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Role of diffusion-weighted MRI in differentiating ischemic etiology and tumor etiology of brain

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Abstract:
- *Many a times clinical presentation of brain tumors mimics that of the stroke and vice versa when patient present with acute neurological manifestations, differentiation of which is very necessary due to their completely different management.*
- *In such critical cases , diffusion-weighted imaging provides information about the physiological properties of the lesion that have been linked to cellularity, structural integrity, and necrotic transformation of brain lesion and thus help us in differentiating stroke from the tumor.*

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AIMS AND OBJECTIVES:
The objectives of the publication titled "DWI " are as follows:
1. To describe the features of intracranial lesions on Diffusion weighted imaging.
2. To compare the diffusion weighted imaging features of these lesion with ADC and T2 FLAIR images so as to help differentiate among them.

Materials And Methods:

PATIENTS:
A prospective study was conducted between January 2020 to December 2020 in Dept. Of Radiodiagnosis, GCS Medical College, Ahmedabad.
Imaging was done with 1.5 tesla GE SIGNA EXPLORER magnetic resonance imaging equipment.

- Inclusion criteria:
All patients with neurological complaints referred to our department.
All patients with diffusion weighted magnetic resonance imaging reference for infarction, hypoxic ischemic injury, infective condition, tumors, demyelination, metabolic and toxic insult to brain, Degenerative disorder irrespective of age and sex were included in the study.

- Exclusion criteria:
- Patients whose data is incomplete.
- Patient who have allergic reaction to contrast medium.

- Implanted electric and electronic devices are a relative contraindication to the magnetic resonance imaging, and in particular: heart pacemakers (especially older types),insulin pumps , implanted hearing aids ,neurostimulators,intracranial metal clips ,metallic bodies in the eye.
- Sutures or foreign bodies are relative contraindications to the MRI because they obscure the visualization of normal anatomy due to artefact effect.
- Patients who are detected to have intracranial bleed were excluded from the study.

All the patients underwent the examination after contraindications for MRI were excluded and consent was taken. All the MRI scans in this study were performed using GE 1.5 tesla SIGNA EXPLORER magnetic resonance imaging equipment.

MRI Protocol consisted of the following:

- A head coil was used.
- Axial diffusion weighted images of the brain.
- Sagittal T1W images of the brain.
- Axial T2W FLAIR images of the brain.
- ADC images were reconstructed from the diffusion weighted images.

Table 1 : Technique for MRI of the brain with DWI.

	DWI	**T2 FLAIR axial**	**T1 Sagittal**
TR	5000	8002	2060
TE	80	86	20
T1		2000	650
Matrix	128 x 192	256 x 320	224 x 384
No. of excitations	2	1	1
Thickness	5 mm	5 mm	5 mm
Section spacing	1.5 mm	1.5 mm	1.5 mm
FOV	24 x 30	24 x 24	24 x 24
Imaging time	45 s	1 min 25 s	1 min 25 s

b values of 0 and 1000s/mm2 were used for diffusion weighting. ADC images were reconstructed from the diffusion weighted images.

I. Introduction:

Diffusion weighted imaging is a specialised magnetic resonance imaging technique that assess local environment at the cellular level to determine changes in the random movement of water protons within and between the intracellular and extracellular spaces. Regions with restricted mobility of water molecules yield a greater DW-MRI signal and appears bright. In ADC maps, regions that contain high water mobility appears bright.

Whereas DWI is most often used to identify acute arterial ischemia, other processes that interfere with or restrict the movement of water can cause notable changes on DWI, including neoplastic lesions,encephalitis,pyogenic abscess and occasional demyelinating diseases.

Tumor cellularity is probably a major determinant of ADC values of brain tumors, although probably not the only one.

Enhancing brain lesion includes abscess and tumors. The centre of the abscesses shows restricted diffusion and thus high signal intensity on DWI as compared to necrotic tumors which show low signal intensity. Thus DWI is useful in providing a greater degree of confidence in distinguishing brain abscesses from cystic or necrotic brain tumors than conventional MRI.(1) Thus, it may increase the diagnostic accuracy when combined with other sequences. Likewise, in Creutzfeldt-Jakob disease, DWI imaging helps differentiate from infarct by showing persistent restricted diffusion.(2)

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.

Table 2: Age wise distribution.

Intra cranial lesions	**Age (in years)**								**Total**
	0-10	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**	**71-80**	
Acute infarct					5	8	13	4	**30**
Subacute infarct					1	1			**02**
Chronic infarct					1	5	8	4	**18**
Hypoxic ischemic injury (HII)	3								**03**

Abscess		1	1	1					**03**
Tuberculoma		1	2	3	2				**08**
Neurocysticercosis (NCC)			1	1					**02**
Extradural empyema				1					**01**
HSV encephalitis			1						**01**
Anaplastic astrocytoma				1	1				**02**
Glioblastoma multiforme						1	2		**03**
Hemangioblastoma					1				**01**
Low grade glioma		1		1	1				**03**
Medulloblastoma		3							**03**
Pilocytic astrocytoma	1								**01**
Lymphoma					1	1			**02**
Arachnoid cyst		1	2	1					**04**
Epidermoid cyst				1	1				**02**
Meningioma			1	2	2	1			**06**
Schwannoma						1			**01**
Multiple sclerosis				1					**01**
ADEM	1								**01**
Periventricular leuckomalacia	1								**01**
PRES		1							**01**
TOTAL	**06**	**08**	**08**	**13**	**16**	**18**	**23**	**08**	**100**

II. **Results :**

The present study was carried out to describe imaging characteristics of various intracranial lesions on DWI and to compare them with ADC and T2 FLAIR images.

Age wise distribution of patients:

The age of the patients with intra cranial lesions ranged from 3 days to 78 years with a mean of 43.97 ± 2.04. The patients involved in the study were divided into 8 age groups viz. 0-10 years, 11-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years , 61-70 and 71-80 years. There were six patients (6%) in 0-10 year age group, eight (8%) in 11-20 year age group, eight (8%) in 21-30 year age group, thirteen (13%) in 31-40 year age group, sixteen (16%) in 41-50 year age group, eighteen (18%) in 51-60 year age group, twenty three (23%) in 61-70 year age group, eight (8%) in 71-80 year age group as given in Table 2.

- In the present study 30 (30%) were females and 70 (70%) males. The mean age among females was 50 years and in males was 44 years. In the present study, majority of the cases were of infarcts which constituted 50 cases (50% of total cases), 3 cases of hypoxic ischemic encephalopathy (3% of total cases) were also included.The other cases were tumors 28 cases (28%) of which 15 (53% of all tumors) were intra axial and 13 (37% of all tumors) were extra axial tumors, 15 infective conditions (15% of total cases), 2 cases of demyelination (2% of total cases) and 2 miscellaneous conditions (2% of total cases). Miscellaneous conditions included 1 case of periventricular leukomalacia and 1 posterior reversible encephalopathy syndrome (PRES) case.
- Infarcts constituted 50 cases (50%) of the total cases in this study. Of this 30 (60% of all the infarct cases) were acute infarcts, 18 (36%) were chronic infarcts and 2 (4%) were subacute infarcts. The age group of patients with infarcts ranged from 43 to 78 years with a mean age of 60 years. There were 12 (24%) females and 38 (76%) males among these cases. In 30 cases (60%) the infarcts were in MCA territory, in 4 cases (8%) they were in ACA territory, in 10 cases (20%) the infarcts were in PCA territory and in 6 cases (12%) they were in basilar artery and vertebral artery territory.
- All 30 cases (100%) of acute infarcts showed true diffusion restriction with hyperintensity on DWI and hypointensity on ADC images.Of these,26 cases (86.66%)showed hyperintensity on T2W images.The remaining 4 cases (13%) showed no signal change on T2W images.
- Of the 18 cases of chronic infarcts, ADC signal was increased in all, suggesting increased water diffusivity. In 8 cases (44.44%), there was hypointensity on DWI and T2 FLAIR images with hyperintensity on ADC images indicating encephalomalacia.T2 shine through was noted in 10 cases (55.55%).None of the cases showed T2 washout.
- Out of 2 cases of subacute infarcts,1 (50%) showed true restriction and 1(50%) showed T2 shine through.
- Three cases of hypoxic ischemic injury were included in this study, age range of 3 days to 15 days. Two cases were preterm neonates and one was a term neonate. All three cases showed true diffusion restriction. 2 of three cases (66.6%) showed hyperintensity on T2 FLAIR images, and 1 (33.4%) did not show any change

on T2 FLAIR images.The extent of abnormality was noted to be more on DWI and ADC images than on T2 FLAIR images.

- Of total 15 Infective conditions included in our study 8 cases are of tubercular granulomas (53.3%), 2 cases of Neurocysticercosis (NCC) granulomas (13.3%), 3 cases of abscess(20%),1 case of extradural empyema (6.7%) and 1 case of HSV encephalitis (6.7%). True restriction of diffusion was noted in 7 (46.66%) cases.This included 2 cases of tubercular granulomas, 3 cases of abscess and 1 case of extradural empyema. Thus 25% of tubercular granulomas, 100% of abscesses and 100% of extradural empyema showed true diffusion restriction. T2 washout was seen in all 2 cases of NCC granulomas and 4 cases (50%) of tubercular granulomas.T2 shine through was seen in 2 case of tubercular granuloma and one case of HSV encephalitis.
- There were 15 cases of intra axial tumors with age ranging from 10 to 68 years with 3 females and 12 males.This included 2 case of anaplastic astrocytoma, 3 cases of glioblastomamultiforme, 1 hemangioblastoma, 3 low grade gliomas, 3 medulloblastomas, 1 pilocytic astrocytoma, and two cases of lymphomas. 5 cases (33.3%) showed true diffusion restriction. Of these 2 were GBM, 2 were medulloblastomas, and one was lymphoma.Thus 66.6% of GBM, 66.6% of medulloblastomas, and 50% of lymphomas showed true restriction of diffusion.

T2 shine through was noted in 8 cases (53.3%). This included all 2 cases of anaplastic astrocytomas, 1 case (33.4%) of GBM, 2 cases (66.6%) of low grade gliomas and 1 (50%) case of lymphoma.T2 washout was seen in one case of hemangioblastoma and 1 case (33.4%) of low grade glioma.

- 13 cases of extra axial tumors with an age range of 14 to 52 years, mean 36 years were included in this study. Of these 4 were females and 9 were males.There were 4 cases of arachnoid cysts, 2 epidermoid cyst, 6 cases of meningiomas and 1 case of schwannoma. True diffusion restriction was noted in 5 cases (38.5%). This included all the cases of epidermoid cyst and 3 cases (50%) of meningiomas.In one case of meningioma, T2 shine through was noted. In 2 (33.3%) cases of meningiomas, T2 FLAIR showed iso to hypo intense signal probably due to high cellularity and presence of calcification. 1 case of schwannoma showed T2 washout.
- Out of 2 cases of demyelination, one was multiple sclerosis and one was a case of ADEM. All the lesions showed hyper intensity on T2 FLAIR images. True diffusion restriction was not noted in any of the cases. T2 washout was seen in one case of multiple sclerosis . No change was noted on DWI or ADC images in the case of multiple sclerosis and in ADEM.
- Miscellaneous other lesions like 1 case of periventricular leukomalacia and 1 case of posterior reversible encephalopathy syndrome were detected. All the lesions showed hyper intensity on T2 FLAIR images. True restriction of diffusion was not noted in any of the cases. T2 washout was seen in one case of PRES. No change was noted on DWI or ADC images in one case of PRES.

III. Discusssion:

Diffusion weighted MRI provides image contrast that is different from that provided by conventional MRI sequences. It provides a technique for mapping proton contrast that reflects the microvascular environment. This imaging technique is sensitive to early ischemic insult. DWI is performed with a pulse sequence capable of measuring water translation over short distances. This water diffusion is much slower in certain pathological conditions as compared with normal brain.(3)

In this study, 100 patients with intracranial lesions detected on DW MRI of the brain were included.

INFARCTS:

The interruption of cerebral blood flow results in rapid(within minutes) breakdown of energy metabolism and ion exchange pumps.This leads to a massive shift of water from the extracellular into the intracellular compartment (cytotoxic oedema) and produces a typical hyperintensity on DWI and hypo-intensity on ADC. Acute ischemia gives perhaps the most dramatic hyperintense changes among all intracerebral pathologies.

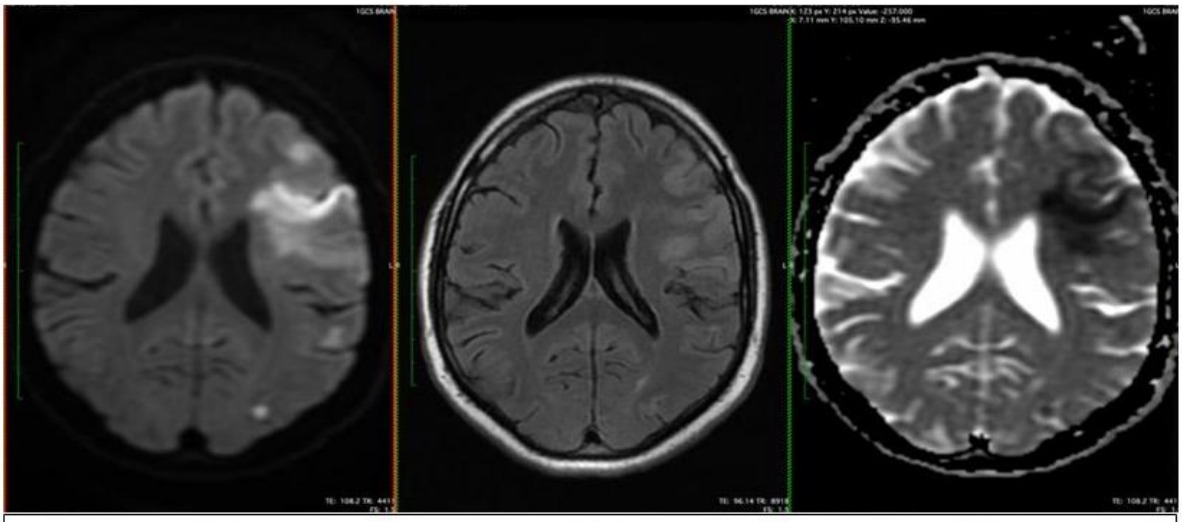
All the 30 cases of acute infarct in our study showed diffusion restriction on DWI images. In 13% of acute infarcts, no change was noted on T2W and FLAIR images (image 3).

The DWI and ADC maps show changes in an ischemic brain within minutes to hours after symptom onset, when no abnormalities are typically seen on conventional MRI and CT. **Thus, DWI was noted to be superior to T2W and FLAIR images in detection of acute infarcts.**

Results of this study are similar with a study done by Gonzalez et al (4) who concluded that DWI is superior to conventional MRI in the diagnosis and characterization of acute infarct.

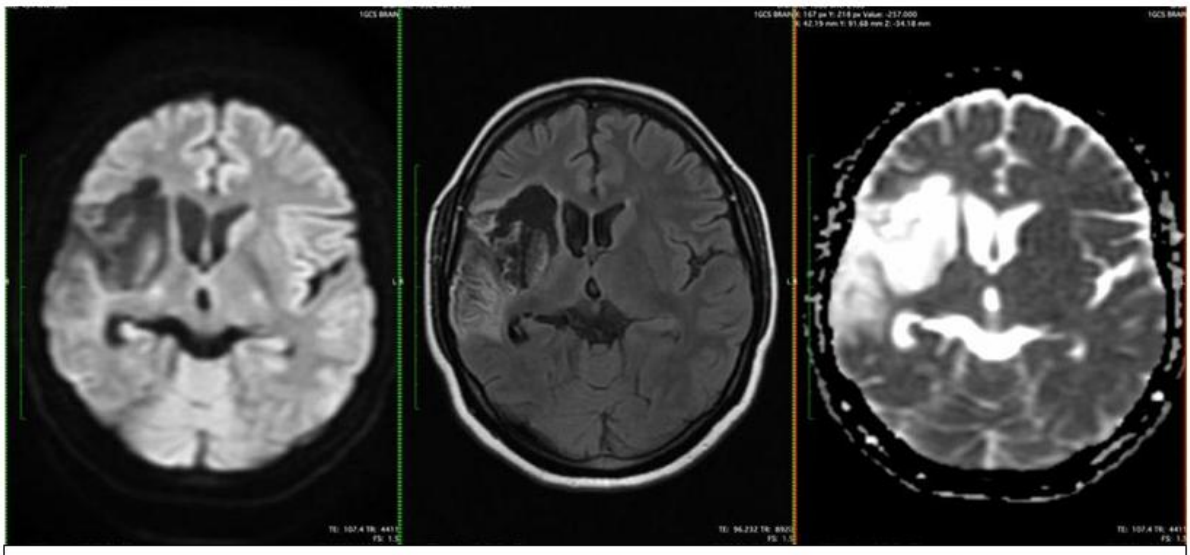
The sensitivity and specificity of DWI in the detection of acute ischemia in our study is 100%. The difference in sensitivity of DWI and conventional MRI sequences is more in the initial time period and decreases as time progresses.

In subacute infarcts and chronic infarcts, abnormal signal was noted on T2WI and on DWI in all patients. Chronic infarcts are characterised by elevated diffusion and appear hypointense on DWI and hyperintense on ADC map.(image 2)



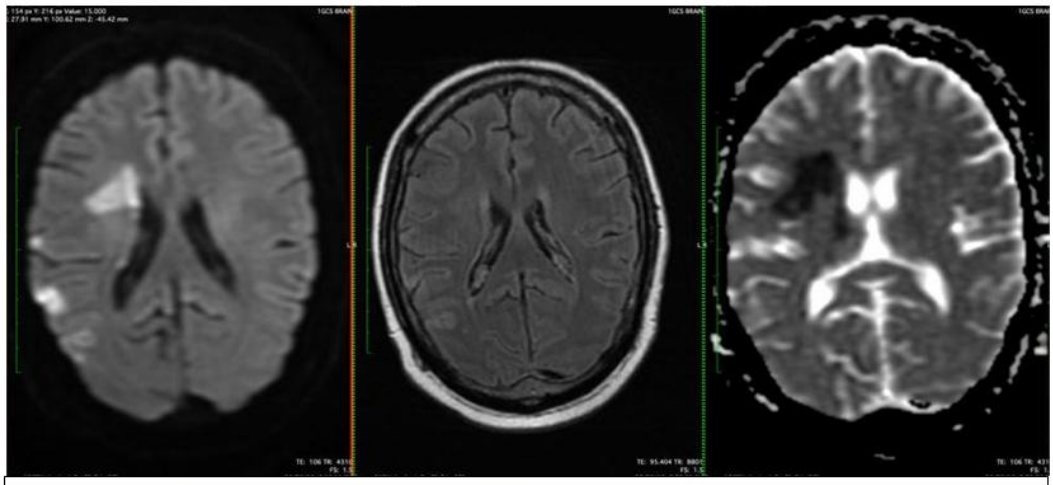
DWI	FLAIR	ADC

Image 1: Case of 45 year old male patient with acute infarct.
The above DWI and ADC images are showing area of diffusion restriction in left parietal region which appears hyperintense on FLAIR images. **Case of acute infarct.**
As it is evident by the above images that the conventional MRI FLAIR image shows only subtle areas of hyperintensity which can be easily missed. This signifies the importance of DWI.



DWI	FLAIR	ADC

Image 2: Case of a 60 year old male patient .
Presence of large CSF intensity area with few FLAIR hyperintense area within involving fronto-parieto-temporal region on right side with associated volume loss & mild ex-vacuo dilatation of frontal & temporal horn of right lateral ventricle.
Case of chronic infarct with few gliotic areas within and associated volume loss.

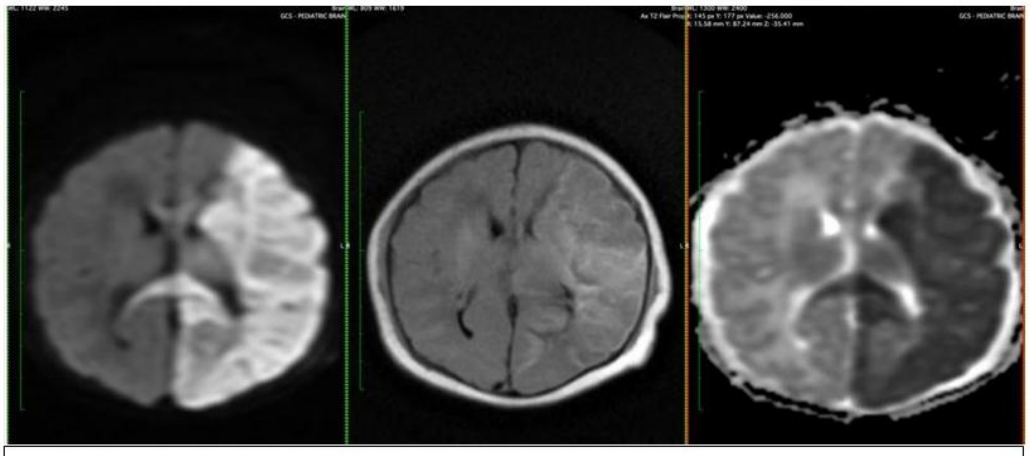


DWI	FLAIR	ADC

Image 3: Case of 56 year old male patient with acute infarct.
The above DWI and ADC images are showing area of diffusion restriction in right parietal and basal ganglia region. (DWI mismatch)
As it is evident by the above images that the conventional MRI FLAIR image shows only subtle areas of hyperintensity which can be easily missed. This signifies the importance of DWI.

Hypoxic ischemic injury:
The mechanism and presentation for hypoxic ischemic injury (HII) is variable and sometimes uncertain. Fu JH et al (5), compared conventional MRI sequences to DWI in the evaluation of HII and found that DWI showed abnormal high signal intensity in the brain in patients in whom the conventional MR sequences were initially normal.

Schaefer et al (6), concluded that HII lesions not seen on routine MR images are identified on DW MR Images. When lesions are identified on conventional images, lesion conspicuity is increased and lesion extent is seen to be larger on DW MR Images. All cases of neonatal HII included in this study showed true diffusion restriction. In 25% of cases there was no abnormality on T2 FLAIR images. The extent of abnormal signal was much more in the remaining 75% of cases on DWI, than that showed by T2W images. (image 4)
The DWI and ADC maps show changes even when no abnormalities are typically seen on conventional MRI and CT. Thus, DWI was noted to be superior to T2W and FLAIR images in detection of hypoxic ischemic injuries.



DWI	FLAIR	ADC

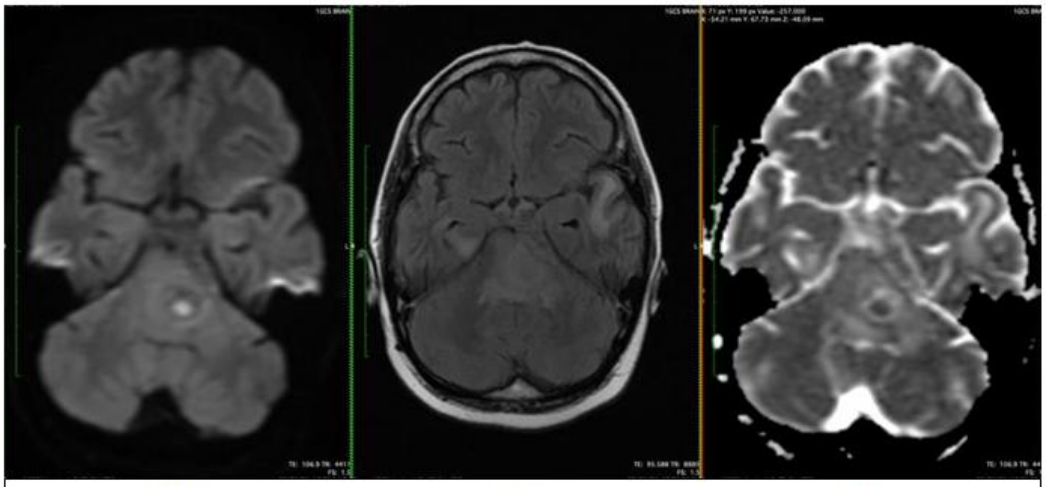
Image 4: Case of a 9 days old female child .
Presence of diffuse altered signal intensity area is seen involving the entire left cerebral hemisphere, left basal ganglia, left half of pons and splenium of corpus callosum which shows true diffusion restriction with signal drop in ADC images. It appears to be hyperintense on T2W and FLAIR images.
The above findings suggestive of hypoxic ischemic encephalopathy (grade - III).

Infections:

Lai et al (1),have showed that abscess cavity shows high signal intensity on DWI and a low signal on ADC image. This is not seen in the necrotic component of brain tumors. They concluded that DWI may enable one to distinguish brain tumors from necrotic tumors.

Also, it helps in the evaluation of partially treated abscesses and to look for their recurrence.

Enhancing brain lesion include abscess and tumors which gives rim enhancement.Therefore, the DWI and ADC findings may be useful in the differential diagnosis of ‘‘ring enhancing’’cerebral masses [7]. In the present study 100% of cases of abscess showed true diffusion restriction. The cystic or necrotic component of none of the tumors included in this study showed restricted diffusion. In 25% of the tubercular granulomas observed in this study, diffusion restriction was noted, probably denoting presence of necrosis (image 5). 50% of tubercular granulomas and 100% of NCC granulomas could not be detected on DWI alone and needed ADC and T2W images for lesion detection probably due to the poor spatial resolution of diffusion weighted imaging. One case (100%) of extradural empyema noted in this study showed true diffusion restriction. The thick nature of this collection causes reduced water diffusivity similar to abscesses.



DWI FLAIR ADC

Image 5: Case of a 29 year old female patient .
Presence of well defined varying size altered signal intensity lesion noted in left inferior cerebellar peduncle and cerebellar vermis. The lesion appears hyperintense on FLAIR images. FLAIR hyperintensity noted surrounding the lesions, s/o Edema.The lesion shows internal area of diffusion restriction suggesting necrotic area. Later On post contrast study, the lesion shows peripheral ring enhancement.
Case of CNS tuberculoma.

Tumors:

Intra axial tumors:

Cruz CH et al (8), showed that highly cellular tumors such as high-grade gliomas and lymphomas can have low ADC values and show restricted diffusion.It was also shown that medulloblastomas may be differentiated from other pediatric brain tumors by presence of diffusion restriction. The solid portion of hemangioblastomas has high ADC values due to their rich vascular spaces.

The findings of this study were similar. 66.6% of GBM, 66.6% of medulloblastomas and 50% of lymphomas showed true diffusion restriction. None of the low-grade gliomas or anaplastic astrocytomas showed restricted diffusion. The single case of hemangioblastoma seen in this study showed high signal on ADC images in its solid component suggesting high water diffusivity.

Extra axial tumors:

Diffusion weighted MRI plays a key role in differentiating arachnoid cyst from epidermoid cysts. Schaefer et al (6), showed that conventional MR cannot be reliably used to differentiate these two lesions as both have CSF like signal intensity on conventional MR sequences.However on DWI epidermoid cysts show diffusion restriction while arachnoid cyst shows CSF like intensity.(image 7-8)

This was also demonstrated in a study by Cruz et al (8), in which epidermoid cysts had ADC values similar to brain parenchyma while arachnoid cysts had ADC values similar to CSF. In the present study all 4 cases of

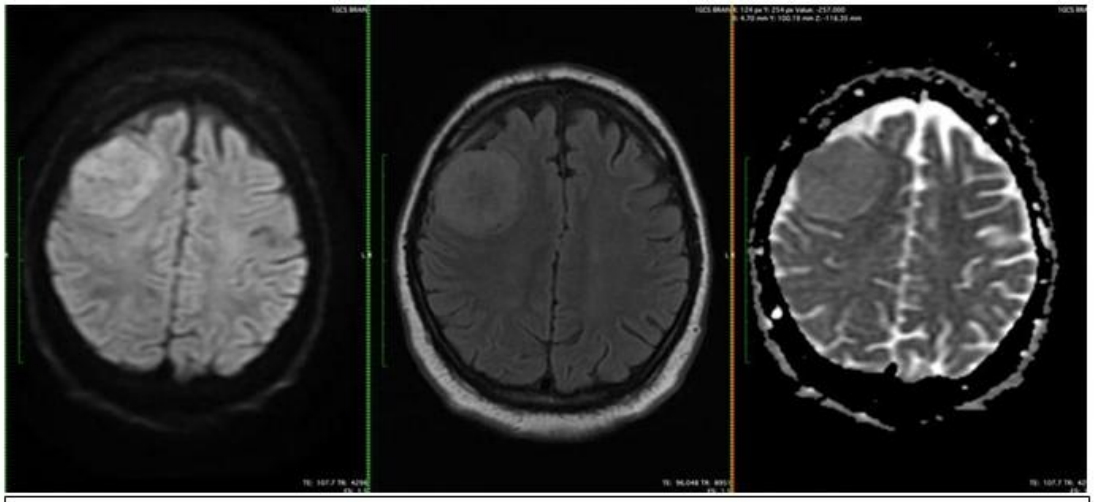
arachnoid cysts had signal similar to CSF on DWI and ADC images. All the cases of epidermoid cyst noted in this study had restricted diffusion.

Tadeusz et al (9) and Cruz et al (8) concluded that most meningiomas are isointense on DWI.(image 6) Only few may show restricted diffusion depending on their cellularity. In their study 23% of meningiomas showed restricted diffusion. This study had similar results with 50% of meningiomas showing true diffusion restriction.

Thus, DWI can differentiate between tumor and infection and can provide information about the cellularity of tumors thereby helping in characterization and grading of tumors.(10)

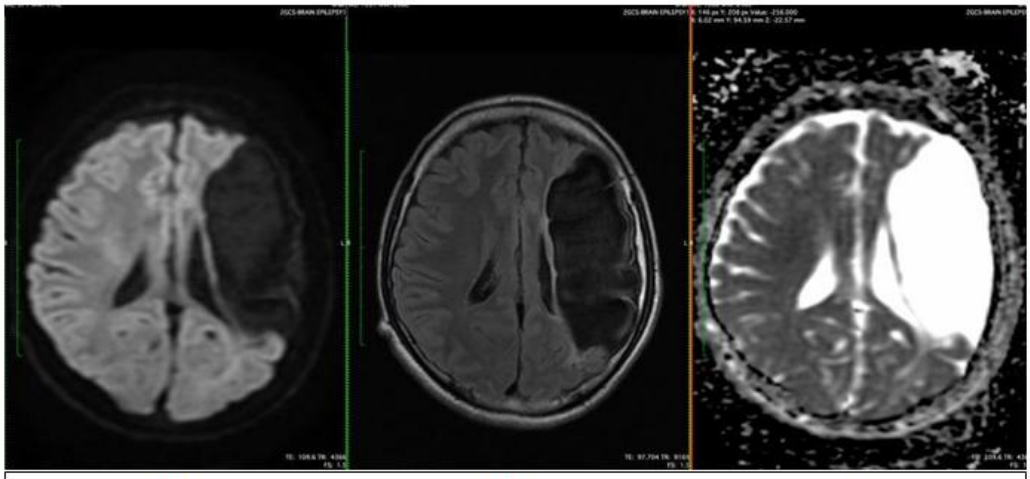
Arachnoid cyst vs epidermoid cyst :

Epidermoid tumours are mainly solid, thus markedly hyperintense on DWI with low ADC values. The ADC values of epidermoid tumours are lower than that of cerebrospinal fluid and equal to or higher than that of brain parenchyma [11e14]. Their high DWI is thought to be related to increased cellularity and viscosity of keratohyalin crystals [11]. Arachnoid cyst has a similar appearance on routine MRI as epidermoid tumours, but DWI can distinguish the them.Epidermoid, being a solid tumour, shows hyperintensity on DWI and has a low ADC map (Figure 8) and this is thought to be caused partly by T2 shine-through. Arachnoid cysts mainly appear as hypointense on DWI and have a high ADC (Figure 7) [13]. Relatedly, DWI has utility in differentiating recurrent tumour CSF-filled cavities postoperatively [15].



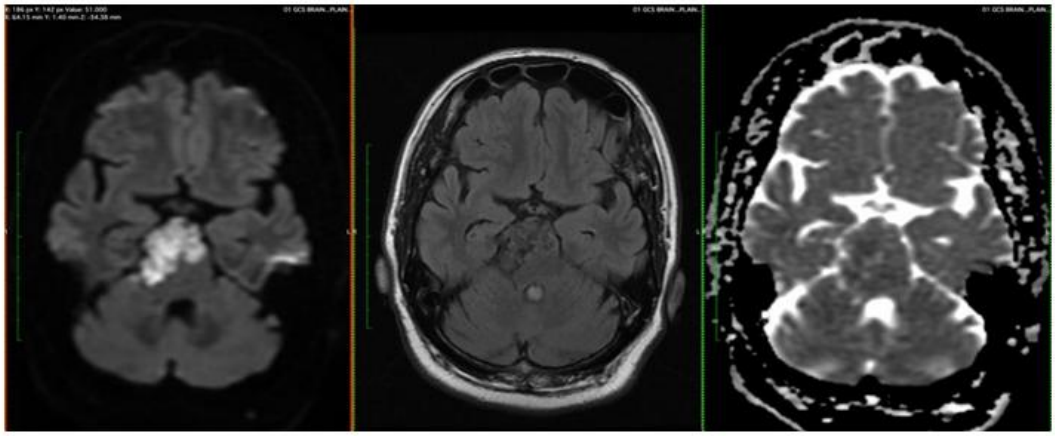
DWI	FLAIR	ADC

Image 6: Case of a 58 year old male patient .
Presence of well defined extraaxial dural based altered signal intensity lesion noted in right parietal region.
The lesion appears hyperintense on FLAIR images.The lesion shows subtle diffusion restriction on DWI.
The lesion causes mass effect in form of compression over adjacent sulci and gyri without any midline shift or compression of ventricles.There is thickening of adjacent dura noted.On post contrast study, the lesion showed homogenous enhancement.
Case of meningioma confirmed by histopathology later.



DWI	FLAIR	ADC

Image 7: Case of a 52 year old female patient .
Large well defined extra axial CSF intensity lesion on FLAIR , DWI and ADC images (no diffusion restriction) noted in left parietal region.
Case of arachnoid cyst.



DWI	FLAIR	ADC

Image 8: Case of a 51 year old male patient .
Extra axial, well defined altered signal intensity lesion involving right cerebello-pontine angle, which appears heterogeneously hyperintense FLAIR images. On DWI and ADC images it shows diffusion restriction.
Complete MRI study showed following findings - The lesion caused mass effect in form of compression on adjacent part of pons,medulla oblongata and right cerebellar penduncles.The lesion involve the quadrigeminal and prepontine cistern. The lesion abuts posterior cerebral artery & encases right vertebral and basilar battery. The lesion abuts the vestibulocochlear and facial nerve on right side near its origin. On post contrast study it does not show enhancement.
Case of epidermoid cyst – later confirmed by histopathology.

Demyelination*:*
Two cases of demyelination seen in this study did not show restricted diffusion and had increased signal on T2 FLAIR images. Studies done by Christiansen P et al (16) and Larsson H et al (17), have shown that most foci of demyelination do not show restricted diffusion.

Multiple sclerosis:
Pilot investigations assessing the role of DWI in the evaluation of multiple sclerosis (MS) have shown that, unlike the reduced ADC values found in regions of acute infarction, which reflect the presence of cytotoxic oedema, the typical DWI abnormality found in MS plaques
is that of truly elevated ADC values [18].In early studies, this increased diffusivity of MS plaques, compared to that of normal white matter, appears to be more pronounced than corresponding T2 signal intensity changes

[19]. However, there can be restriction of diffusion at the margin of the demyelinated plaque.In the setting of an acute demyelinating plaque, the predominant finding may be that of high DWI and low ADC, which may mislead the radiologist into diagnosing subacute stroke. In this scenario, serial imaging is critical as MS plaques appear to convert to their characteristic high ADC values [20].

IV. Conclusion:

Diffusion weighted MRI is a valuable technique that provides unique information about the physiological state of brain tissue. By using a combination of various MR sequences coupled with DWI and ADC images a valuable diagnosis may be provided to the clinicians. In this study the signal characteristics of various lesions on DWI, ADC, T2FLAIR and T1W images were studied.

Diffusion weighted MRI has been proven to be of excellent use in the characterization of infarcts and in the detection of acute infarcts. It is especially useful in the initial few hours of the ischemic insult when conventional MR sequences may be inconclusive and may not detect the infarct.

Also in the cases of hypoxic ischemic injuries- DWI and ADC images showed changes even when no changes were noted on conventional MRI sequences.

DWI also provided valuable information about tumor cellularity and thus helped in characterization of tumors and grading of tumors.

While conventional MRI may be inconclusive in the differentiation of epidermoid cyst from arachnoid cyst, DWI shows diffusion restriction in the former and helps in differentiation between the two.

Diffusion weighted images also helps to differentiate infections and tumors.

Thus, DW MRI is very helpful, necessary and superior to conventional MRI in differentiating and characterizing various intracranial lesions.

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