

Role of Diffusion Weighted MRI in Differential Diagnosis of Non-Infarct Brain Pathologies

Kavita U. Vaishnav¹, Zaryab M. Qureshi²

¹Associate Professor, ²Third Year Resident Doctor, Department of Radiology, AMC MET Medical College and L.G. Hospital, Ahmedabad-380008, India

Corresponding author: Dr. Kavita U. Vaishnav, Associate Professor, Department of Radiology, AMC MET Medical College and L.G. Hospital, Ahmedabad-380008, India

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ABSTRACT

Introduction: Diffusion weighted imaging (DWI) has a wide range of applications in the evaluation of intracranial pathological conditions. It provides a specific diagnosis in few situations, and adds to the information provided by conventional sequence in many others. This study was conducted to evaluate role of DWI in differentiating non-infarct pathologies of the brain which shows restriction of diffusion such as infectious, neoplastic and demyelinating diseases, encephalopathies, leukodystrophies, vasculitis and vasculopathies, haemorrhage and trauma.

Material and Methods: The present study was conducted in department of Radiology at AMC MET Medical College and L.G.Hospital. Participants after understanding the study protocol and procedure were asked to give their written consent for the study.

Results: In this study, only 32.7% infective lesions showed bright signals on diffusion weighted sequences, however, it was 100% sensitive for cerebral abscesses. 41% metabolic lesions showed bright signal on DWI, among which the most common posterior reversible encephalopathy syndrome showed 64.4% sensitivity. 74.2% epidermoid cysts showed bright signals on DWI. Only 4.8% brain tumours appear bright on DWI sequences, although sensitivity for detection of lymphoma was found to be 50%. Only about 2.6 % granulomatous lesions appeared bright on diffusion weighted images.

Conclusion: DW MRI helps in differentiating and characterizing non infarct intracranial lesions.

Keywords: DWI, ADC (Apparent Diffusion Coefficient)

INTRODUCTION

Diffusion weighted imaging (DWI) is based on the sensitivity of MR to microscopic mobility of water molecules within tissues. It consists of a DW image, also called the diffusion trace, and an apparent diffusion coefficient (ADC) map. In tissues, DWI probes the movement of water molecules, which occurs largely in the extracellular space. However, the movement of water molecules in the extracellular space is not entirely free, but is modified by interactions with hydrophobic cellular membranes and macromolecules. Hence, diffusion in biological tissue is often referred to as "apparent diffusion". The net displacement of molecules diffusing across an area of tissue per second is called the apparent diffusion coefficient (ADC). In areas of restricted diffusion, the ADC is low, whereas in areas of free diffusion it is high. ADC is a value that describes microscopic water diffusibility in the presence of factors that restrict diffusion within tissues. Brain tissues with low ADC appears relatively hypointense, whereas regions with higher ADC values appears hyperintense.

Diffusion tensor imaging (DTI) is not the most scope of this paper, is an extension of DWI that gives additional information

about brain tissue structure by measuring functional anisotropy, or the directional component of water diffusion. DTI has recently been used in demyelinating diseases, white matter injury and also in some cases of neoplasms. Lesions with long T2 relaxation times have artifactual high signal because of the heavily T2 weighting of the DW image, called the T2 shine-through effect, mimicking restricted diffusion. This artifact could also be overcome by means of upper b values or by the ADC map which does not have shine-through effect.⁵

MATERIAL AND METHODS

The study was conducted in the department of radiodiagnosis of AMC MET Medical college and L.G. Hospital, Ahmedabad. The study was carried out prospectively on all patients referred to the department of radiology for MRI brain study excluding those patients with MRI findings suggestive of infarcts from a period of April 2020 to July 2021. All MRI studies were done on Siemens Magnetom Essenza 1.5 T MRI and high resolution T1 and T2 weighted images, FLAIR, diffusion weighted and susceptibility weighted images were acquired.

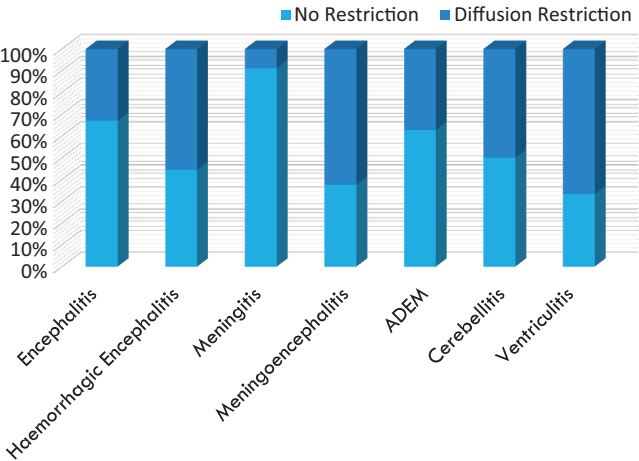


Figure-1: Inflammations

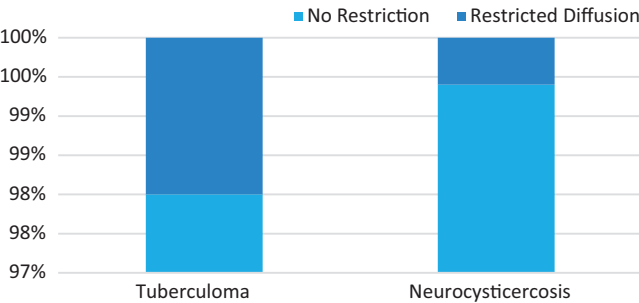


Figure-2: Granulomatous Inflammations

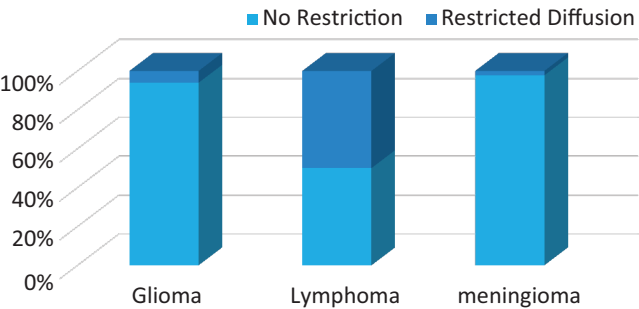


Figure-3: Tumours

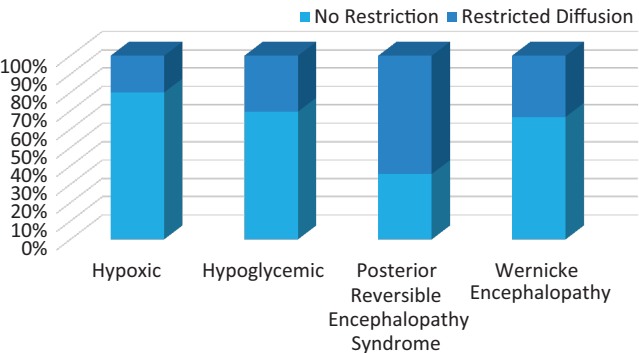


Figure-4: Encephalopathy

Inclusion criteria

All patients with diffusion weighted magnetic resonance imaging reference for hypoxic ischemic injury, infective condition, tumors, demyelination, metabolic & toxic insults to brain. Degenerative disorder irrespective of age and sex were included in the study.

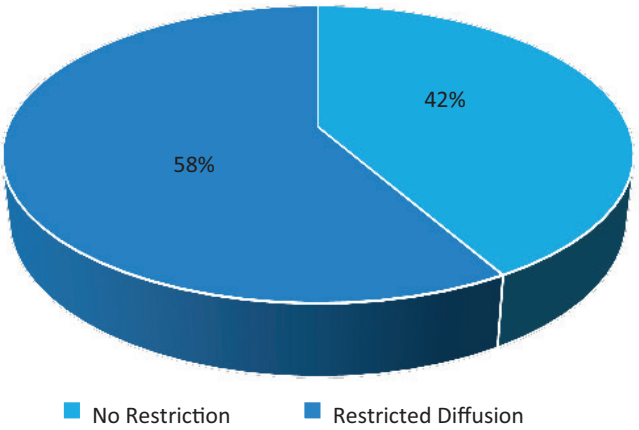


Figure-5: Osmotic Demyelination

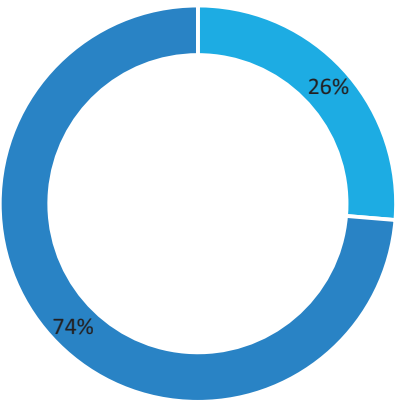


Figure-6: Epilepsy

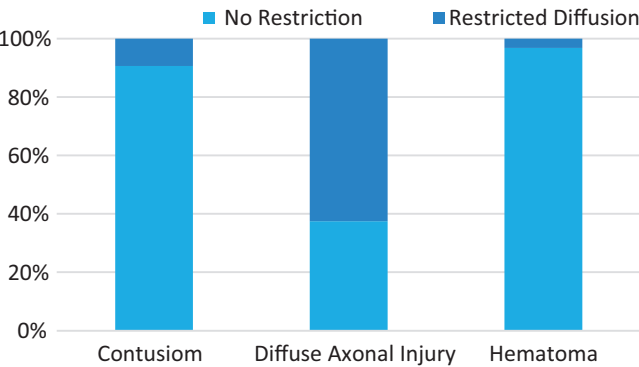


Figure-7: Trauma

Exclusion criteria

- Patients with infarct lesions in brain
- Patient who have aneurysmal clip in their brain
- Patient with claustrophobia
- Patient having orthopedic implant

Patients underwent the examination after the contraindications for MRI were excluded and consent was taken. All the MRI scans in this study were performed using 1.5T MRI scanner.

MRI Protocol consisted of the following

- A head coil was used
- Axial diffusion weighted images of the brain
- Sagittal T1W images of the brain

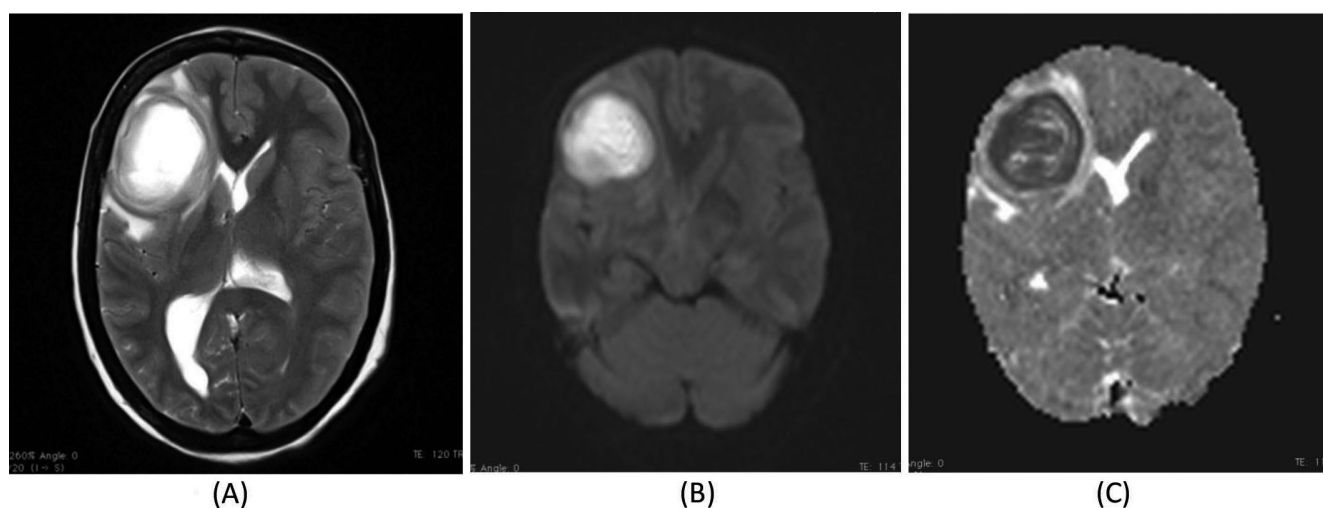


Figure-1: Axial T2W image of right frontal lobe abscess appearing hyperintense with hypointense rim and extensive perilesional edema (A), appearing bright on DWI (B), dark on ADC (C).

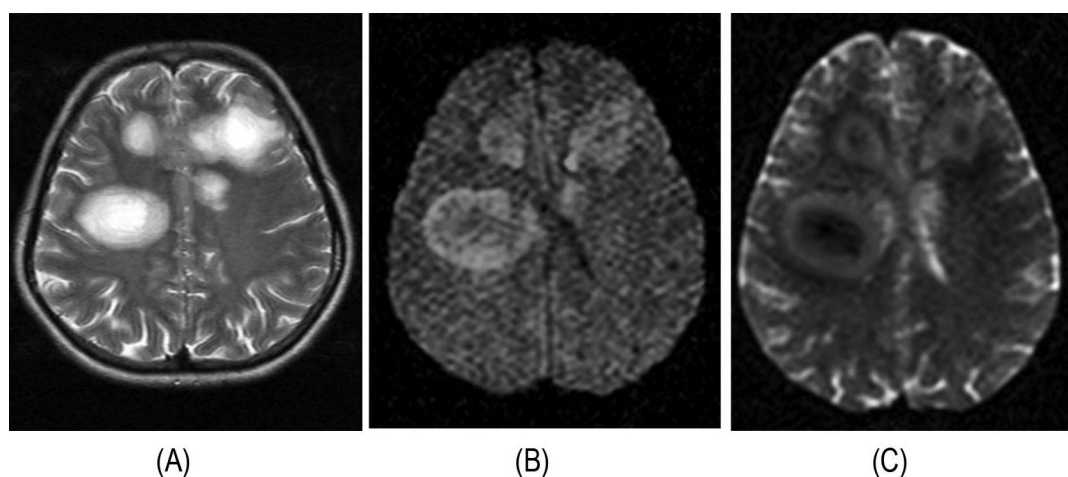


Figure-2: Axial T2W of acute disseminated encephalomyelitis appearing as multiple hyperintense lesions in left frontal and right fronto-parietal areas (A), bright on DWI (B) and dark on ADC (C).

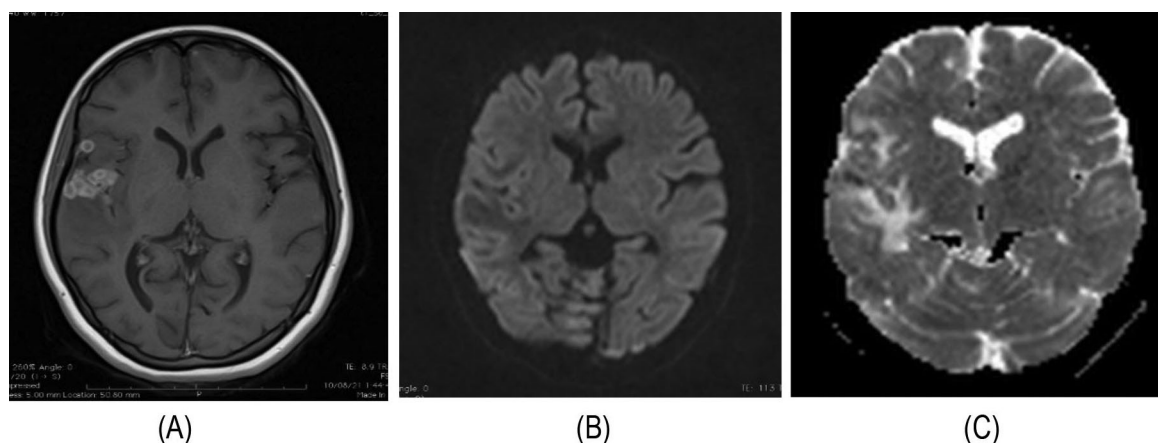


Figure-3: Axial T1W post contrast image of tuberculoma showing ring enhancement (A) and dark on DWI image (B), bright on ADC (C).

- Axial T2W FLAIR images of the brain
- ADC images were reconstructed from the diffusion weighted images.

All patients clinically suspected of intracerebral hemorrhage, intracranial tumours, extra axial masses, cerebral abscesses

and encephalitis, demyelination, sustained seizure activity, metabolic or toxic insults to the brain and leukodystrophy were included in this study. Patient was placed in supine position and brain coil was used. MRI features of lesion detected were studied- site (intra or extra axial) margins,

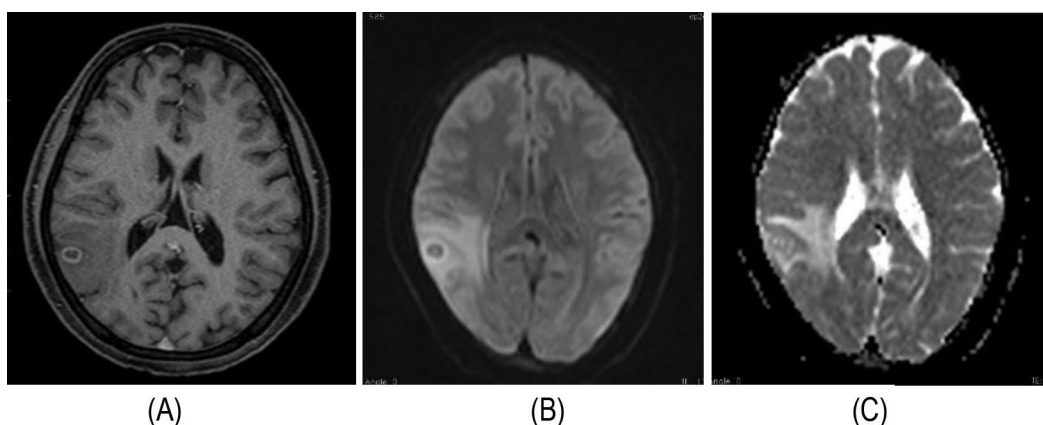


Figure-4: Axial post contrast T1W image of neurocysticercosis showing peripherally enhancing nodular lesion in right parietal region (A), on DWI (B) and on ADC (C).

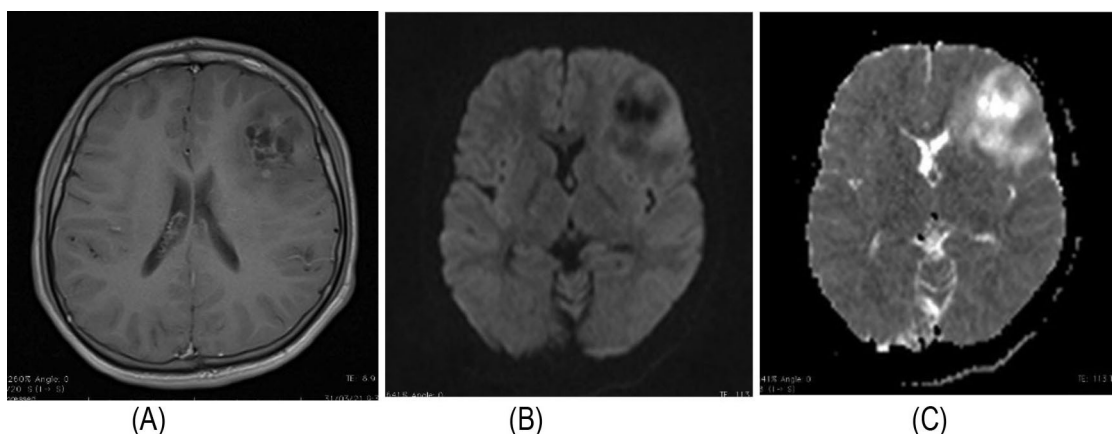


Figure-5: Axial post contrast T1W image of low-grade glioma which appears as heterogeneously mildly enhancing altered signal intensity lesion in left frontal region (A), dark on DWI (B) and bright on ADC (C)

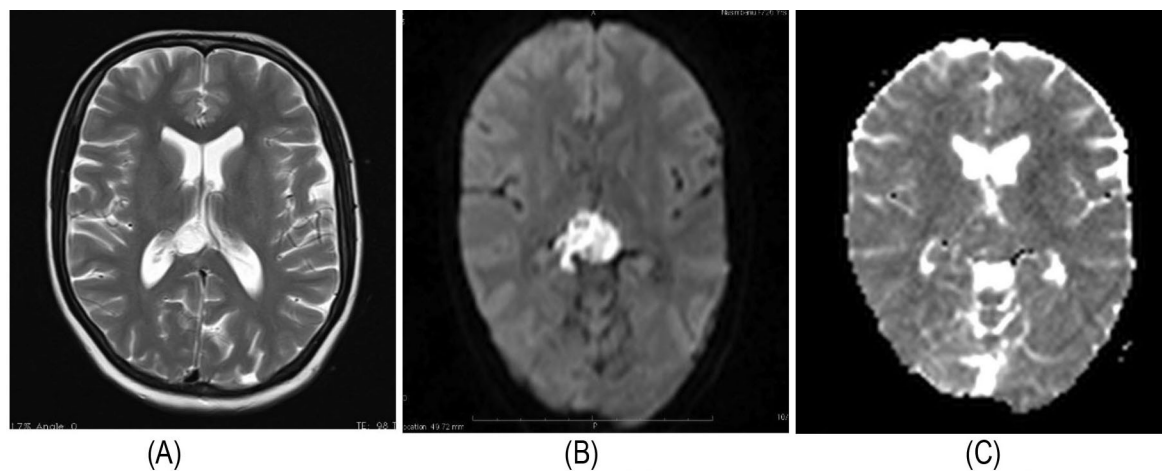


Figure-6: Axial T2W image of epidermoid cyst in right ambient cistern which is isointense to CSF on T2W image (A), showing bright on DWI (B) and dark on ADC (C).

perilesional edema, appearance on DWI and ADC T1W1, T2W1, FLAIR images, presence of calcification or hemorrhage, any enhancement in contrast study. Non-ionic intravenous contrast gadopentetate dimeglumine was administered in patients with normal renal function tests wherever necessary. The recommended dosage of gadopentetate dimeglumine injection is 0.2 mL/kg (0.1 mmol/kg) administered intravenously. Though in general

protocol, all required sequences were taken.

RESULTS

In this study, inflammatory conditions were 73 cases of encephalitis (38.2%), 9 cases of hemorrhagic encephalitis (4.7%), 57 cases of meningitis (29.8%), 8 cases of meningoencephalitis (4.1%), 35 cases of ADEM (18.3%), 6 cases of Cerebellitis (3.1%) & 3 cases of ventriculitis (1.5%).

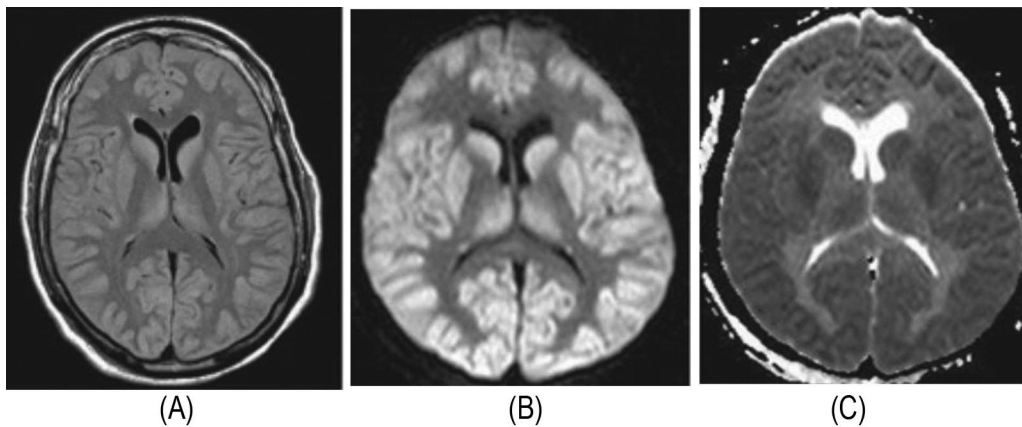


Figure-7: Axial FLAIR image of perinatal hypoxic ischemic encephalopathy showing hyperintensity in bilateral basal ganglia and thalami (A), bright on DWI (B) and dark on ADC (C).

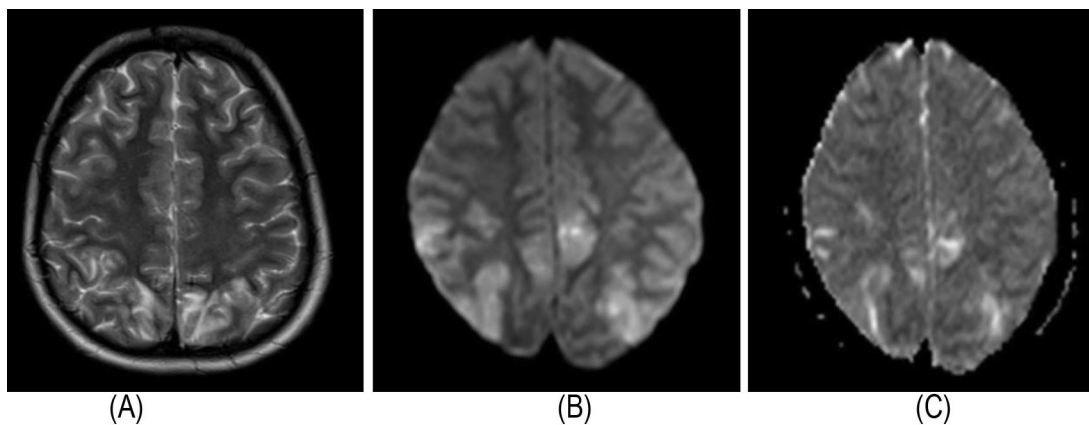


Figure-8: Axial T2W image of posterior reversible encephalopathy syndrome showing hyperintensity on T2W image in bilateral parieto-occipital region (A), showing bright signal on DWI (B) & on ADC (C)

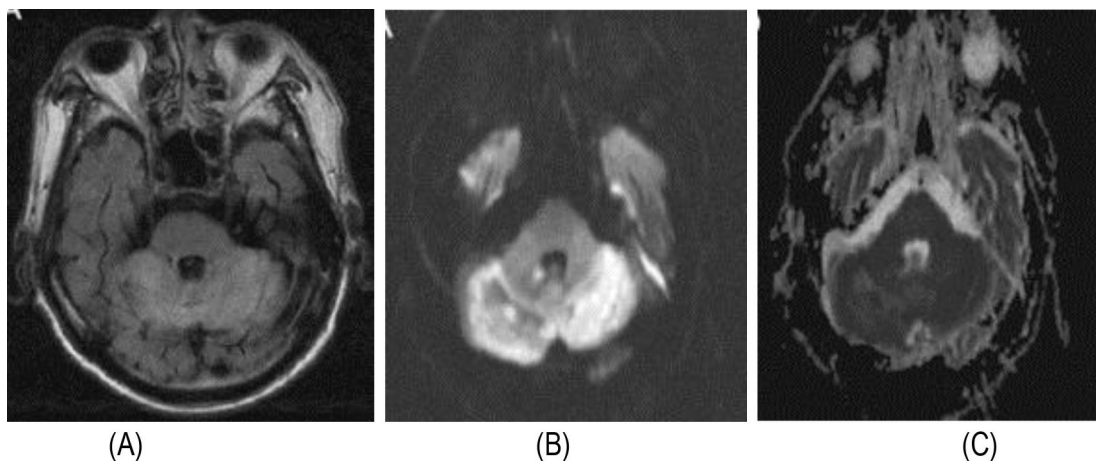


Figure-9: Axial FLAIR image of Wernicke's encephalopathy showing hyperintensity in bilateral cerebellar hemisphere (A), hyperintense on DWI image (B) and hypointense on ADC (C).

Out of these 29.8% cases showed diffusion restriction. All cases of cerebral abscesses show diffusion restriction showing 100% sensitivity of DWI. In case of granulomatous inflammations consisting of 11 cases of tuberculoma (50%) and 11 cases of neurocysticercosis (50%) only 2.6% of the cases show diffusion restriction (fig-1).

In tumors cases include glioma 33 (26.4%), lymphoma 4 (3.2%) & meningioma 88 (70.4%). Out of these Only 4.8% brain tumours appear bright on DWI sequences, although

sensitivity for detection of lymphoma was found to be 50%. 74.2% epidermoid cysts showed bright signals on DWI (fig-2,3).

Metabolic lesions include hypoxic encephalopathy 75 (46.8%), hypoglycemic encephalopathy 23 (14.3%), PRES 59 (36.8%) & wernicke's encephalopathy 3 (1.8%) (fig-3).

In case of demyelinating diseases, osmotic demyelination 7 (58.3%) out of 12 cases show diffusion restriction (fig-4).

In epileptic patients, 28 (73.6%) out of 38 cases show

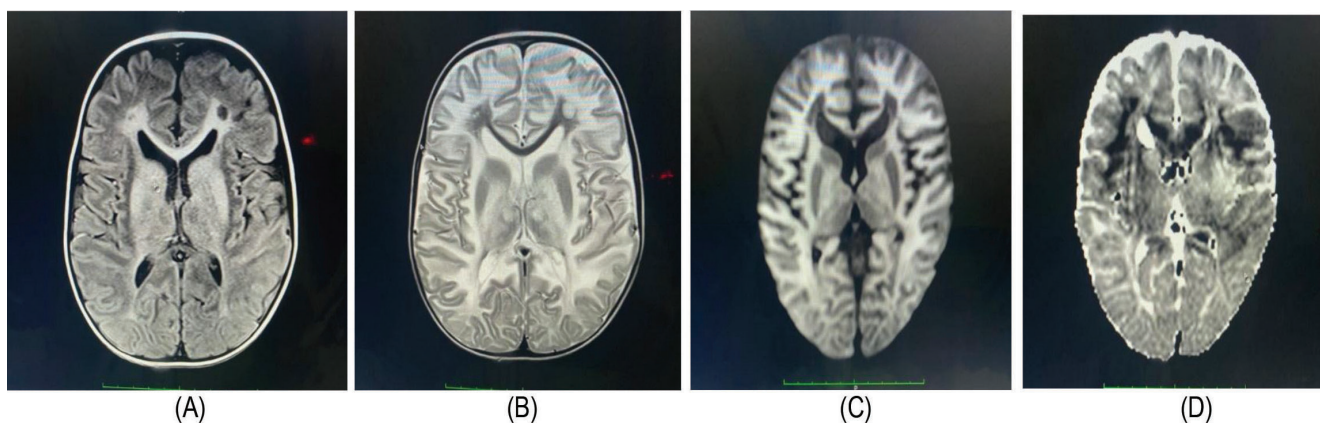


Figure-10: Axial T1W image of Canavan's disease showing hyperintensity involving peri-ventricular & subcortical white matter, thalami & capsular regions on (A), T2W (B) and showing diffusion restriction on DWI (C), low signal on ADC (D).

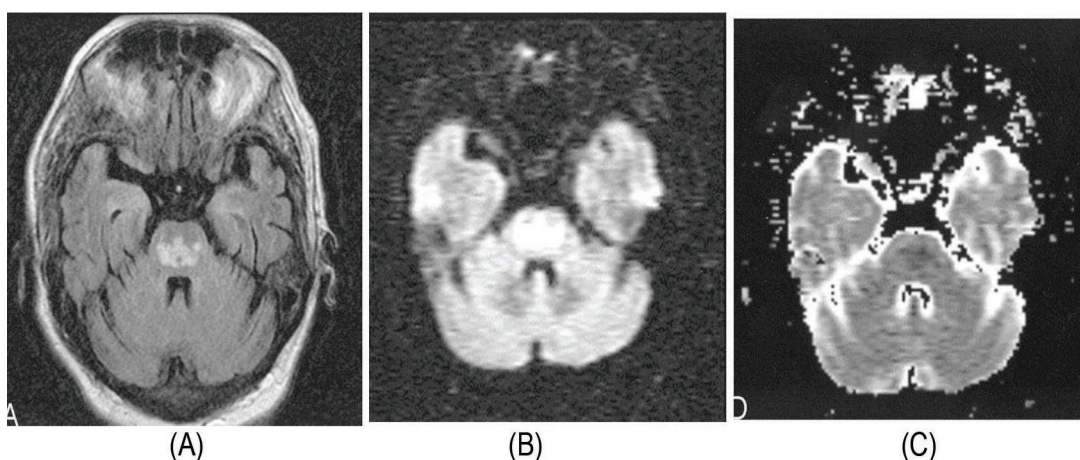


Figure-11: Axial FLAIR image of osmotic myelinosis showing pontine hyperintensity (A), hyperintense on DWI image (B) and hypointense on ADC (C)

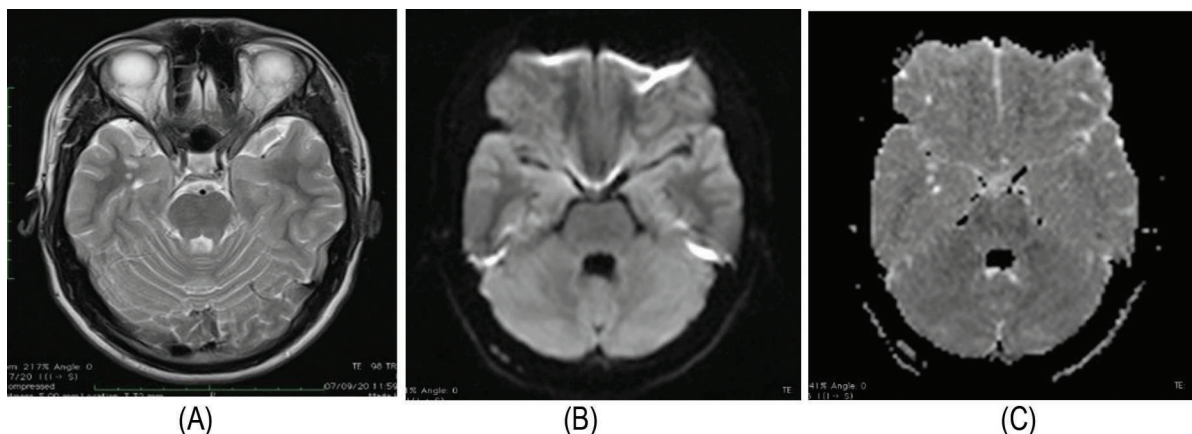


Figure-12: Axial T2W image of epilepsy showing hyperintensity in right medial temporal (A), DWI image (B) & On ADC (C)

diffusion restriction (fig-5).

In cases of trauma, contusion comprises of 32 (23.8%), diffuse axonal injury 8 (5.9%) and hematoma 94 (70.1%). Out of these only 8.2 % of cases show diffusion restriction (fig-6,7).

DISCUSSION

Diffusion weighted imaging (DWI) features a broad selection of applications within the evaluation of intracranial pathological conditions. It provides a selected diagnosis

in few situations, and adds to the knowledge provided by conventional sequence in many others.

Tissue characterization becomes possible by comparing the differences in apparent diffusion between tissues. For example, a tumor exhibits more restricted apparent diffusion as compared to a cyst because intact cellular membranes in a tumor would hinder the free movement of water molecules. As DWI is most often used to identify acute arterial ischemia, processes that interfere with or restrict

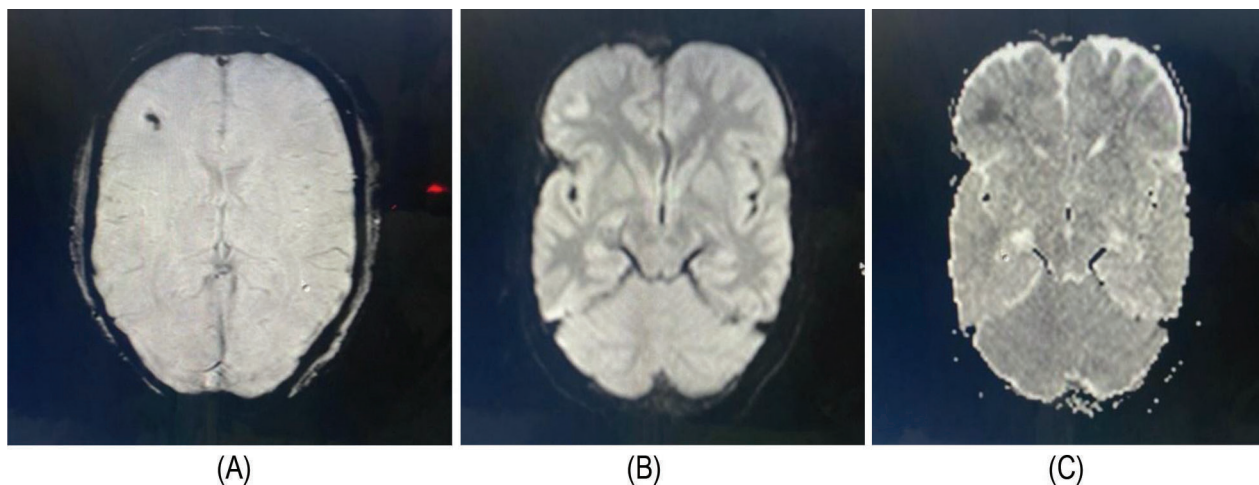


Figure-13: Axial SWI image of haemorrhage in right frontal region showing hypointensity (A), bright on DWI image (B) and dark on ADC image (C).

the movement of water can cause notable changes on DWI, including neoplastic lesions, encephalitis, pyogenic abscesses and occasional demyelinating diseases. Reduced diffusion can be seen in highly cellular tumours such as lymphoma, meningioma and glioblastoma. Oedema is a non-specific reaction of brain parenchyma to different factors which can, to some extent, be differentiated by DWI. Cytotoxic oedema is due to abnormal cellular uptake of water and myelin oedema is due to intramyelinic accumulation of vacuolated or free water which has high signal intensity on the diffusion trace, with decreased ADC as results of isotropically restricted water diffusion. On the opposite hand, vasogenic oedema is caused by increased permeability of the blood brain barrier, and interstitial oedema is caused by subependymal water diffusion in acute hydrocephalus have intermediate signal on the DW image with increased ADC.

Infections

Brain abscesses are cystic lesions with a thick, rim-shaped contrast enhancing capsule, surrounded by massive vasogenic edema. This appearance on MR images sometimes cannot be differentiated from cystic necrotic tumors with similar clinical findings, therefore its differential diagnosis is crucial for the necessity of prompt treatment. Brain abscesses show very high signal on DW image associated with decreased ADC (Fig. 1). The restricted diffusion in abscesses are due to the high viscosity of the proteinaceous fluid and hypercellularity of the pus consisting of bacteria and inflammatory cells.^{2,6-8}

In viral encephalitis typical MRI findings include hyperintensity of affected white matter and cortex on T2W imaging. DWI shows restricted diffusion due to cytotoxic oedema, however less intense as compared to infarction.

In Acute disseminated encephalomyelitis MRI findings show regions of high signal in subcortical locations on T2W and FLAIR sequences; the thalami and brainstem can also be involved, with surrounding edema. DWI shows peripheral restricted diffusion; the center of the lesion, although high on T2 and low on T1, does not have increased restriction on DWI (Fig. 2)

Granulomatous inflammations

- Tuberculomas: DWI typically shows central low signal,

but if liquid necrosis is present centrally then high signal may be seen.

- Neurocysticercosis: Typically, CSF density lesion is noted on MRI; hyperintense scolex is sometimes seen. Signal drop-out is seen on susceptibility weighted images (SWI).

Neoplastic lesions

Brain neoplasms show varying signal on the DW image and the ADC map. Tumours with higher cellularity or higher grade show increased signal on the DW image and a marked reduction in ADC values.^{8,14}

a) Primary tumours

- Low grade gliomas, because of their low cellularity, have a significantly higher ADC values compared to high grade gliomas and lymphomas (Fig. 5). They show high signal on T2 which is related to edema, demyelination & other degenerative changes.
- Lymphomas are highly cellular tumors. Typical MR findings are slightly hyperintense lesions compared to normal brain tissue on T2-weighted images usually in the cerebral, basal ganglia and thalamus.
- DWI is helpful in differentiating primary central nervous system lymphomas from angiotropic large cell lymphoma which is frequently accompanied by diffusion abnormalities due to brain ischemia.

b) Metastases

- Metastases show variable signal (generally iso- or hypointense) in the DWI. Rarely high signal intensity in the DW image with decreased ADC may be seen, due to hypercellularity, extracellular methemoglobin or sometimes increased protein concentration in the form of highly viscous mucin in cystic metastases.

Epidermoid cyst

- These are rare congenital lesions arising from the inclusion of ectodermal tissue into the neural tube. Cerebellopontine angle is the most common location.
- Typical MR imaging findings are well-defined, lobulated masses, slightly hyperintense or isointense to

the cerebrospinal fluid on T1 and T2-weighted images with no internal contrast enhancement (Fig.7).

- The lesions show diffusion restriction on the DW image with mixed signal on the ADC map.

Encephalopathies

a) Hypoxic ischemic encephalopathy (HIE)

- It is a general term describing the infarct-like lesions as a result of ischemia, anoxia or hypoglycemia, presenting with restricted diffusion representing cytotoxic edema.
- Perinatal hypoxic ischemia causes structural and functional damage to the brain of the neonate, commonly effecting the basal ganglia, thalami and white matter, usually sparing the cerebellum.
- ADC in neonates is 30–50% higher compared with adults, because normal neonatal white matter is less myelinated and structured and contains more water. Directly after a severe ischemic insult, ADC in neonates decreases.^{3,24}

b) Posterior reversible leukoencephalopathy syndrome

- Characterized by T2- hyperintense areas predominantly within the cortex and subcortical white matter of the parieto-occipital lobes on MR imaging with evidence of cytotoxic oedema in DWI (Fig. 8).²⁵
- Microhemorrhages and endothelial cell damage, both vasogenic and cytotoxic edema may be seen due to increased blood–brain barrier permeability.

c) Toxic encephalopathy

- Immune-suppressive drugs such as cyclosporine, interferon alfa and tacrolimus, immunoglobulin therapy and methotrexate may cause transient encephalopathy.^{2,27–30}

d) Wernicke encephalopathy

- It is a disorder resulting from thiamine deficiency. Typical MR imaging findings are hyperintense lesions surrounding the third ventricle, mamillary body, aqueduct and thalami on the T2-weighted, FLAIR and DW images, attributable to both cytotoxic and vasogenic edema.³²

Leukodystrophies

- These are genetic diseases, most commonly of metabolic origin, which disturb normal myelination of the white matter.
- DWI differentiates vasogenic edema and myelin edema.
- Among leukodystrophies high grade myelin edema is encountered in Krabbe disease, Canavan disease, maple syrup urine disease.

Demyelinating diseases

- Multiple sclerosis is the most common demyelinating disease. DWI and diffusion-tensor imaging may improve lesion detection with standard T2-weighted techniques. On DWI acute lesions may show high ADC due to vasogenic oedema, and myelin destruction with axonal preservation; or low ADC due to intramyelin oedema.^{2,37} Chronic MS plaques do not show diffusion restriction.²
- Osmotic myelinolysis is characterized by regions of demyelination throughout brain, most commonly in

the pons. Extrapontine myelinolysis is most commonly seen in the basal ganglia, thalami and gray-white matter junctions. Characteristic MR findings of central pontine myelinolysis are symmetric T2-hyperintense lesions involving the basilar pons and sparing of peripheral areas of pons and descending corticospinal tracts. DWI shows areas of increased ADC similar to MS lesions. However, depending on the age of the lesions, degree of ADC elevation may vary³⁸ and lesions with decreased ADC may be seen³⁹

Epilepsy

Seizures induces cellular swelling and fluctuations in the extracellular water. Typical postictal MR imaging findings are uni or bilateral high signal in the cortical or limbic structures particularly in the hippocampus on T2-weighted images. Detectable MR spectroscopic findings have also been documented. In DWI, first signs of cytotoxic edema are usually followed by signs of vasogenic edema in the postictal period⁴⁰ (Fig. 12)

Vasculitis and vasculopathies

- Behcet's disease is an inflammatory multisystem disease. Involvement of central nervous system causes lesions secondary to vasculitis, mainly with venular involvement, and dural sinus thrombosis. On DWI the lesions are either iso- or hyperintense with high ADC. The pattern with high signal on both diffusion and ADC images is attributable to vasogenic edema due to the disrupted blood–brain barrier associated with acute inflammatory response.⁴¹
- Systemic lupus erythematosus is another cause of cerebral vasculopathy which affects the arterioles and capillaries. On DWI lesions representing both infarcts and vasogenic edema can be seen.

Haemorrhage

Spontaneous intracerebral haemorrhage is most frequently seen in the form of deep haemorrhage secondary to hypertension. Non-enhanced CT is still the technique of diagnostic choice, while MR imaging gives additional information about the stage of the haemorrhage depending on the signal intensity of the blood products typically changing over time. Recently DWI has been used to differentiate haemorrhage from infarction in hyperacute stroke and to identify perihematoma ischemia or oedema⁴² (Fig. 13). In DWI the core of an acute hematoma is hyperintense with decreased ADC. However, T2-shine-through, T2 black-out effects and susceptibility artifacts from blood products contribute to the appearance on DW image and ADC values. Therefore, DWI should be read with great caution in haemorrhagic lesions.⁴³ Conjoint use of DWI with T2- and T2*-weighted images is mandatory.⁸

Trauma

MR imaging findings in posttraumatic patients are T2-hyperintense lesions due to diffuse axonal injury at gray-white matter junctions, in the white matter and in the brain stem. T2*- weighted imaging improves detection of hemorrhagic lesions.⁴⁴ DWI can depict shearing injuries not visualized with FLAIR, T2-weighted fast spin echo and

T2*-weighted gradient echo sequences.⁴⁵ Lesions with low ADC may be related to trauma-induced brain ischemia, on the other hand lesions with high ADC represents increased amount of extracellular water.⁴⁶

CONCLUSION

Diffusion weighted MRI is a very useful technique that provides unique information about the physiological state of brain tissue. By using a combination of various MR sequences along with DWI and ADC images a valuable diagnosis may be provided to the clinicians. DWI remains a valuable and effective tool in differential diagnosis of non-infarct lesions of the brain, especially infections, metabolic lesions and epidermoid cysts in which conventional imaging maybe equivocal.

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