demyelinating conditions which have different clinical courses but similar MRI features. ADEM and NMO have less diffuse tissue damage compared to MS which can distinguish them from MS [5]. MRI findings in typical MS are T2/FLAIR hyperintense lesions noted in periventricular, cortical or juxtacortical, infratentorial and spinal cord [6]. Among the suspected patients of MS, the demonstration of disease dissemination on dual-echo in space and time and CE T1WI is considered as imaging criteria for diagnosis [6,7].

The NMO lesions are reported as confluent hyperintensities on T2-weighted images or Fluid-Attenuated Inversion Recovery [FLAIR] images seem to be asymmetrically scattered mostly in periependymal areas [7].

In patients with ADEM, disseminated, bilateral, asymmetrical T2/FLAIR hyperintense white matter lesions are seen. The appearance of ADEM on MRI, has some overlapping features with conditions such as MS and CNS vasculitis. Sparing of periventricular region and the absence of "Dawson finger" appearance is said to differentiate ADEM from MS and CNS angiography would help to differentiate ADEM from CNS vasculitis [7].

The T1 weighted, FLAIR, T2 weighted and pre and post single dose gadolinium T1 weighted imaging are the fixed MRI sequences used in the assessment of multiple sclerosis. Hyperintense lesions in T2 weighted imaging and FLAIR sequences are observed to be non specific and might be due to different reasons like edema, axonal loss, gliosis and demyelination or Wallerian degeneration. Active inflammation increases the permeability of the contrast producing hyper signal intensity on CE T1WI images and it is also considered the standard radiological marker of inflammatory activity in multiple sclerosis (MS) [8]. But post CE T1WI images are considered as delicate instrument in detecting this type of CNS damage. Because of disease chronicity, there might be requirement of multiple doses

of Gadolinium-Based Contrast Agents (GBCAs) to be used during the disease follow-up which might put the patients under the increased risk of nephrogenic syndrome in patients with Acute Renal Failure (ARF) and Chronic Renal Failure (CRF) [9]. In addition, the use of such contrasts in the pregnant women is enigmatic. Thus, the current study was conducted to assess the signal intensity on Diffusion Weighted Imaging (DWI) sequence in patients with clinically suspected cases of demyelinating diseases of brain in comparison to the enhancement status of CE T1WI Imaging sequence.

MATERIALS AND METHODS

This descriptive cross-sectional study was carried out in the Department of Radiodiagnosis in collaboration with Department of Neurology at VMMC and Safdarjung hospital, New Delhi, India, over a time frame of two years from June 2015 to June 2017. Prior to starting the study, clearance was obtained from the Institutional Ethics Committee and a written, informed consent were obtained from each subject.

Sample size calculation: As per the statistics available, the average number of patients presenting with features suggestive of inflammatory demyelinating diseases to the Department of Radiology varies around 15 to 20 per year, hence the sample size of 40 has been considered. Convenient sampling method was adopted.

Inclusion criteria: Patients between the age group two years to 50 years presenting with features suggestive of inflammatory demyelinating diseases comprising multiple sclerosis, neuromyelitis optica and acute disseminated encephalomyelitis according to revised diagnostic criteria [10,11,12] were included in the study.

Exclusion criteria: Patients presenting with acute CNS infections, known/suspected cases of CNS tuberculosis, hypoxic ischaemic encephalopathy, patients with history of head trauma and stroke within the past six months were excluded from the study. Patients with neurodegenerative diseases, psychiatric illness were excluded from the study.

Procedure

Magnetic resonance imaging examination was carried out with PHILIPS 1.5 TESLA ACHIEVA machine. MR imaging of the brain was done using Fast Spin Echo (FSE) T1 weighted imaging (T1WI), T2 weighted imaging (T2WI) and Fluid Attenuated Inversion Recovery (FLAIR) imaging sequences in axial, coronal and sagittal planes. CE T1WI in axial, coronal and sagittal planes were done using 0.1 mmol/kg body weight of Gadolinium based contrast agent. DWI was acquired with a single- shot echo planar spin-echo sequence in three orthogonal directions with a b value of 1000 sec/mm^3 and a baseline image with a b value of 0 sec/mm^3. Apparent Diffusion Coefficient (ADC) values were calculated by the software and ADC maps were generated. DWI was performed prior to administration of contrast with an identical slice thickness (5 mm) and position to T1WI, T2WI and T2/ FLAIR imaging.

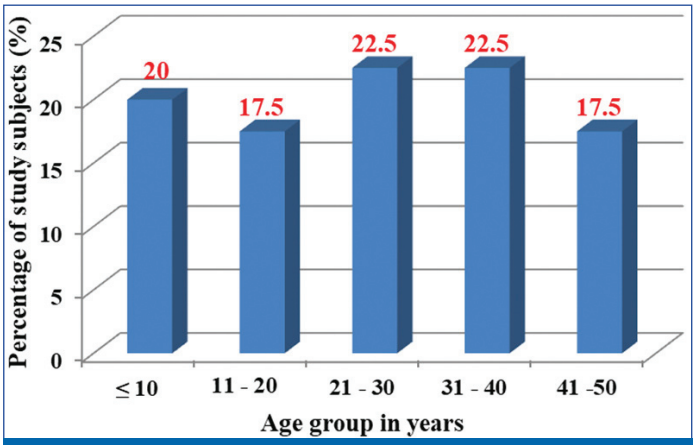
The demyelinating lesions were first labeled on T2WI and FLAIR with their sizes being no less than 3 mm for better delineation on CE T1WI and DWI. The number, distribution and morphology of demyelinating lesions on T2/FLAIR in the cortical gray matter, white matter, deep gray matter and brainstem were determined in each subject. On CE T1WI demyelinating lesions were labelled as either enhancing or non enhancing. On DWI and ADC maps, the signal intensity of the lesions was determined as either hyperintense or non hyperintense (isointense or hypointense) to the surrounding normally appearing white matter. The area of perilesional edema, if any was not evaluated.

STATISTICAL ANALYSIS

All the data were collected and entered into Microsoft Excel software. The categorical variables were presented in proportions (%) and continuous variables were presented as Mean±Standard deviation. Qualitative variables were assessed for significance using Fisher's-exact test and validity of the hyperintense signals and Diffusion Restriction (DR) on DWI was assessed with the contrast enhancement on gold standard technique of CE T1WI. Sensitivity, specificity, Negative Predictive Value (NPV), Positive Predictive Value (PPV) and accuracy were the validity measures which were assessed. The analysis was done using SPSS software version 18.0. A p-value of less than 0.05 was considered as statistically significant. Kappa statistics was used to assess the agreement between the hyperintense signals and DR on DWI with contrast enhancement on CE T1WI.

RESULTS

The mean age of the study subjects were 26.5±13.8 years. Most of the subjects were in the age group of 21 to 40 years (45%) with female preponderance (58%) [Table/Fig-1].



[Table/Fig-1]: Distribution of study subjects based on age.

Majority of the lesions in inflammatory demyelinating diseases were supratentorial but in neuromyelitis optica where only infratentorial lesion was noted in 50% (1/2) and in other 50% (1/2), no lesions could be visualised [Table/Fig-2].

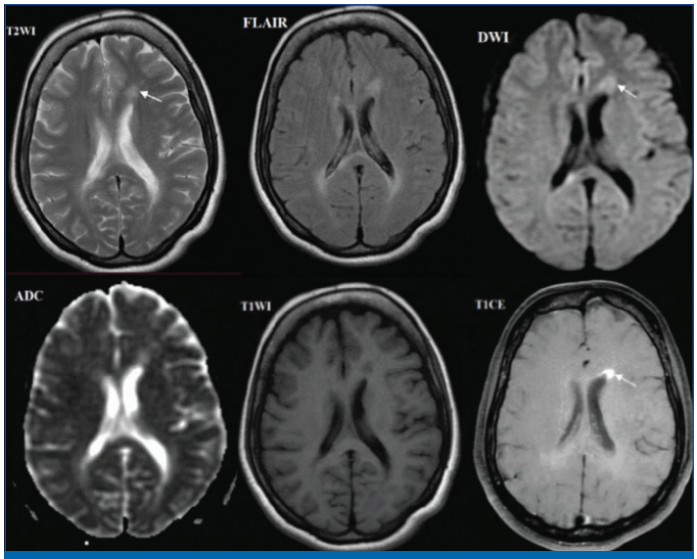
Location of lesions	MS¥ (n=386) n (%)	NMO¥ (n=1) n (%)	ADEM¥ (n=154) n (%)	Total (n=541) n (%)
Supratentorial	370 (95.9)	00 (0)	148 (96.1)	518 (95.7)
Infratentorial	16 (4.1)	01 (100)	06 (3.9)	23 (4.3)

[Table/Fig-2]: Location of lesions among the study subjects with inflammatory demyelinating diseases.
¥MS: Mutiple sclerosis; NMO: Neuromyelitis optica; ADEM: Acute disseminated encephalomyelitis

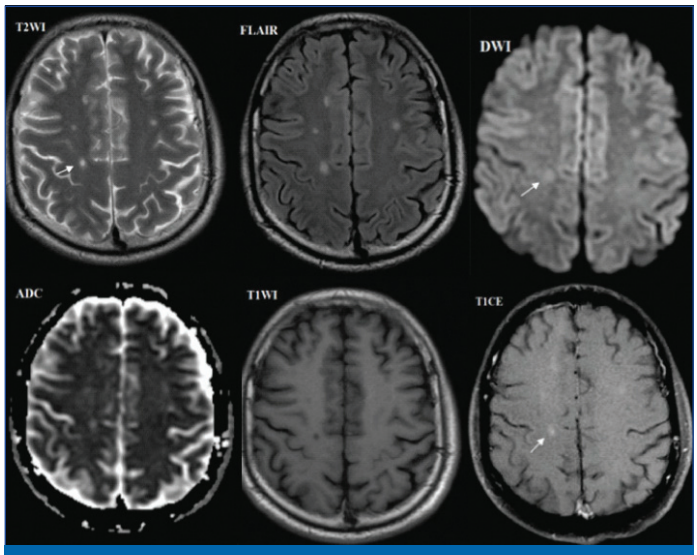
There were a total of 73 contrast enhancement lesions. Among 73 lesions, 100% of hyperintense lesions on DWI showed contrast enhancement overall in various inflammatory demyelinating diseases of brain [Table/Fig-3,4]. They showed significant moderate level of agreement [Table/Fig-5A]. However, no agreement was seen in case of diffusion restriction when compared to CE T1WI [Table/Fig-5B].

The hyperintense signals as shown by DWI were 100% sensitive in each demyelinating diseases of multiple sclerosis and acute disseminated encephalomyelitis. It indicates that the probability of the lesions showing hyperintense signals on DWI also showing contrast enhancement on CE T1WI is 100% indicating that hypointense signals rules out the demyelinating diseases. Negative predictive value of 100% also shows that, chances of non enhancing lesions also showing hypointense signals is 100% [Table/Fig-6A].

However the specificity of diffusion restrictions on DWI, shows that the probability of the restricted diffusion in those with enhancing lesions is 100%. Its positive predictive value also shows that all the study subjects who tests positive for restricted diffusion will have enhancing lesions in inflammatory demyelinating diseases [Table/Fig-6B,7].



[Table/Fig-3]: Case of multiple sclerosis with axial MR images showing T2/FLAIR hyperintense lesions in left periventricular white matter and splenium of corpus callosum with the lesion in left periventricular white matter showing increased diffusion and contrast enhancement (arrows).
T2WI: T2 weighted imaging; FLAIR: Fluid attenuated inversion recovery; DWI: Diifusion weighted imaging; ADC: Apparent diffusion coefficient; T1WI: T1 weighted imaging; T1CE: T1 contrast-enhanced



[Table/Fig-4]: Case of multiple sclerosis with axial MR images showing multifocal ovoid T2/FLAIR hyperintense lesions in bilateral corona radiata showing increased diffusion and contrast enhancement (arrows).
T2WI: T2 weighted imaging; FLAIR: Fluid attenuated inversion recovery; DWI: Diifusion weighted imaging; ADC: Apparent diffusion coefficient; T1WI: T1 weighted imaging; T1CE: T1 contrast-enhanced

Hyperintense on DWI	Enhancing lesions on CE T1W1		Kappa
	Present	Absent	
Multiple sclerosis (n=51)			
Yes	38 (100)	05 (38.5)	0.62 (0.003)*
No	00 (0)	08 (61.5)	
Acute disseminated encephalomyelitis (n=22)			
Yes	12 (100)	4 (40)	0.71 (<0.001)*
No	0 (0)	6 (60)	
Overall (n=73)			
Yes	50 (100)	09 (39.1)	0.68 (<0.001)*
No	00 (0)	14 (60.9)	

[Table/Fig-5A]: Agreement for hyperintensity on DWI with enhancement on CE T1W1.
*indicates statistical significance at p<0.05 on applying Kappa statistics; DWI: Diffusion weighted imaging; CE T1WI: Contrast-enhanced T1 weighted imaging

DISCUSSION

Focal demyelinating lesions can be picked up easily by the conventional MRI images but they lack histopathological specificity,

Diffusion restriction on DWI	Enhancing lesions on CE T1W1		Kappa
	Present n (%)	Absent n (%)	
Multiple sclerosis (n=51)			
Yes	04 (10.5)	00 (0)	0.06 (0.56)
No	34 (89.5)	13 (100)	
Acute disseminated encephalomyelitis (n=22)			
Yes	02 (16.7)	00 (0)	0.15 (0.48)
No	10 (83.3)	10 (100)	
Overall (n=73)			
Yes	06 (12)	00 (0)	0.08 (0.16)
No	44 (88)	23 (100)	

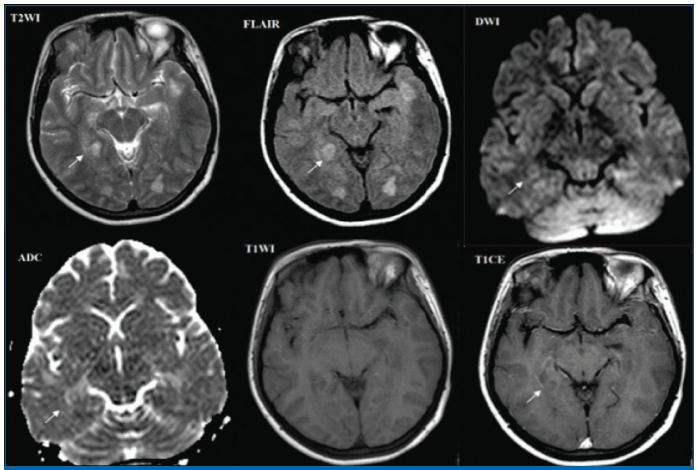
[Table/Fig-5B]: Agreement for diffusion restriction on DWI with enhancement on CE T1W1.
DWI: Diffusion weighted imaging; CE T1WI: Contrast-enhanced T1 weighted imaging

Variables	CE T1WI vs hyperintense lesions-DWI§		
	Multiple sclerosis	Acute disseminated encephalomyelitis	Overall
Sensitivity	100% (90.8% to 100%)	100% (73.5% to 100%)	100% (92.9% to 100%)
Specificity	61.5% (31.6% to 86.1%)	60% (26.2% to 87.8%)	60.9 % (38.5% to 80.3%)
Positive predictive value	88.4% (79.3% to 93.8%)	75% (58.4% to 86.5%)	84.7% (76.9% to 90.2%)
Negative predictive value	100% -	100% -	100% -
Accuracy	90.2% (78.6% to 96.7%)	81.8% (59.7% to 94.8%)	87.7% (77.9% to 94.2%)

[Table/Fig-6A]: Validity of hyperintense lesions on DWI with enhancement on CE T1W1.
CE T1WI: Contrast-enhanced T1 weighted imaging; DWI: Diffusion weighted imaging; §The values in the parenthesis indicates 95% ;CI: Confidence interval

Variables	CET1WI vs DR-DWI§		
	Multiple sclerosis	Acute disseminated encephalomyelitis	Overall
Sensitivity	10.5% (2.9% to 24.8%)	16.7% (2.1% to 48.4%)	12% (4.5% to 24.3%)
Specificity	100% (75.3% to 100%)	100% (69.2% to 100%)	100% (85.2% to 100%)
Positive predictive value	100% -	100% -	100% -
Negative predictive value	27.7% (25.5% to 29.9%)	50% (43.7% to 56.3%)	34.3% (32.1% to 36.7%)
Accuracy	33.3% (20.8% to 47.9%)	54.5% (32.2% to 75.6%)	39.7% (28.5% to 51.9%)

[Table/Fig-6B]: Validity of Diffusion restriction on DWI with enhancement on CE T1W1.
CE T1WI: Contrast-enhanced T1 weighted imaging; DR: Diffusion restriction; DWI: Diffusion weighted imaging; §The values in the parenthesis indicates 95%; CI:Confidence Interval



[Table/Fig-7]: Case of ADEM with axial MR images showing T2/FLAIR hyperintense lesion in right medial temporal lobe showing peripheral diffusion restriction and subtle peripheral contrast enhancement (arrows).
T2WI: T2 weighted imaging; FLAIR: Fluid attenuated inversion recovery; DWI: Diifusion weighted imaging; ADC: Apparent diffusion coefficient; T1WI: T1 weighted imaging; T1CE: T1 contrast-enhanced

like inflammation, edema, axonal loss and gliosis, which are areas of high signal intensity. Such associations of the pathologic substrate and clinical status of the patients can be determined using DWI [13]. Though Contrast-Enhanced MRI (CE-MRI) has been the imaging modality of choice for MS, acquiring multiple scans with gadolinium-based contrast agents in its due course of the disease is not a preferred choice. Hence utilisation of DWI in comparison to contrast enhanced imaging has been considered recently and this study was conducted.

Overall, there were 51 lesions of multiple sclerosis, 22 lesions of acute disseminated encephalomyelitis and only two lesions of neuromyelitis optica as detected by the contrast enhanced imaging. As there were very less lesions of neuromyelitis optica, authors have omitted that demyelinating disease in eliciting the validity of the DWI versus contrast enhanced imaging.

Papais-Alvarenga RM et al., noted the mean age at disease onset as 32.7 years. Females formed the majority in their study similar to the present study; however, the mean age was slightly lesser in this study with mean being 26.5 years and this difference in the age might be due to different study settings [14].

Wang KY et al., have described that periependymal dorsal brainstem lesions and cerebellar lesions which are adjacent to the fourth ventricle, mainly in the region of the area postrema within dorsal medulla are most precise imaging findings for NMOSD in the brain. Moreover, they have said that cortical lesions are less likely in MS [15]. Similarly in this study NMO lesions were found infratentorially in the brainstem. Huang Y et al., have considered those having NMO with no brain abnormalities as one of the study groups to assess which brain region was associated with higher relapse number. Similarly, in this current study, few subjects who were suspected of NMO had no brain lesions [16].

Inflammatory demyelinating diseases are mostly detected as a T1 hyperintense signal change on contrast. 100% of hyperintense lesions in this study showed contrast enhancement overall in demyelinating lesions and even in multiple sclerosis and acute disseminated encephalomyelitis separately. They showed significant moderate level of agreement. Similarly Lo CP et al., found all of the enhancing lesions to be hyperintense on DWI [17].

Lo CP et. al., also showed that hyperintensity on DWI was significantly linked to contrast enhancement on CE T1WI. The validity measures viz., sensitivity, specificity, PPV, NPV and accuracy for DWI to predict the occurrence of enhancement of the demyelinating lesions on CE T1WI were noted to be 100%, 67.9%, 32.3%, 100%, and 72.1%, respectively [17], which were almost similar to this current study noted as 100%, 60.9%, 84.7%, 100% and 87.7% [Table/Fig-8]. However the proportions are almost similar or higher in this study and that might be due to the difference in the distribution of type of lesions in their study. Authors have also found hyperintense signals by DWI to be 100% sensitive in each demyelinating diseases of multiple sclerosis and acute disseminated encephalomyelitis. 100% sensitivity indicates that hypointense signals rules out the demyelinating diseases and 100% negative predictive value shows that, chances of non-enhancing lesions also showing hypointense signals as 100%. The use of T1 enhanced sequences along with the injection of contrast allows selective identification of inflammatory lesions activity recognised based on their enhancement and they appear as an early event and are consistent with lesions of MS [18]. Meftahi GH et al., reported sensitivity and specificity of 86% and 62.5% respectively in detecting active plaques in MS [19]. Similarly in the present study the sensitivity and specificity were 100% and 61.5% respectively and the values were almost in line with study by Meftahi GH et al., [Table/Fig-8].

According to Arashloo FT et al., sensitivity, specificity, PPV, NPV and accuracy of DWI signal intensity in enhancing plaques of multiple sclerosis were 69%, 67%, 79%, 55% and 68% respectively [20]. Whereas in the present study, values were recorded to be 100%, 61.5%, 88.4%, 100% and 90.2% respectively however the values in this study were higher except for the specificity which was slightly less in this study [Table/Fig-8].

Various studies	Validity measures of DWI to predict the occurrence of enhancement of demyelinating lesions on CE T1WI				
	Sensitivity	Specificity	PPV	NPV	Accuracy
Present study (for all demyelinating lesions)	100%	60.9%	84.7%	100%	87.7%
Lo CP et al., [17] (for all demyelinating lesions)	100%	67.9%	32.3%	100%	72.1%
Our study (for multiple sclerosis)	100%	61.5%	88.4%	100%	90.2%
Meftahi GH et al., [19] (for multiple sclerosis)	86%	62.5%	-	-	-
Arashloo FT et al., [20] (for multiple sclerosis)	69%	67%	79%	55%	68%

[Table/Fig-8]: Diagnostic accuracy values of DWI to predict the occurrence of enhancement of demyelinating lesions on CE T1WI as reported in previous studies v/s present study [17,19,20].
DWI: Diffusion weighted imaging; CET1WU: Contrast-enhanced T1 weighted imaging; PPV: Positive predictive value; NPV: Negative predictive value

Abou Zeid N et al., found ring enhancing lesions and peripheral diffusion restriction to be more common in the inflammatory demyelinating diseases compared to tumors or abscesses [21]. In the current study, the specificity of diffusion restrictions on DWI was 100%. which shows that the probability of the restricted diffusion in those with enhancing lesions of inflammatory demyelinating diseases was 100% Its positive predictive value also shows that all the study subjects who tests positive for restricted diffusion will have enhancing lesions in demyelinating inflammatory diseases. In literature, glutamate mediated excitotoxicity has been explained as the pathophysiological basis for the restricted diffusion in acute demyelinating lesions and involved mechanism have been considered to be the induction of cytotoxic edema for many neurological conditions like diffuse axonal injury, wallerian degeneration and ischaemic stroke. It is similarly doubted if the diffusion restriction is a part of an inflammatory infiltrate or cytotoxic edema because of similarities in the imaging appearances of lesions in fulminant demyelinating processes [21,22]. However, no agreement was seen in case of diffusion restriction when compared to CE T1WI in the present study and that might be due to the fact that all contrast enhanced lesions might not show restricted diffusion as the ones in the acute phase only might show restricted diffusion on DWI. Hence in DWI, the hyperintense lesions can be considered as a better screening indicator and diffusion restriction can be considered as a diagnostic indicator.

Limitation(s)

The lesions of spinal cord could not be studied due to operational feasibility. Non significant agreement for diffusion restriction may possibly be due to low sample size. Additionally time interval between the onset of symptoms and acquisition of MRI varied among subjects and this might have influenced the results.

Inclusion of MR imaging of the spine in future studies for evaluation of inflammatory demyelinating diseases is recommended to facilitate better understanding, identification and differentiation of various inflammatory demyelinating diseases. Previous studies have shown better diagnostic performance for demonstration of simultaneous presence of both gadolinium enhancing and non enhancing lesions in multiple sclerosis when MRI of brain was obtained within first 30 days of symptom onset [23,24]. Hence authors recommend similar study in a larger setting and recruiting patients with recent onset of symptoms. Further studies with dedicated imaging of optic nerves and spinal cord in patients of NMO with larger sample size are required for adequate characterisation of lesions.

CONCLUSION(S)

All the enhancing lesions of demyelinating lesions on CE T1WI showed hyperintense signals on DWI. With the sensitivity and NPV of signal intensity status in DWI being 100% and the relatively low PPV shows that DWI may not replace CE T1WI imaging but may serve as a screening MRI sequence where the use of gadolinium based contrast agents is a concern. The specificity and PPV of diffusion restriction being 100% and considering the biological plausibility, it can be considered as a diagnostic indicator importantly during the active phase of demyelinating processes.

REFERENCES

[1] Rao TMV, Prasad UG. Clinical profile of 50 adults with demyelinating diseases of central nervous system-A prospective observational study. IAIM. 2016;3(11):143-50.
[2] Koudriavtseva T, Renna R, Plantone D, Caterina Mainero. Demyelinating and thrombotic diseases of the central nervous system: Common pathogenic and triggering factors. Front Neurol. 2015;6:63.
[3] Pandit L, Mustafa S. Epidemiology and clinical features of demyelinating disorders in India. Neurol Clin Neurosc. 2021;9(4):266-73.
[4] Hemond CC, Bakshi R. Magnetic resonance imaging in multiple sclerosis. Cold Spring Harb Perspect Med. 2018;8(5):a028969.
[5] Rovira À, Wattjes MP, Tintoré M, Carmen Tur, Tarek A Yousry, Maria PS, et al. MAGNIMS consensus guidelines on the use of MRI in multiple sclerosis-clinical implementation in the diagnostic process. Nat Rev Neurol 2015;11(8):471-82.
[6] Wildner P, Stasiołek M, Matysiak M. Differential diagnosis of multiple sclerosis and other inflammatory CNS diseases. Mult Scler Relat Disord. 2020;37:101452.
[7] Larassati H, Estiasari R, Yunus RE, Parizel PM. State-of-the-art review: Demyelinating diseases in Indonesia. Multiple Sclerosis International 2021;2021:1278503.
[8] Michoux N, Guillet A, Rommel D, Mazzamuto G, Sindic C, Duprez T. Texture analysis of T2-weighted MR images to assess acute inflammation in brain MS lesions. PLoS One. 2015;10(12):e0145497.
[9] Chien CC, Wang HY, Wang JJ, Kan WC, Chien TW, Lin CY, et al. Risk of acute kidney injury after exposure to gadolinium-based contrast in patients with renal impairment. Ren Fail. 2011;33(8):758-64.
[10] Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Annals of Neurology. 2011;69(2):292-302.
[11] Hara T. [Acute disseminated encephalomyelitis (ADEM): Its diagnostic criteria and therapy]. Nihon rinsho. Japanese Journal of Clinical Medicine. 2013;71(5):887-92. PMID: 23777100.
[12] Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015;85(2):177-89.
[13] Rueda-Lopes FC, da Cruz LCH, Doring TM, Emerson L Gasparetto. Diffusion-weighted imaging and demyelinating diseases: New aspects of an old advanced sequence. Am J Roentgenol. 2014;202(1):W34-42.
[14] Papais-Alvarenga RM, Vasconcelos CCF, Carra A, Ibis Soto de Castillo, Sara Florentin, Fernando Hamuy Diaz de Bedoya, et al. Central nervous system idiopathic inflammatory demyelinating disorders in South Americans: A descriptive, multicenter, cross-sectional study. PLoS One, 2015;10(7):e0127757.
[15] Wang KY, Chetta J, Bains P, Balzer A, Lincoln J, Uribe T, et al. Spectrum of MRI brain lesion patterns in neuromyelitis optica spectrum disorder: A pictorial review. Br J Radiol. 2018;91(1086):20170690.
[16] Huang Y, Zhang L, Lin Y, Wang Y, Zhang B, Men X, et al. Clinical outcomes of neuromyelitis optica with brain magnetic resonance imaging abnormalities. Journal of Neurology, Neurological Science and Disorders. 2015;1(1):10-14.
[17] Lo CP, Kao HW, Chen SY, Chu CM, Hsu CC, Chen YC, et al. Comparison of diffusion-weighted imaging and contrast-enhanced T1-weighted imaging on a single baseline MRI for demonstrating dissemination in time in multiple sclerosis. BMC Neurol. 2014;14(1):01-07.
[18] Rovira A, Tintoré M, Alvarez-Cermeño JC, Izquierdo G, Prieto JM. Recommendations for using and interpreting magnetic resonance imaging in multiple sclerosis. Neurología. 2010;25(4):248-65.
[19] Meftahi GH, Pirzad Jahromi G, Azari A, Ghaemmaghami P. Detection of active plaques in multiple sclerosis using 3 and 12 directional diffusion-weighted imaging: Comparison with gadolinium-enhanced MR imaging. Journal of Biomedical Physics & Engineering. 2020;10(6):737-44.
[20] Arashloo FT, Hanzaei FF, Sedighi B, Amjad G, Younesi L. Efficacy of diffusion-weighted imaging in symptomatic and asymptomatic multiple sclerotic plaques. J Family Med Prim Care. 2019;8(7):2409-13.
[21] Abou Zeid N, Pirko I, Erickson B, Weigand SD, Thomsen KM, Scheithauer B, et al. Diffusion-weighted imaging characteristics of biopsy-proven demyelinating brain lesions. Neurology. 2012;78(21):1655-62.
[22] Balashov KE, Lindzen E. Acute demyelinating lesions with restricted diffusion in multiple sclerosis. Mult Scler. 2012;18(12):1745-53.
[23] Rovira À, Swanton J, Tintoré M, Huerga E, Barkhof F, Filippi M, et al. A single, early magnetic resonance imaging study in the diagnosis of multiple sclerosis. Archives of Neurology. 2009;66(5):587-92.
[24] Tur C, Tintoré M, Rovira A, Nos C, Río J, Téllez N, et al. Very early scans for demonstrating dissemination in time in multiple sclerosis. Mult Scler. 2008;14(5):631-35.

PARTICULARS OF CONTRIBUTORS:
1. Consultant Radiologist, Department of Radiology, Gopala Gowda Shantaveri Memorial Hospital, Mysore, Karnataka, India.
2. Consultant and Associate Professor, Department of Radiology, Vardhaman Mahavir Medical College and Safdarjung Hospital, New Delhi, India.
3. Associate Professor, Department of Radiology, Adichunchungiri Institute of Medical Sciences, Mandya, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Mohan Kumar,
S4, Second Floor, Malu Apartment, Industrial Area, Jewargi Cross,
Gulbarga, Karnataka, India.
E-mail: mohankumar235@gmail.com

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