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Diffusion-Weighted Imaging (DWI) and Diffusion Tensor Imaging (DTI) in Diagnosis of White Matter Diseases of the Brain

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ABSTRACT

Background: Many White matter diseases involve a diverse range of disorders, either due to improper myelin formation or the loss of previously acquired myelin, with the underlying causes of several of these diseases still being not well understood. This study sought to establish the diagnostic advantage provided by diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI) in the diagnosis of WMD.

Methods: The case control study involved 50 patients with ages ranging from 5 to 75 and 30 healthy individuals as controls, all of whom exhibited neurological symptoms, sensory issues, or visual difficulties. Magnetic resonance imaging was conducted on all patients.

Results: There was a statistically significant difference between the two groups regarding DWI at a significance level of $P < 0.05$. In the context of DTI, fractional anisotropy values were found to be substantially lower in cases compared to the control group, with a p-value less than 0.05. Furthermore, the mean diffusivity value was significantly higher in cases than in the control group, with a probability of less than 0.05. Conversely, FA values were significantly lower in the corticospinal tract and corpus callosum tract of diseased individuals compared to disease-free controls ($P<0.05$).

Conclusions: DWI and DTI are non-invasive imaging methods that identify subtle structural tissue alterations not visible on standard MRI scans. Across all white matter conditions examined, a decrease in FA values was observed, accompanied by a rise in MD values relative to the control group

Keywords: *Diffusion-Weighted Imaging, Diffusion Tensor Imaging, White Matter Diseases, Brain*.

1. INTRODUCTION

The human central nervous system's white matter is composed of a complex network of approximately several trillion nerve connections. The majority of these connections are enveloped by a fatty substance called myelin, which contributes to the white appearance of the WM and accounts for roughly 50% of its dry weight [1].

WM diseases encompass a broad range of disorders, which can be distinguished by either impaired myelin formation (dysmyelination) or destruction of previously formed myelin sheaths (demyelination) [2]. The cause of myelin destruction are still not well understood. Demyelinating disorders are classified into four main categories: autoimmune, infectious, vascular, and toxic-metabolic processes [3].

The widespread use of brain magnetic resonance imaging (MRI) has led to a greater recognition of adult-onset WMD, which affects 50–98% of elderly patients, likely as a result of small vessel disease [2].

Abnormalities in diffusion indicate changes to the random movement of water molecules within tissues, offering valuable insights, enhancing MRI's sensitivity as a diagnostic tool, reducing the range of possible diagnoses, providing information on prognosis, supporting treatment planning and assessing the effectiveness of treatment [4,5].

An advanced MRI technique known as DTI allows for the quantitative assessment of tissue microstructure; it utilises the diffusion rate of water molecules to visualise bundles or tracts of neural fibres in the white matter [6].

DTI technique has been considered as the most effective method for characterizing WM organization, WM integrity is one of the most sensitive indicators of axon damage or demyelination [7].

Commonly measured DTI scalar parameters include fractional anisotropy (FA) and mean diffusivity (MD) [8].

The objective of this study was to establish the additional benefits of diffusion-weighted imaging (DWI) and DTI in the diagnosis of WMD.

Patients and Methods

This case-control study was conducted on 50 patients spanning an age range of 5 to 75 years, who exhibited neurological symptoms such as headache, lack of concentration, fatigue, dizziness or cognitive dysfunctions, mood or memory changes, sensory changes such as numbness and tingling, ataxia and balance problems, vision troubles and sudden onset of paresis or paralysis and 30 healthy individuals as control. The research took place between April 2022 and April 2024 after having received approval from the Ethical Committee of Tanta University Hospitals, Tanta, Egypt, with the approval code 35430/4/22. Written consent was obtained from the patient or the patients' relatives after providing appropriate information. Exclusion criteria were patients with brain tumors or congenital WMD, who have had metallic devices placed in their body that are incompatible to MRI machine such as heart pacemaker and aneurysm clip and claustrophobic patients.

All patients were subjected to complete history taking, clinical examination, neurological examination [sensory or motor abnormality, gait or balance changes and signs of lateralization] and MRI assessment by using MRI unit (GE) 1.5 Tesla in Radio-diagnosis department

Patient preparation

Prior to examination, the patient had removed all metal items such as pins and earrings and emptied their bladder to prevent irritation during the examination process. The patient was positioned in a supine position during the examination, lying comfortably to prevent excessive movement throughout the exam. The coronal, sagittal, and axial planes, along with a head-first orientation, were utilised for imaging. The slice thickness measured 6 mm, the matrix dimensions were 256 x 256, and the field of view spanned 220-240 mm. Examinations were conducted in a supine position using a standard circularly polarized head coil with a head support pillow positioned to minimize patient movement.

The MRI protocol comprised axial T1WI, axial T2WI, axial FLAIR images, DWI with an apparent diffusion coefficient (ADC) value, and DTI, which utilized a single shot, spin-echo echoplanar sequence with 40 encoding directions and a diffusion weighting factor of 800s/mm2. TR (10951, TE 67, matrix 128 x128, FOV 224 X 224 mm, number of excitations 2, slice thickness: 2.0/00 and flip angle 90 (degrees).

Every DTI was moved to the workstation. The GE software designed to produce colour orientation maps, FA maps, ADC maps, MD maps, and 3D fibre tractography maps was used to post-process the images.

Thickness of slice: 6 mm for Tl WI (TR 450, TE 15, matrix 80 x 81, FOV 230 XI 77), T2WI (TR 3612, TE 100, matrix 208 x 127, FOV 230 X 177), and FLAIR (TR 6000, TE 120, matrix 240 x 111, FOV 230 X 184).

The direction and anatomy of the tracts are visualized in directionally encoded FA maps, in which specific colours are allocated to tracts traversing the three orthogonal planes: red signifies tracts running from right to left, green signifies anteroposterior tracts, and blue signifies craniocaudal tracts. A three-dimensional display of tracts was generated. A region of interest was identified and marked along the path of the fiber tract on a colour-coded FA map, which was displayed in either a single or multiple axial, sagittal, or coronal sections. The software subsequently generates a 3D visualisation of the designated tract by tracing it automatically. A ROI (or seed) was placed on a patch of abnormal signal intensity visible in FLAIR images, as well as in FA, ADC, and MD maps from individual or consecutive axial, sagittal, or coronal sections. Color-coded DTI maps were then analyzed by comparing the FA and MD values with corresponding values in healthy tracts. In the control group, a ROI (or seed) was placed on corresponding sites of affection in the diseased group, matching the same age and sex, to measure FA, ADC, and MD values for comparative analysis.

2. METHOD OF TRACKING OF STUDIED TRACTS:

Statistical analysis

Statistical analysis was performed using the SPSS v26 software, developed by IBM Inc. (based in Chicago, IL, USA). The quantitative variables were represented as mean and standard deviation (SD) and were compared between the two groups using an unpaired Student's t-test. The qualitative variables were displayed in terms of frequency and percentage and were subsequently analyzed with the Chi-square or Fisher's exact test, depending on the situation. A two-tailed P value of less than 0.05 was deemed statistically significant.

3. RESULTS

Demographic data were enumerated in this table. **Table 1**

Table 1: Distribution of the two studied groups according to demographic data

		Cases (n=50)	Control (n=30)
Age (years)		35.30 ± 14.38	35.30 ± 14.38
Sex	**Male**	18(36.0%)	15(50.0%)
	Female	32(64.0%)	15(50.0%)

Data are presented as mean ± SD or frequency (%).

Distribution of studied cases according to complaint, diagnosis, site of foci and plaques, number of foci/plaques, detection of foci and/or patches in T1WI, T2WI and FLAIR sequences and appearance of foci and/or plaques on DWI in cases group were enumerated in this table. **Table 2**

Table 2: Distribution of the studied cases according to complaint, diagnosis, site of foci and plaques, number of foci/plaques, detection of foci and/or patches in T1WI, T2WI and FLAIR sequences and appearance of foci and/or plaques on DWI in cases group

		Cases (n=50)
Compliant	**Visual problem**	10(20.0%)
	Headache	10(20.0%)
	Fatigue	5(10.0%)
	Confusion	15(30.0%)
	Slurred speech	4(8.0%)
	Seizures	8(16.0%)
	Mood changes	11(22.0%)
	Abnormal sensation	11(22.0%)
	Lack of concentration	10(20.0%)
	Muscle weakness	7(14.0%)
	Paraplegia	2(4.0%)
Diagnosis	**Multiple sclerosis**	9(18.0%)
	SLE vasculitis	7(14.0%)
	Lacunar infarction	7(14.0%)
	ADEM	6(12.0%)
	PRES	6(12.0%)
	Rheumatoid vasculitis	6(12.0%)
	HIV encephalopathy	4(8.0%)
	Venous infarction	3(6.0%)
	NMO	2(4.0%)

Site of plaques	**PVWM**	41(82.0%)
	DWM	31(62.0%)
	CC	20(40.0%)
Site of foci	**Supratentorial**	35(70.0%)
	Supra and infratentorial	15(30.0%)
Number of foci / plaques	**1--5**	7(14.0%)
	5--10	20(40.0%)
	10--15	23(46.0%)
Detection of foci and/or patches in T1WI, T2WI and FLAIR sequences	**T1WI**	17(34.0%)
	T2WI	50(100.0%)
	FLAIR	50(100.0%)
Appearance of foci and/or plaques on DWI	**Free diffusion**	20(40.0%)
	Some restricted	15(30.0%)
	Restricted	15(30.0%)

Data are presented as frequency (%). SLE: Systemic lupus erythematosus, ADEM: Acute disseminated encephalomyelitis, PRES: Posterior reversible encephalopathy syndrome, HIV: Human immunodeficiency virus, NMO: Neuromyelitis optica, PVWM: Periventricular white matter, DWM: Deep white matter, DWI: Diffusion-weighted imaging, CC: Corpus callosum.

A significant difference between the two groups was observed in relation to DWI (P<0.05). In DTI comparisons, the fractional anisotropy (FA) was noticeably lower in cases than in the control group, with a p-value less than 0.05. Furthermore, the mean diffusivity (MD) value was significantly higher in cases than in the control group. **Table 3**

Table 3: Comparison between the two studied groups according to DWI and DTI parameters

		Cases (n=50)	**Control (n=30)**	**Test of sig.**	**p**
DWI	**Free diffusion**	20(40.0%)	30(100.0%)	28.800*	**<0.001***
	Some restricted	15(30.0%)	0(0.0%)		
	Restricted	15(30.0%)	0(0.0%)		
DTI	**FA value**	0.348±0.096	0.572±0.055	13.233*	**0.001*<**
	MD value	$10.05e^{-10}$±$3.11e^{-10}$	$8.73e^{-10}$±$8.03e^{-10}$	3.757*	**0.001*<**

Data are presented as frequency (%). * Significant P value <0.05. DWI: Diffusion-weighted imaging, DTI: Diffusion tensor imaging, FA: Fractional anisotropy, MD: Mean diffusivity.

In every case group, the FA value was considerably lower than that of the control group (P<0.05). In every case group, the MD value was considerably greater than that of the control group (P<0.05). **Table 4**

Table 4: Comparison between MS, lacunar infarction, rheumatoid vasculitis, SLE vasculitis, PRES, ADEM and HIV encephalopathy cases and control according to different DTI parameters

	MS (n=9)	**Control (n=30)**	**Test of sig.**	**P**
FA value	0.335±0.113	0.572±0.055	6.048*	**<0.001***

MD value	$10.27e^{-10}$±$4.65e^{-10}$	$8.73e^{-10}$±$8.03e^{-10}$	2.575*	**0.032***
	Lacunar infarction (n=7)	**Control (n=30)**	**Test of sig.**	**P**
FA value	0.350 ± 0.054	0.572 ± 0.055	9.607	**<0.001***
MD value	$9.98e^{-10}$	$8.77e^{-10}$	2.937*	**0.006***
	Rheumatoid vasculitis (n=6)	**Control (n=30)**	**Test of sig.**	**P**
FA value	0.312 ± 0.074	0.572 ± 0.055	9.958*	**<0.001***
MD value	10.06e-^{10}	$8.77e^{-10}$	5.376*	**<0.001***
	SLE vasculitis (n=7)	**Control (n=30)**	**Test of sig.**	**P**
FA value	0.338±0.125	0.572±0.055	4.828*	**0.002***
MD value	$10.05e^{-10}$	$8.77e^{-10}$	2.556*	**0.042***
	PRES (n=6)	**Control (n=30)**	**Test of sig.**	**P**
FA value	0.288±0.093	0.572±0.055	10.180*	**<0.001***
MD value	$10.36e^{-10}$	$8.77e^{-10}$	2.936*	**0.032***
	ADEM (n=6)	**Control (n=30)**	**Test of sig.**	**P**
FA value	0.242±0.067	0.572±0.055	12.912*	**<0.001***
MD value	$10.55e^{-10}$	$8.77e^{-10}$	2.989*	**0.027***
	HIV encephalopathy (n=4)	**Control (n=30)**	**Test of sig.**	**P**
FA value	0.278±0.090	0.572±0.055	9.273*	**<0.001***
MD value	$9.83e^{-10}$	$8.77e^{-10}$	2.399*	**0.022***

Data are presented as mean ± SD or median. * Significant P value <0.05. FA: Fractional anisotropy, MD: Mean diffusivity, SLE: Systemic lupus erythematosus, ADEM: Acute disseminated encephalomyelitis, PRES: Posterior reversible encephalopathy syndrome, HIV: Human immunodeficiency virus, MS: Multiple sclerosis.

FA values were significantly lower in CST and CC tract of diseased cases than control cases (P<0.05). **Table 5**

Table 5: Comparison between the two studied groups according to CST and CC tract affection

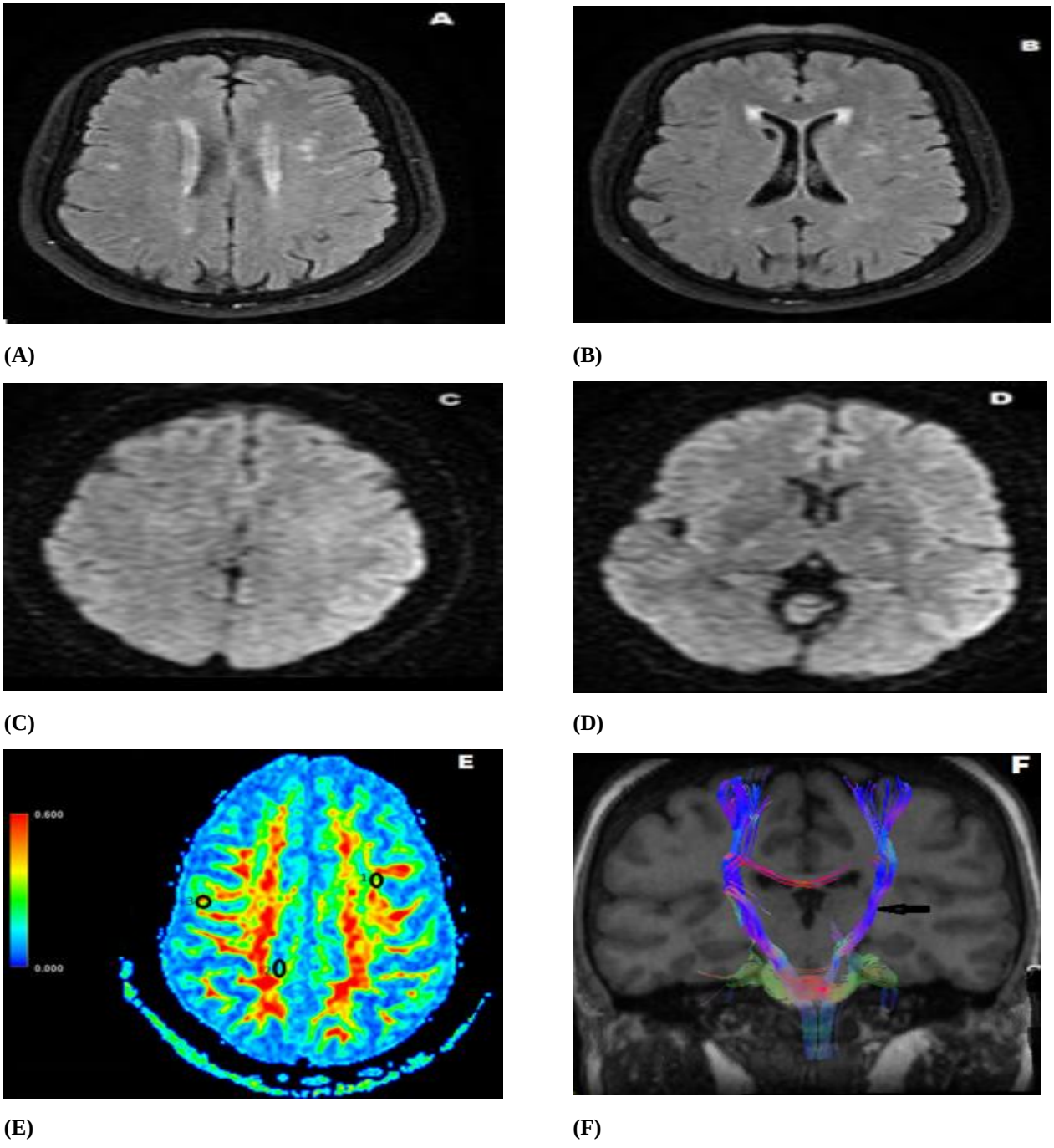
	Cases (n=50)	**Control (n=30)**	**Test of Sig.**	**p**
CST affection	33(66.0%)	0(0.0%)	26.351*	**<0.001***
CC affection	38(76.0%)	0(0.0%)	32.813*	**<0.001***

Data are presented as mean ± SD. * Significant P value <0.05. CST: Corticospinal tract, CC: Corpus callosum

Case 1: 55 years old male patient was complaining from slurred speech, confusion and numbness in his right upper limb. Given history of hypertension and previous stroke 2 years ago.

Area	**FA**	**MD**	**ADC**
ROI (1)	0.445	$9.324e^{-10}$	$8.74e^{-10}$
ROI (2)	0.324	$8.943e^{-10}$	$8.24e^{-10}$
ROI (3)	0.372	$9.023e^{-10}$	$8.821e^{-10}$

Diagnosis: multiple old lacunar infarctions is considered with affection of DTI parameters in the form of decrease FA, increase MD values in comparison to control case of the same age and sex. Area of encephalomalacia in right caudate nucleus representing old ischemic stroke. **Figure 1**



(A) **(B)**

(C) **(D)**

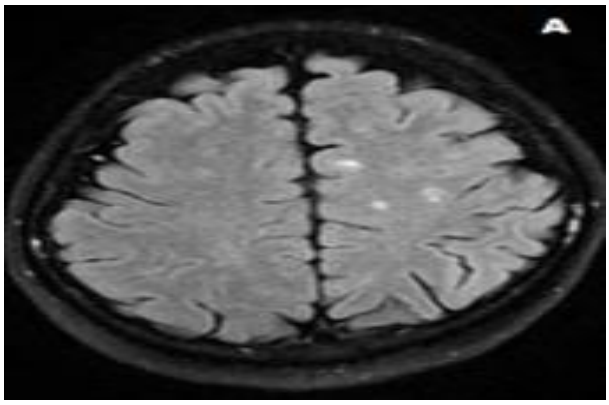
(E) **(F)**

Figure 1: Axial FLAIR (A) showed multiple hyperintense foci distributed on both high parietal regions, (B) showed hypointense area of cerebrospinal fluid like signal in right caudate nucleus, axial diffusion-weighted imaging (C-D) showed no diffusion restriction, (E) fractional anisotropy map and (F) corticospinal tractography showed decrease in fiber density of left corticospinal tract in comparison to the right side with fractional anisotropy 0.431

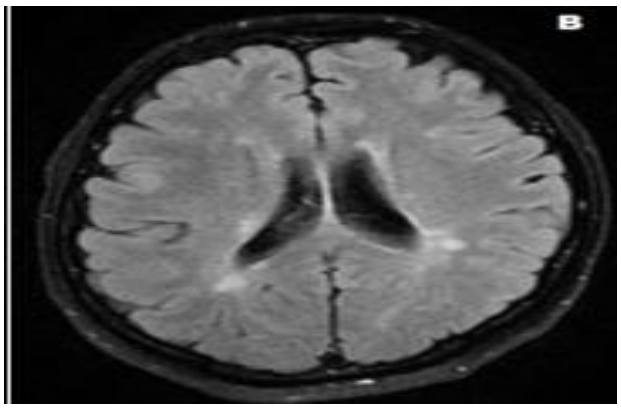
Case 2: 44 years old Female patient complaining from cognitive and mood changes, clinically diagnosed SLE for 6 years and she was under treatment.

Area	FA	MD	ADC
ROI (1)	0.508	$9.890e^{-10}$	$9.560e^{-10}$
ROI (2)	0.467	$9.780e^{-10}$	$9.923e^{-10}$
ROI (3)	0.312	$9.987e^{-10}$	$9.460e^{-10}$
ROI (4)	0.208	$8.467e^{-10}$	$10.102e^{-9}$
ROI (5)	0.288	$8.213e^{-10}$	$10.340e^{-9}$

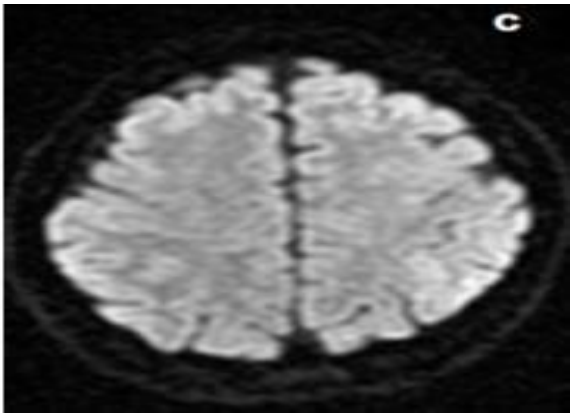
Diagnosis: lupus angiitis is considered with affection of DTI parameters in the form of decrease FA, increase MD values in comparison to a control case of the same age and sex. **Figure 2**



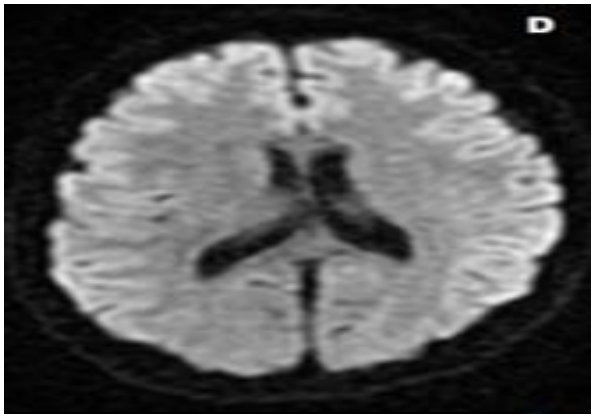
(A)



(B)



(C)



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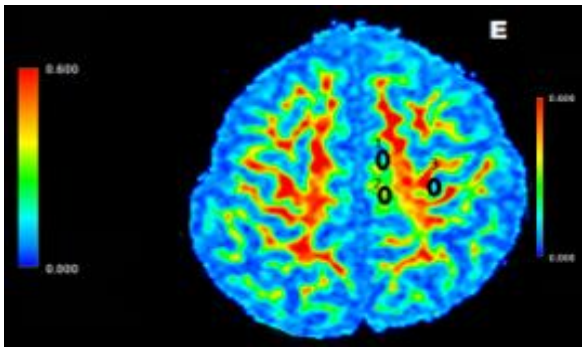

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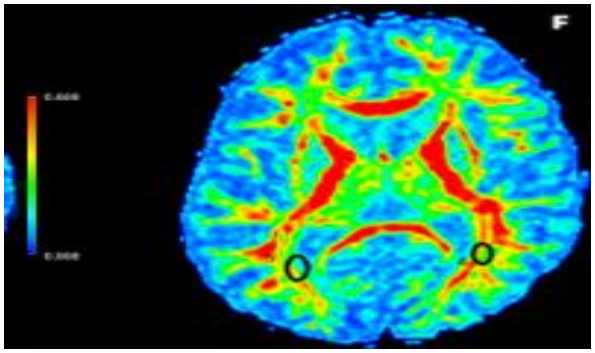

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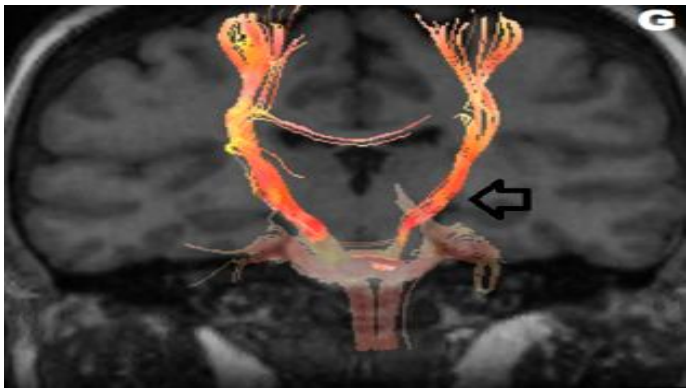

(G)

Figure 2: Axial FLAIR (A-B) multiple foci of hyperintense signal in left high parietal and deep periventricular close to both occipital horns of lateral ventricle, (C-D) diffusion weighted images showed no diffusion restriction, fraction anisotropy map (E-F) showed five region of intersts were drawn on the hyperintense foci which were noted on FLAIR images with affection of diffusion tensor imaging parameters and corticospinal tractography (G) showed decrease in fiber density of left corticospinal tract in comparison to right side, fractional antiscopy 0.456

4. DISCUSSION

The WM is the network of nerve fibres that facilitates communication and information sharing between various grey matter regions [9].

In this study, the site of the plaques was supratentorial only in 35 of cases and supra and infratentorial in location in 15 of cases, this agreed Frischer, J. M. et al. [11] found that most of the lesions are predominately seen supratentorial in location. In our study, only 34% of these cases had foci and/or patches were detected on T1WI, and whole of these foci and/or patches were detected in T2WI and FLAIR images in 100% of cases. This was concordant with Riphagen, J. M. et al. [12] found that FLAIR image has superiority over T1WI in detection of WM abnormalities. In our study, 40% of cases showed no diffusion restriction of WM foci and/or plaques on DWI, 30% showed diffusion restriction of all foci and/or plaques and 30% showed diffusion restriction of some foci and/or plaques. A study by Adam, A.et al. [13] found that diffusion restriction of the lesions depends on its acuity which help to know the course of the diseases, progression and follow up. All cases of control group showed no diffusion restriction on DWI. In comparison to studied group there was significant difference with $p< 0.001$. This agreed with Okorie, C. K. et al. [14] said that DWI has been described as the optimal imaging technique for diagnosing acute ischemic stroke and different WMD.

It was found that the FA value of cases group of different WMD was 0.348 while FA value on control group was 0.572 which means decrease in FA in diseased cases on comparison to normal ones with significant difference, $P<0.001$. Filippi, M., et al. [15] found that decrease in FA of focal WM lesions in their study. A significant difference was found on MD values on comparison of cases and control groups with $P<0.001$. MD value of cases group was 10.05e-10 ± 3.11e-10 while on control group was 8.73e-10 ± 8.03e-10 with increase in MD in diseased cases on comparison to normal ones. This is agreed with Min, Z. gang et al. [16] found that increase in MD value with $P< 0.0001$.

In agreement with our results comparison between MS, lacunar infarction, rheumatoid vasculitis, SLE vasculitis, PRES, ADEM and HIV encephalopathy cases and control according to different DTI parameters, Filippi, M., et al. [15] found that

decrease in FA and increase in MD values in cases of MS. Zhao, D. Q. et al. [18] found that in cases of lacunar infarctions, there was a decrease in FA value (0.35± 0.003) in patients' group than control group (0.95± 0.006) with p value<0.001 while increase in MD value in in patients' group than control group (0.73± 0.004) with p<0.0001. Phukan, P. et al. [19] found that in patients with rheumatoid vasculitis, there was a decrease in mean value of FA while comparing with mean value of FA on control group with statistically significant difference, P value less than 0.001.A statistically significant difference was found on MD values with P value less than 0.001. Liang, S. Y. et al. [20] found that reduced FA values (0.35 vs 0.40, p = 0.001) and increased MD (1.71 vs 1.48, p = 0.009) in cases of SLE vasculitis than those of controls. Anderson, R. C. et al. [21] found that decrease in FA (0.338 ± 0.125) and increase in MD (1034 x 10-12) in PRES cases. Chen, C. I., et al. [22] found that there is decease in FA value 0.16 ± 0.05 in ADEM.

HIV encephalopathy cases, there is decrease in FA value (0.278 ± 0.090) while comparing with FA value on control group (0.572 ± 0.055) with significant difference, P<0.001. A significant difference was found on MD values with P=0.022, MD value was high (9.75e-10 ± 7.61e-10) than control group (8.73e-10 ± 8.03e-10). This is concordant with Ma, J., et al. [23] found that lower FA (p < 0.0001) and higher MD (p<0.0001) than the control group.

CST affection of its fibers in 66% of cases and normal in the remaining 34%. The range of FA of the CST in control cases was 0.56 ± 0.02 while in cases of MS was 0.34±0.01, in cases of lacunar infarctions was 0.30±0.05. We noticed reduction of FA values of the involved tract of diseased cases than control cases with significant difference between them. This is concordant with Kerbrat, A. et al. [24] found that the lesion FA in the CST was higher in patients 3.6 ± 2.7% and 2.9 ± 2.4% of MS

In this study, the CC tract was traced with affection of its fibers in 76% of cases and normal in the remaining 24%; 9 cases of them had MS, 7 cases had lacunar infarctions. The range of FA of the CC in control cases was 0.65 ± 0.02 while in cases of MS was 0.56±0.01, in cases of lacunar infarctions was 0.57±0.04, so there was a reduction of FA values of the involved tracts than control cases that with a significant difference between them. This is agreed with Fabri, M.et al. [25] found that reduction of FA of CC in cases with MS to 0.46±0.03.

One of the study's limitations was the very small sample size, which may have affected the findings. However, this shortcoming should be lessened by the compound's clinical presentation, radiological investigations, and laboratory testing. The findings ought to be confirmed in a more extensive, well planned investigation.

5. CONCLUSIONS

Noninvasive imaging methods like DTI can identify microstructural tissue alterations that are not apparent with traditional MRI and describe the diffusion characteristics of water molecules. in WM. The DTI enables a more precise differential diagnosis and an earlier diagnosis, which permits an earlier and more focused therapeutic intervention, particularly when correlated with clinical and laboratory results. In our study, we observed a decrease in fraction anisotropy value and an increase in MD value in various studied WMD. However, more research is required to address some of our shortcomings, such as the limited sample size, in order to gain a better understanding of the potential uses of DTI in the study of patients with various WMD.

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There is no conflict of interest.

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