IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 2 Ser.3 (February. 2023), PP 14-36
www.iosrjournals.org

Localization of epileptogenic foci using diffusion tensor imaging (DTI)

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Abstract:
Introduction: *Diffusion tensor imaging (DTI) is a magnetic resonance (MR) imaging technique that measures the magnitude and direction of water diffusion along three principle eigenvectors (x, y, and z), as well as provides insight into the microstructure of both grey and white matter. Imaging in the field of epilepsy surgery remains an important tool in identifying regions where the seizure focus may present as a resectable area and is especially helpful in children with temporal lobe epilepsy.*
Materials and Methods: *The present study is a cross-sectional, observational study undertaken for the localization of epileptogenic foci using diffusion tensor imaging (DTI) in patients being referred to the department of Radiodiagnosis, NRI Medical College, and GH Chinnakakani. All the study patients were investigated on a 1.5-Tesla MRI.*
Results: *In our study of 50 patients, GTCS was observed in 48% of the patients. Conventional MRI revealed no abnormalities in 64% of the cases, 22% had ischemic changes, 10% had HIE, and 4% had a few T2 hyperintense foci. There is a significant difference in mean ADC and FA values in patients with seizure foci in hippocampal and parahippocampal regions, the internal capsule, SLF, ILF, and UF as per the t-test (P=0.000).*
Conclusions: *DTI was discovered to be sensitive to various microstructural changes associated with epilepsy. DTI can easily detect white matter changes in patients with MR imaging-negative epilepsy. We conclude that it is an important radiological tool in presurgical epilepsy evaluation and for surgical planning.*
Key Word: *DTI, white matter tracts, apparent diffusion coefficient (ADC), fractional anisotropy (FA), hippocampal and parahippocampal regions, internal capsule, superior longitudinal fasciculus (SLF), inferior longitudinal fasciculus (ILF), and uncinate fasciculus (UF).*

Date of Submission: 22-01-2023 Date of Acceptance: 05-02-2023

I. Introduction

Paroxysmal spells are frequently caused by central nervous system (CNS) events, psychiatric causes, or cardiac disturbances. Transient events with movements include syncope, convulsive syncope, convulsive concussion, rigors, sleep-related events, movement disorders, and psychogenic non-epileptic seizures. Epileptic seizures are one type of paroxysmal event [1]. An epileptic seizure is a brief occurrence caused by abnormally increased synchronous neuronal activity in the brain. Central nervous system (CNS) events, psychiatric causes, or cardiac disturbances are common causes of paroxysmal spells. Syncope, convulsive syncope, convulsive concussion, rigors, sleep-related events, movement disorders, and psychogenic non-epileptic seizures are examples of transient events with movements. Paroxysmal events include epileptic seizures[1].

A seizure is a brief period of abnormally increased synchronous neuronal activity in the brain. There are two types of classifications: partial and generalised. In a partial seizure, one area of the cortex is activated at the start, which may result in motor or sensory phenomena. Partiallyconvulsive seizures will quickly generalise and spread to all cortical areas. The onset of generalised seizures is caused by diffuse cortical activation. Partial-onset seizures with rapid secondary generalisation are the most common type of seizures in adults[2]. Complex partial seizures, which have dyscognitive characteristics, are frequently associated with altered consciousness. These can manifest as lip-smacking or mild amplitude extremity movements, or as isolated confusion. Epilepsy

is characterised by recurrent unprovoked seizures. Whether a first or recurring seizure is needed for diagnosis and treatment.

According to the World Health Organization (WHO), 80% of the 50 million people worldwide who have epilepsy are from developing countries. Epilepsy accounts for 0.5% of the global disease burden, accounting for 7,307,975 DALYs in 2005[3]. In India, there were over 10 million epileptic patients. It affects about 1% of the population[4]. Rural areas have a higher prevalence than urban areas. Conventional MRI with existing epilepsy protocol has a sensitivity of just over 50% in detecting epileptogenic foci. As a result, additional sequences such as diffusion tensor imaging (DTI) are required for an accurate epilepsy diagnosis.

DTI is a non-invasive MRI technique that provides information about the microstructure of white matter (WM). It aids in characterising the various orientation properties of the water-molecule diffusion process. To study pathological and normal brain areas, it generates parameters such as the apparent diffusion coefficient (ADC) and fractional anisotropy (FA). MR tractography is extremely useful in non-invasively detecting the trajectories of vital WM tracts in the brain. The current study sought to ascertain the role of DTI in detecting epilepsy in a rural Indian setting.

II. Materials And Methods

Study Design: Cross-sectional, observational study
Study Location: This was a tertiary care teaching hospital based study done in Department of Radiodiagnosis, at NRI Medical College & GH, Chinnakakani.
Study Duration: December 2021 to December 2022.
Sample size: 50 patients.
Sample size calculation:
The sample size is calculated as:
$N=Z^2PQ/E^2$,
N-samplesize,
P=0.01%,
E-Error: 3%,95% confidence limits,
N=43(minimum sample size). So, we included 50 patients in this study. All 50 patients provided consent for the study.
Subjects & selection method:The study population was drawn from patients who are referred to department of Radiodiagnosis, NRI Medical College and GH, Chinnakakani from December 2021 to December 2022.

INCLUSION CRITERIA:
1. Patients with epilepsy
2. Any gender.
3. Patients of any age
4. Patients who provided informed consent to participate in the study.

EXCLUSION CRITERIA:
1. Pregnant and lactating women
2. Patients with cardiac pacemakers, prosthetic heart valves, cochlear implants or any metallic implants(contraindications for MRI)
3. Patients having history of claustrophobia.
4. Patients with incomplete data
5. Patients with intracranial lesions

Procedure methodology :
The present study is a cross-sectional, observational study undertaken to localise the epileptogenic foci using DTI in patients who have been referred to the department of Radiodiagnosis, NRI Medical College, and GH, Chinnakakani.
All the study patients were investigated on1.5 Tesla GE signa Excite MRI system with a phased array head coil using conventional MRI sequences and DTI sequence.

Age, gender, conventional MRI findings, laterality of focus, final MRI Diagnosis with location of focus, mean FA and ADC values of hippocampus and para hippocampal regions, superior longitudinal fasciculus(SLF), inferior longitudinal fasciculus(IFL), uncinated fasciculus, internal capsule were assessed for all patients. Statistical tests were done using epi info software, Microsoft excel 2019.

Imaging protocol and analysis:

The scanning protocol is axial sections of T1, T2, FLAIR, DWI, SWI, and DTI, oblique and coronal T2 of the temporal lobe, oblique 3D T1, sagittal T2, and high-resolution thin sections of coronal T2 FLAIR.

DTI images were acquired in the axial plane with a spin echo planar imaging sequence. Diffusion-sensitive gradients are applied in 25 directions: The duration of the DTI sequence is 5 minutes and 19 seconds.

All DTI images were transferred to the workstation, where image reconstruction and post-analysis were done. Regions of interest (ROI) of the same size were kept on a color-coded FA map that is superimposed over isotropic T1WI over bilateral hippocampi, the anterior limb, genu, and posterior limb of the internal capsule, the frontal and occipital regions of the SLF, the temporal and occipital regions of the ILF, and the uncinate fasciculus. FA and ADC values from regions of interest were noted.

ROIs were kept on axial images at the foramen of Munroe for the anterior limb, genu, and posterior limb of the internal capsule. For frontal and occipital regions of SLF, ROIs were kept on axial images when the region was maximally seen. For the hippocampus, parahippocampal white matter and uncinate fasciculus coronal images were used. Parasagittal images help to locate ILF.

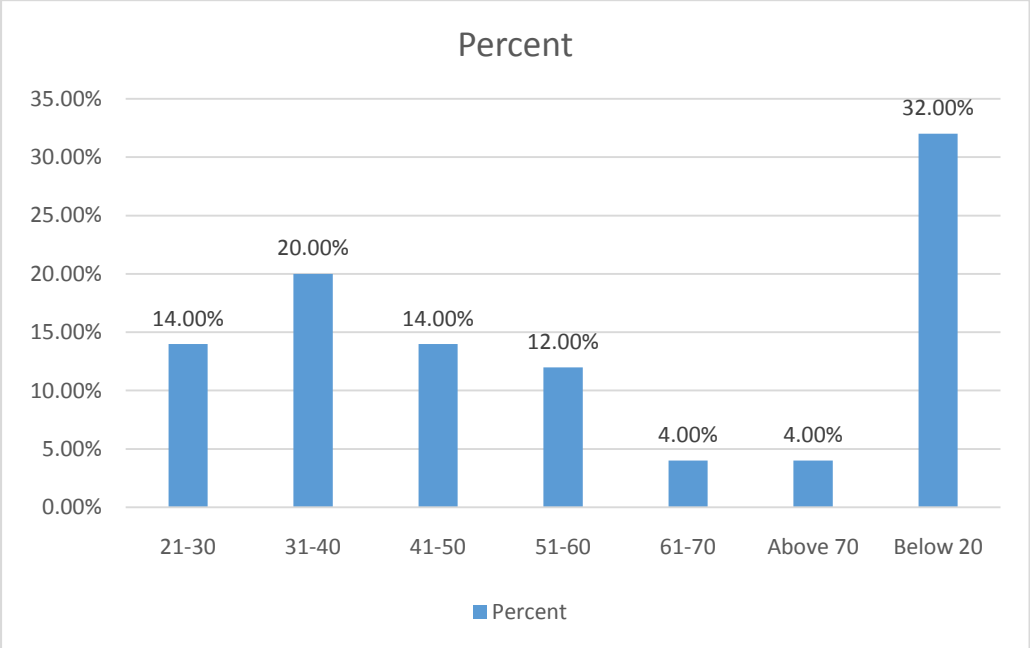
Statistical analysis: The data collected was entered into Excel 2019, and analysis was done using Excel and the software Epi Info. The results were expressed in the form of descriptive and inferential statistics. A probability value below 0.05 was considered statistically significant. Frequencies and percentages were also used. Continuous variables were calculated using the mean and SD. Categorical parameters were determined using the chi-square test. Numerical values were assessed using the T-test.

III. RESULTS

The current study included 50 patients with epilepsy.

Age group:32% patients were aged below 20 years. 20% were aged 31-40 years, 14% were aged 21-30 years, 14% were aged 41-50 years and 12% were aged 51-60 years.

Graph 1: Age group



Mean age:

The mean age was 32.3 years. Age ranged from 2 years to 78 years. The median age was 32 years.

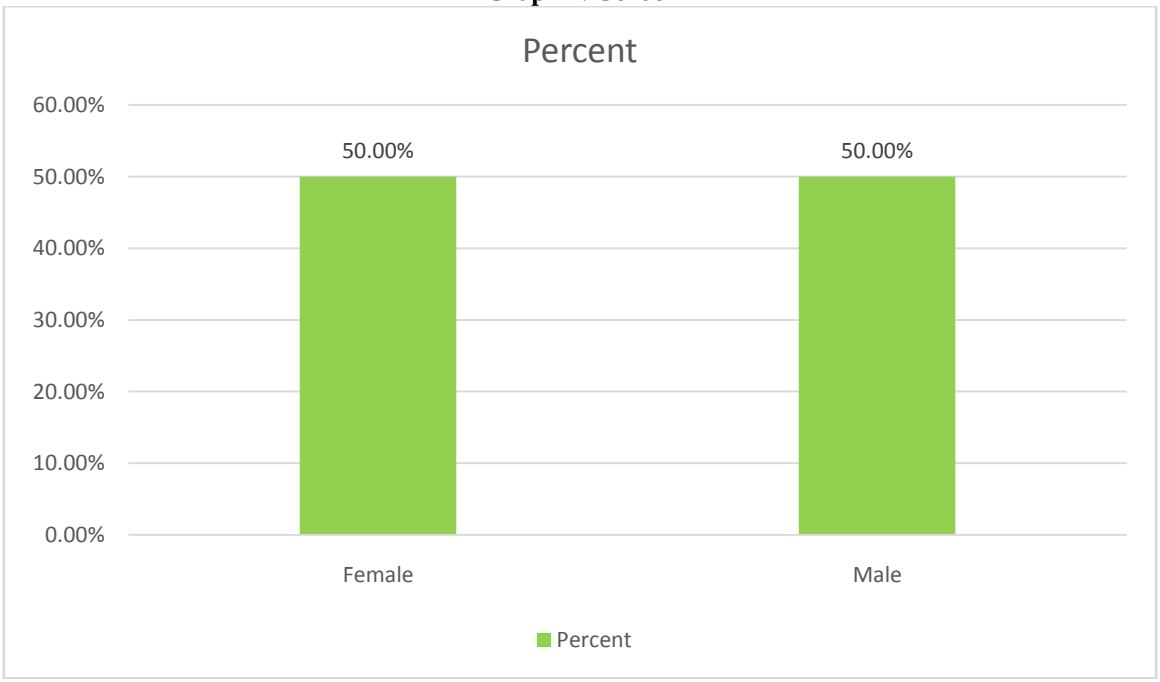
Table 2: Mean age and age range

Obs	Total	Mean	Variance	Std Dev
50.0000	1618.0000	32.3600	379.4596	19.4797

Minimum	25%	Median	75%	Maximum	Mode
2.0000	16.0000	32.0000	47.0000	78.0000	14.0000

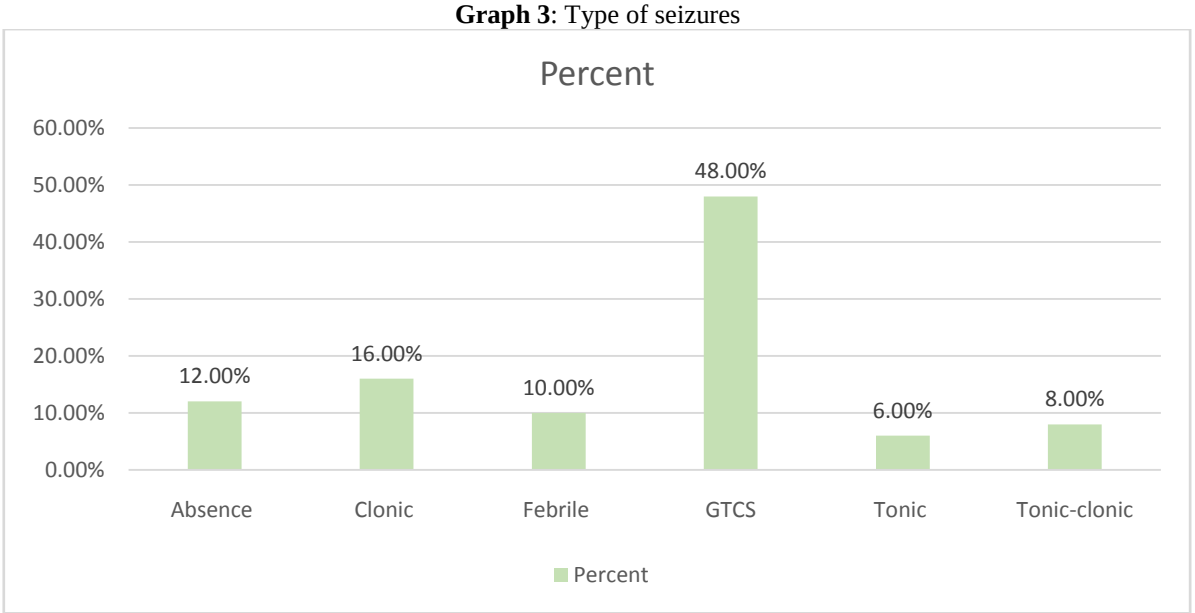
Gender:
This study had 50% males & 50% females. This indicates that there is no gender preponderance for epilepsy

Graph 2: Gender



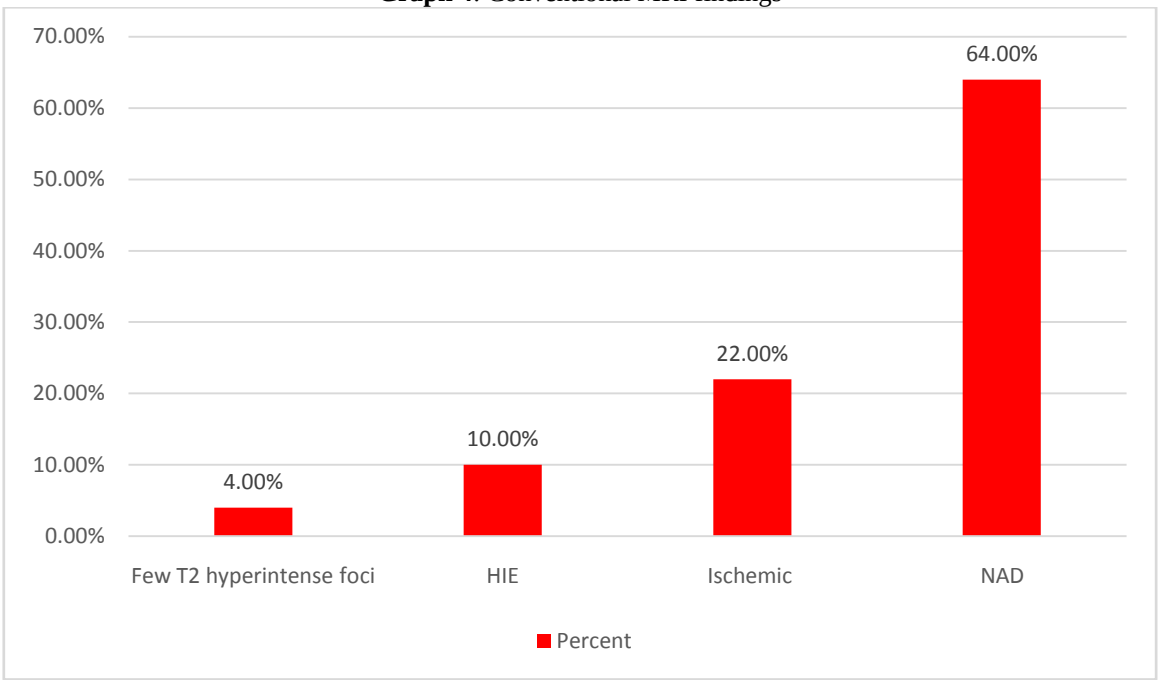
Type of seizures:
GTCs was seen in 48% of patients, clonicseizures were seen in 16% of patients, absence seizure were seen in 12% of patients, febrile seizures were seen in 10% of patients and tonic clonic seizures were seen in 8% of patients.

Graph 3: Type of seizures



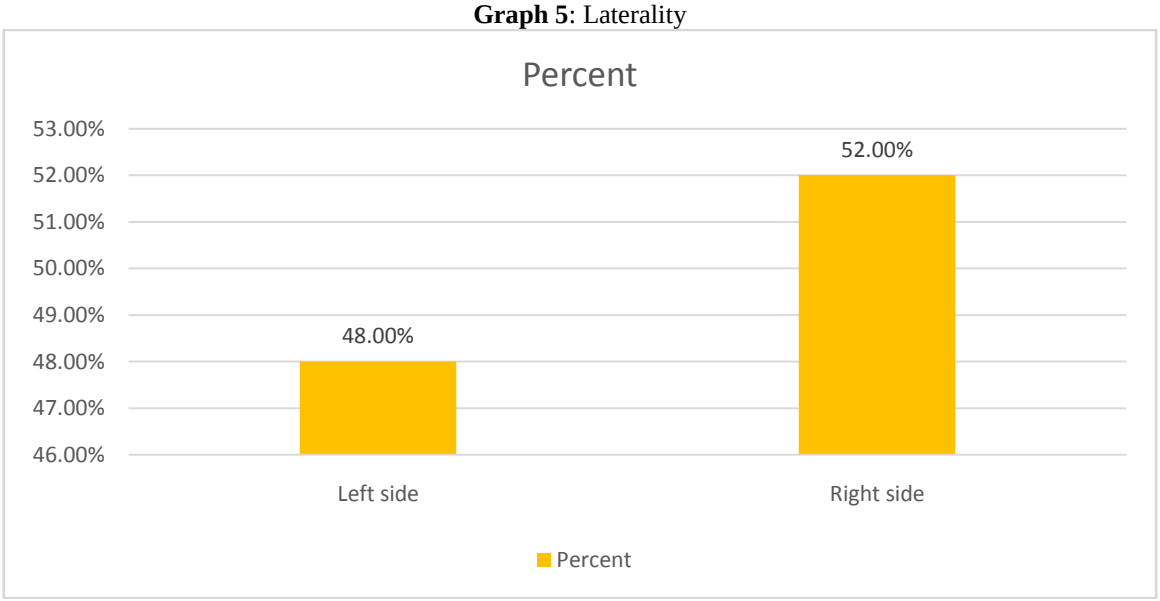
Conventional MRI:
64% had no abnormalities deducted from conventional MRI. 22% had Ischemic changes, 10% had HIE and 4% had FewT2 hyperintense foci in MRI.

Graph 4: Conventional MRI findings



Laterality:
52% patients had seizure focus on right side and 48% had on the left side.

Graph 5: Laterality

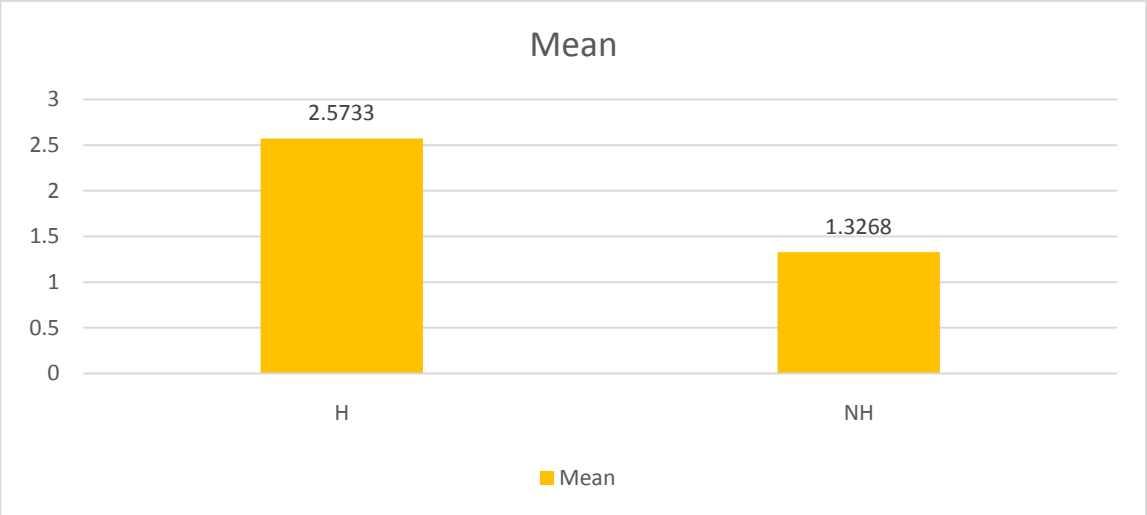


Mean ADC levels in Hippocampi:
There is a significant difference in mean ADC levels in patients with seizure foci in Hippocampal& Non-Hippocampal regions as per t test (P=0.000). The mean ADC is more in hippocampal region.

Table 1: Mean ADC levels- Hippocampi

MEAN ADC				
Group	Obs	Mean	Variance	Std Dev
H	9.0000	2.5733	0.0844	0.2905
NH	41.0000	1.3268	0.0440	0.2098
Method		t Value	Pr> |t|	
Pooled		15.03	0.0000	

Graph 6: Mean ADC hippocampi



Mean FA B/L hippocampi:

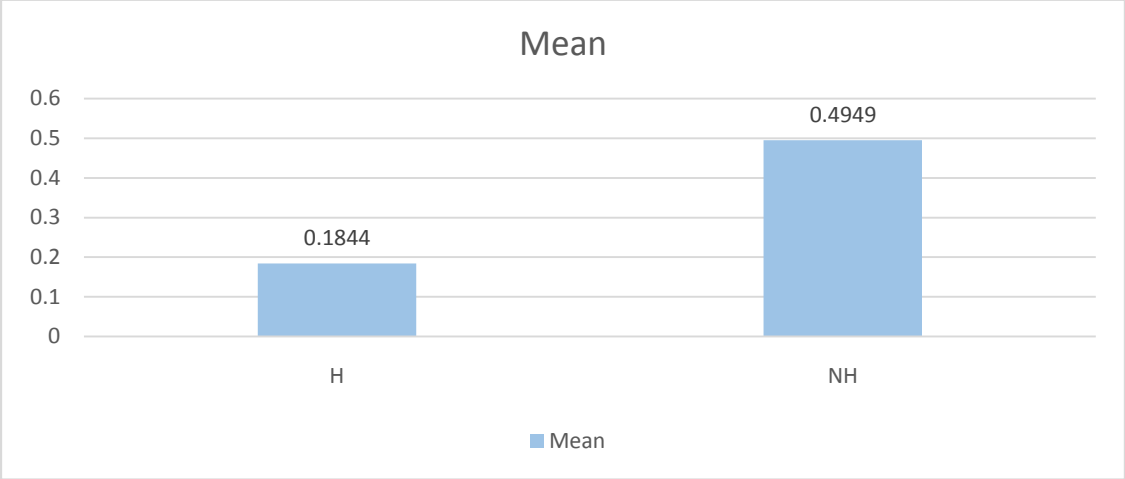
There is significant difference in mean FA in patients with seizure foci in Hippocampal & Non-Hippocampal regions groups as per t test (P=0.000). The mean FA is less in Hippocampal region

Table 2: Mean FA Hippocamp

Mean FA B/L				
Region	Obs	Mean	Variance	Std Dev
H	9.0000	0.1844	0.0031	0.0557
NH	41.0000	0.4949	0.0110	0.1051

Method	Variances	DF	t Value	Pr> |t|
Pooled	Equal	48	-8.55	0.0000

Graph7: Mean FA Hippocampi



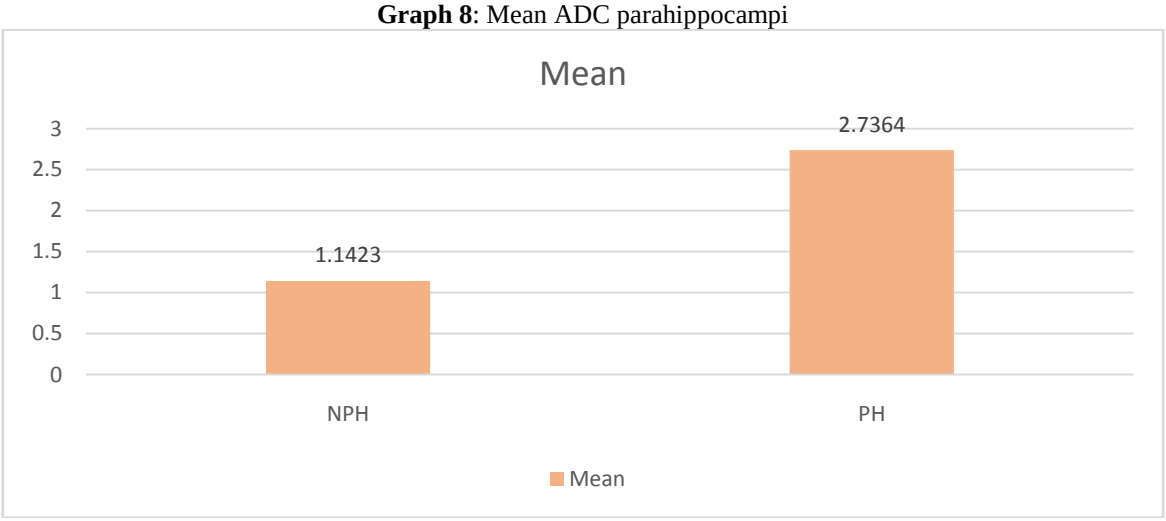
Mean ADC Parahippocampus region:
There is a significant difference in mean ADC in the patients with seizure foci in parahippocampal& Non-parahippocampal regions (P=0.000). The mean ADC was more in the pararahippocampal region in patients with seizures foci in the parahippocampal region.

Table 3: Mean ADC parahippocampi

Mean ADC PH				
Region	Obs	Mean	Variance	Std Dev
NPH	39.0000	1.1423	0.0443	0.2106
PH	11.0000	2.7364	0.0425	0.2063

Method	t Value	Pr> |t|
Pooled	-22.27	0.0000

Graph 8: Mean ADC parahippocampi

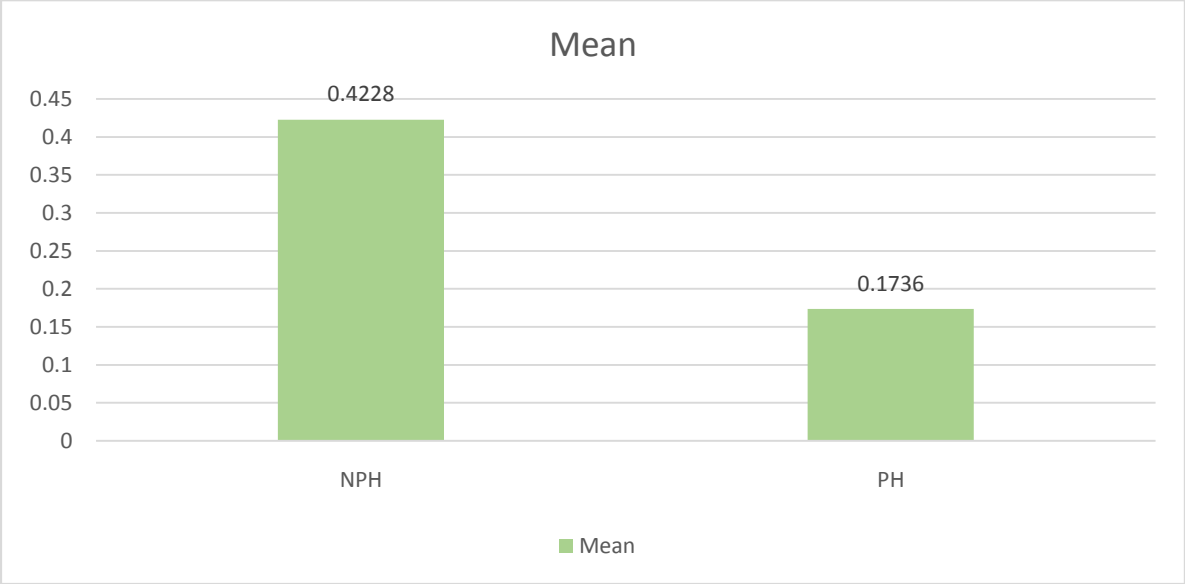


Mean FA PH:
There is a significant difference in mean FAinthe patients with seizure foci in parahippocampal& Non-parahippocampalregions as per t test (P=0.000).

Table 4: Mean FA in Parahippocampal area

MEAN FA- PH region					
Region	Obs	Total	Mean	Variance	Std Dev
NPH	39.0000	16.4900	0.4228	0.0288	0.1696
PH	11.0000	1.9100	0.1736	0.0017	0.0418
DF	t Value	Pr> |t|			
48	4.8	0.0000			

Graph 9: Mean FA in Parahippocampal



Mean ADC internal capsule

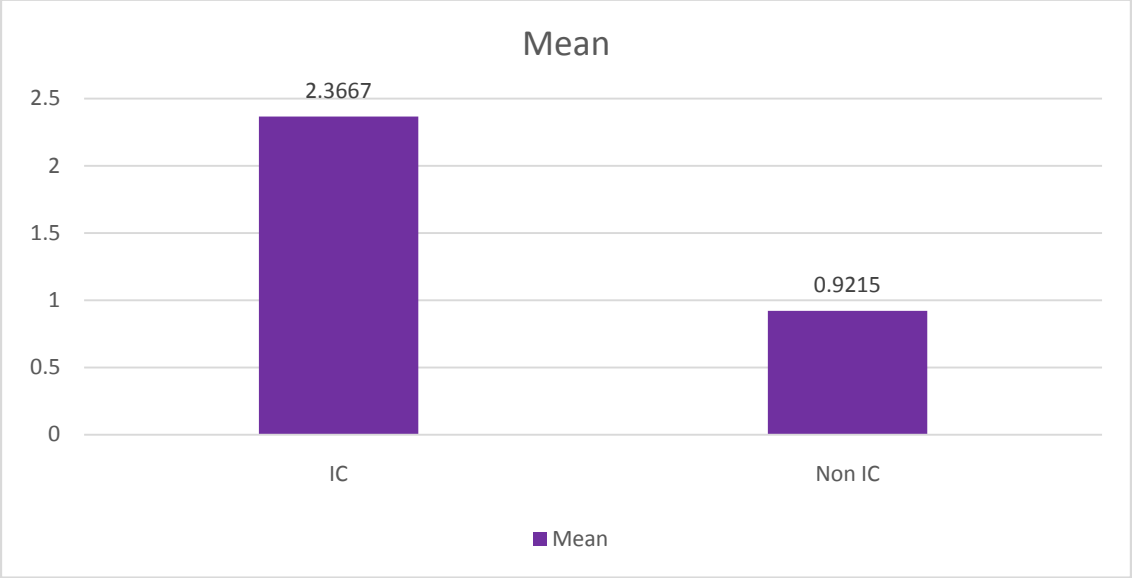
There is a significant difference in mean ADC in patients with seizure foci in internal capsule& non-internal capsule areas as per t test (P=0.000). The mean ADC was more in the internal capsule in patients with seizure foci in internal capsule.

Table 5: Mean ADC in internal capsule

Mean ADC internal capsule				
Region	Obs	Mean	Variance	Std Dev
IC	3.0000	2.3667	0.0533	0.2309
Non IC	47.0000	0.9215	0.0742	0.2725

DF	t Value	Pr> |t|
48	8.96	0.0000

Graph 10: Mean ADC in internal capsule



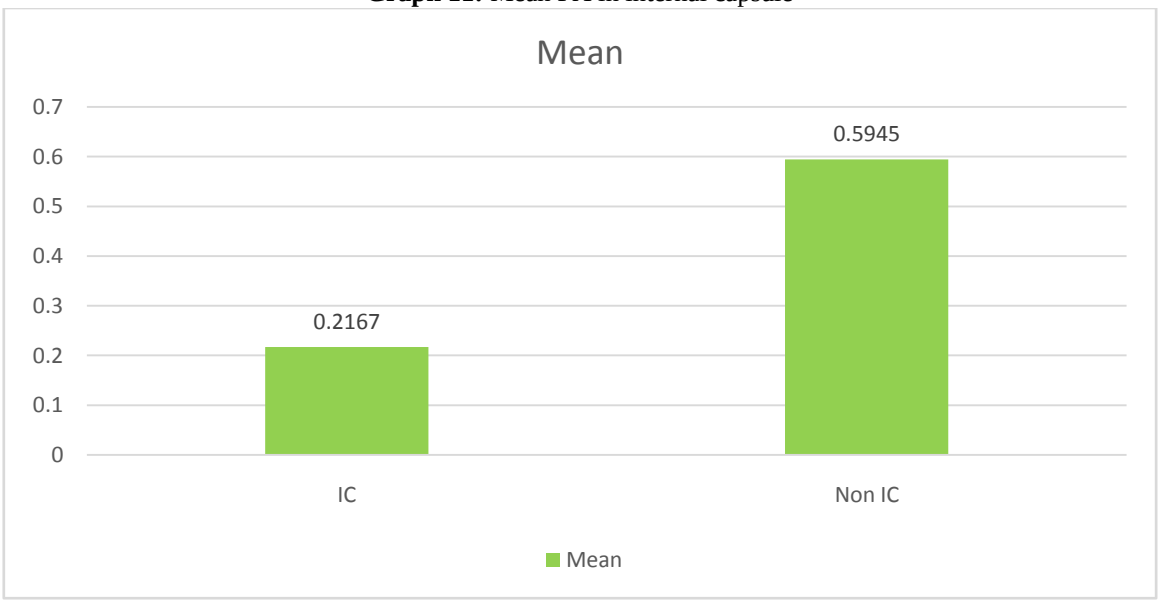
Mean FA internal capsule:
There is a significant difference in mean FA in patients with seizure foci in internal capsule& non-internal capsule areas as per t test (P=0.000).

Table 6: Mean FA in internal capsule

MEAN FA IC				
Region	Obs	Mean	Variance	Std Dev
IC	3.0000	0.2167	0.0001	0.0115
Non IC	47.0000	0.5945	0.0185	0.1362

DF	t Value	Pr> |t|
48	-4.76	0.0000
44.08	-18.03	0.0000

Graph 11: Mean FA in internal capsule



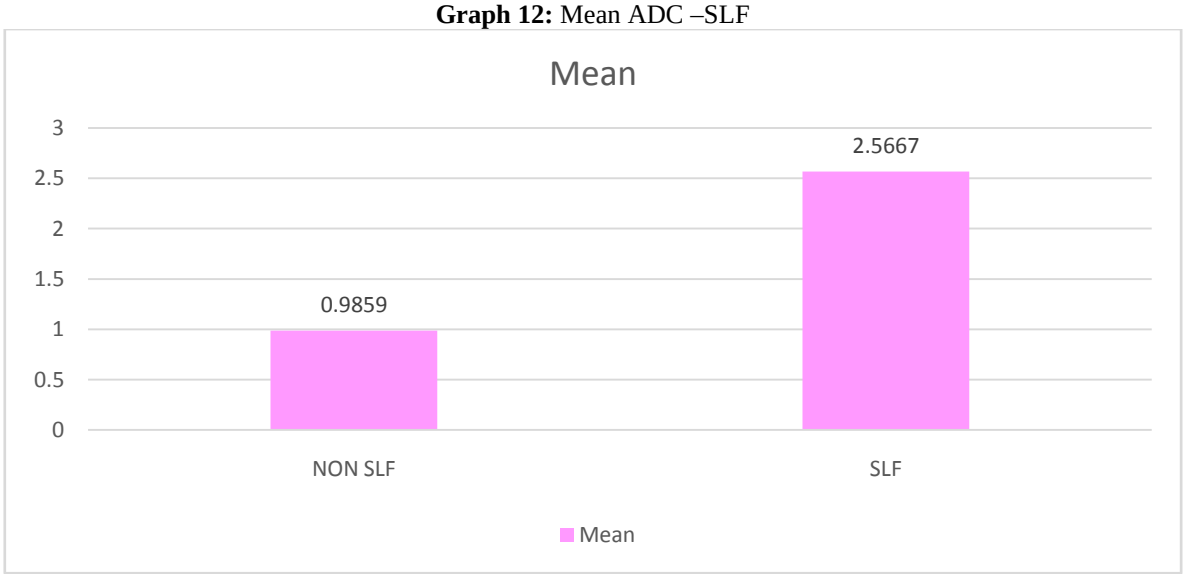
Mean ADC SLF:
There is a significant difference in mean ADC inpatients with seizure foci in SLF& Non SLF areas as per t test (P=0.000). The mean ADC in SLF region is more in patients with seizure foci in SLF.

Table 7: Mean ADC -SLF

MEAN ADC SLF				
Group	Obs	Mean	Variance	Std Dev
NON SLF	44.0000	0.9859	0.0890	0.2984
SLF	6.0000	2.5667	0.1307	0.3615

DF	t Value	Pr> |t|
48	-11.89	0.0000

Graph 12: Mean ADC –SLF



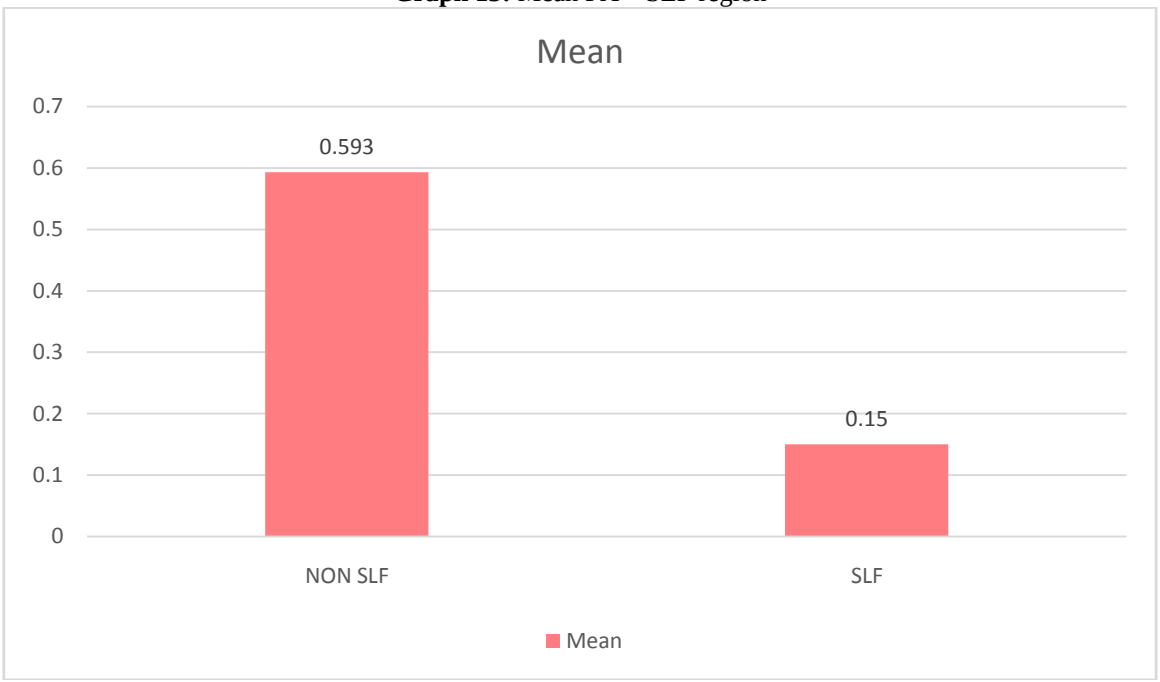
Mean FA SLF
There is significant difference in mean FA in patients with seizure foci in SLF& Non SLF areas as per t test (P=0.000). The mean FA in SLF region was less in patients with seizure foci in SLF.

Table 8: Mean FA – SLF region

MEAN FA SLF				
Region	Obs	Mean	Variance	Std Dev
NON SLF	44.0000	0.5930	0.0205	0.1432
SLF	6.0000	0.1500	0.0002	0.0155

DF	t Value	Pr> |t|
48	7.50	0.0000

Graph 13: Mean FA – SLF region



Mean ADC ILF

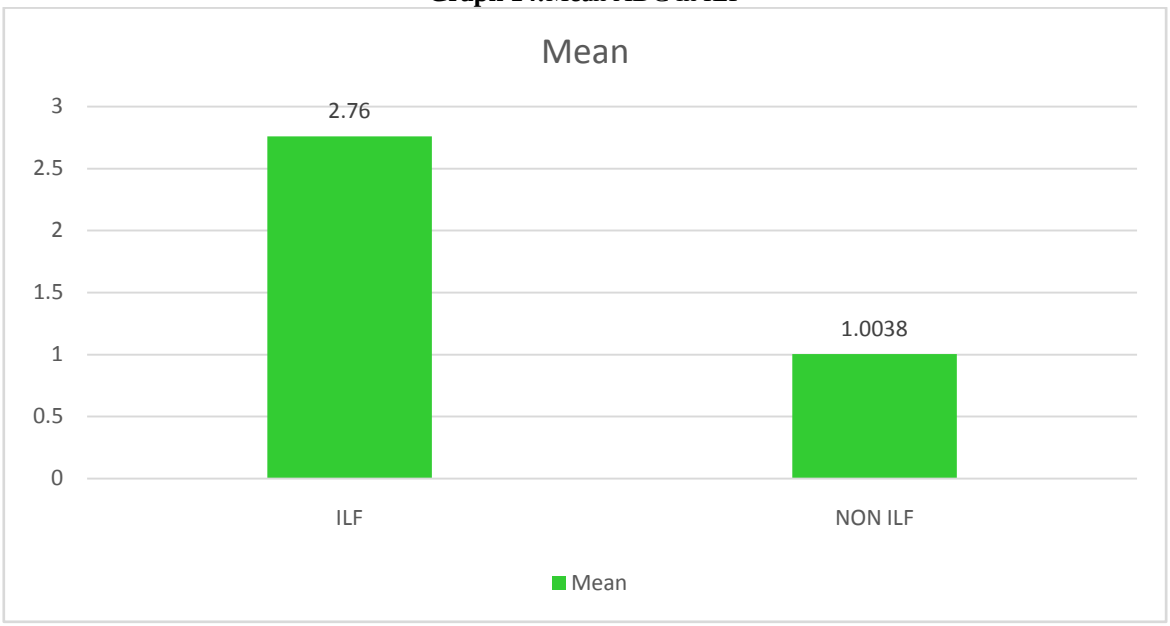
There is significant difference in mean ADC in patients with seizure foci in ILF& Non ILF areas as per t test (P=0.000). Mean ADC in ILF is more in patients with seizure foci in ILF.

Table 9: Mean ADC in ILF

MEAN ADC ILF				
Region	Obs	Mean	Variance	Std Dev
ILF	5.0000	2.7600	0.1430	0.3782
NON ILF	45.0000	1.0038	0.0757	0.2751

DF	t Value	Pr> |t|
48	13.07	0.0000

Graph 14: Mean ADC in ILF



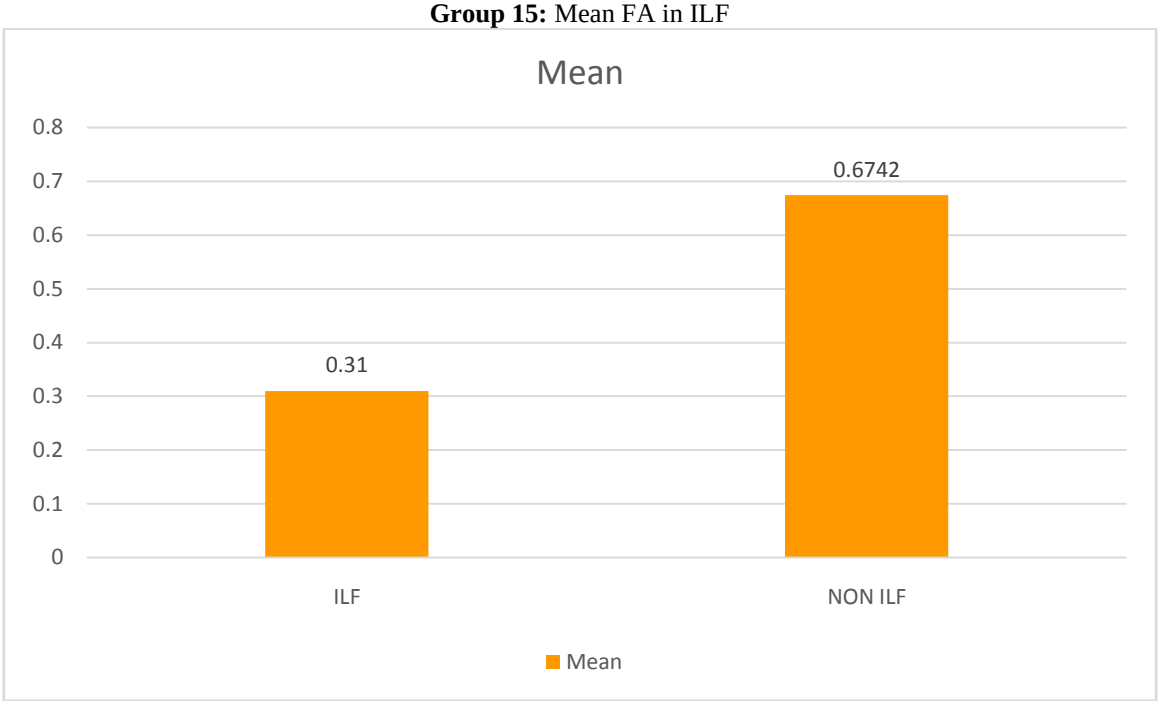
Mean FA ILF:
There is significant difference in mean FA in patients with seizure foci in ILF& Non ILF areas as per t test (P=0.000).

Table 10: Mean FA- ILF

Mean FA ILF				
Group	Obs	Mean	Variance	Std Dev
ILF	5.0000	0.3100	0.0232	0.1523
NON ILF	45.0000	0.6742	0.0287	0.1695

DF	t Value	Pr> |t|
48	-4.60	0.0000

Group 15: Mean FA in ILF



Mean ADC UF:

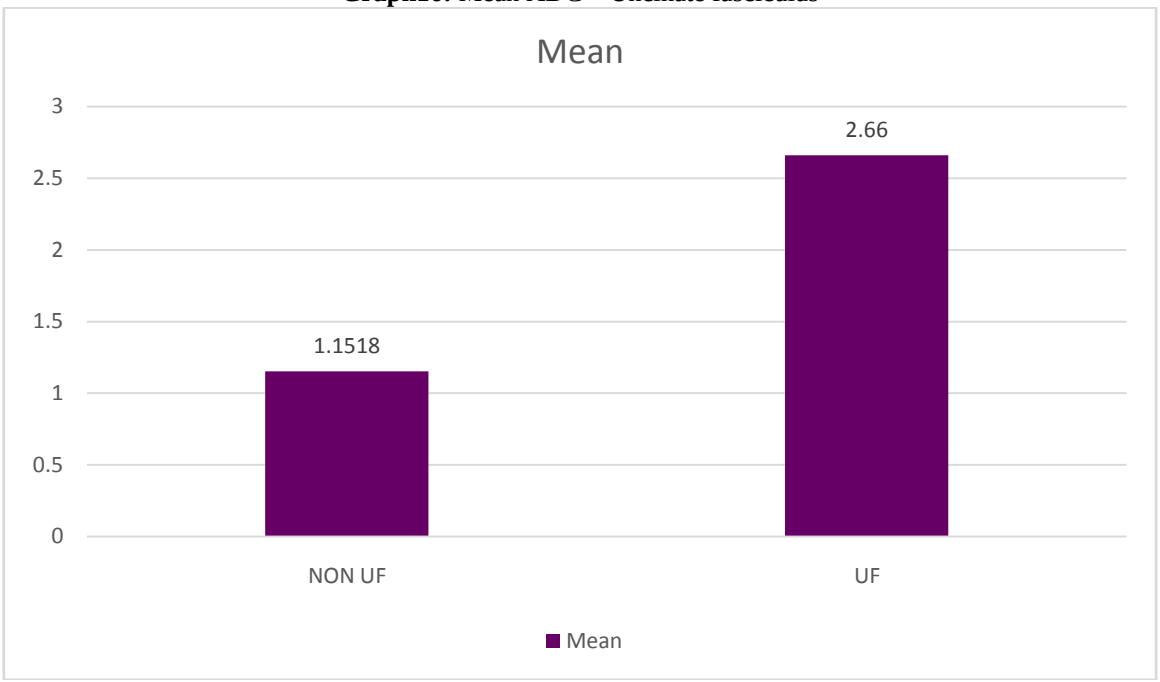
There is significant difference in mean ADC in patients with seizure foci in UF and non UF &regions as per t test (P=0.000). Mean ADC in UF patients was more is more in patients with seizure foci in UF.

Table 11: Mean ADC – Uncinate fasciculus

MEAN ADC UF				
Region	Obs	Mean	Variance	Std Dev
NON UF	45.0000	1.1518	0.0571	0.2389
UF	5.0000	2.6600	0.0180	0.1342

DF	t Value	Pr> |t|
48	-13.79	0.0000

Graph16: Mean ADC – Uncinate fasciculus



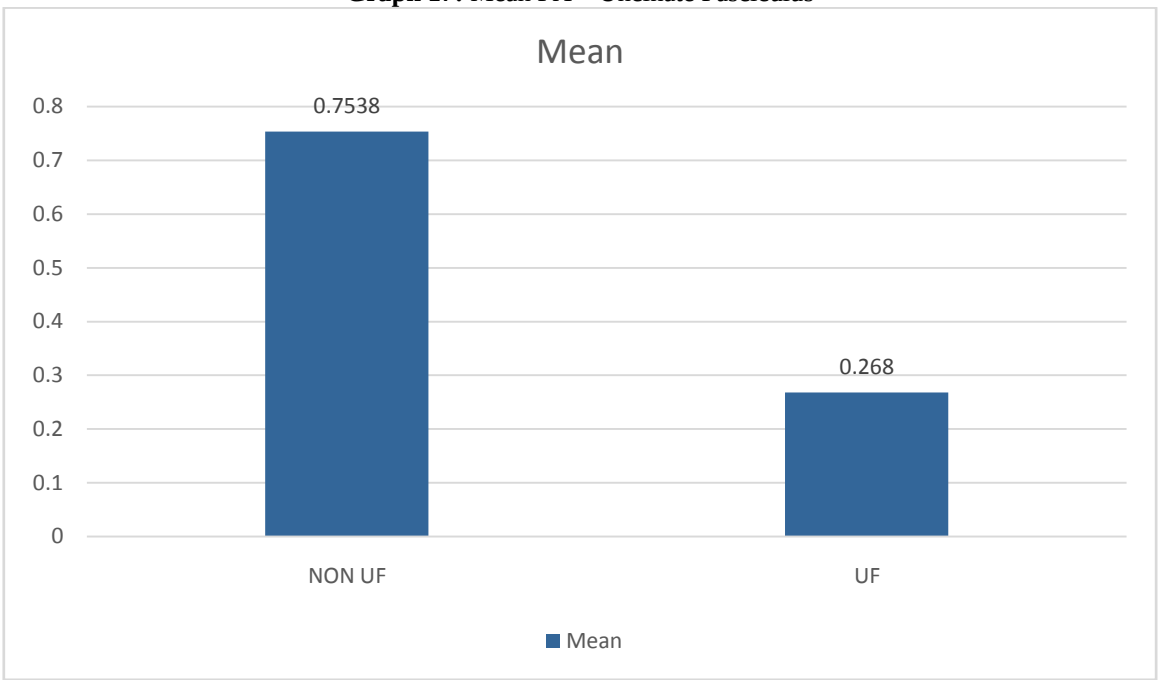
Mean FA UF:

There is significant difference in mean FA in patients with seizure foci in UF and non UF areas, per t test (P=0.000). The mean FA was less in UF is more in patients with seizure foci in UF

Table 12: Mean FA – Uncinate Fasciculus

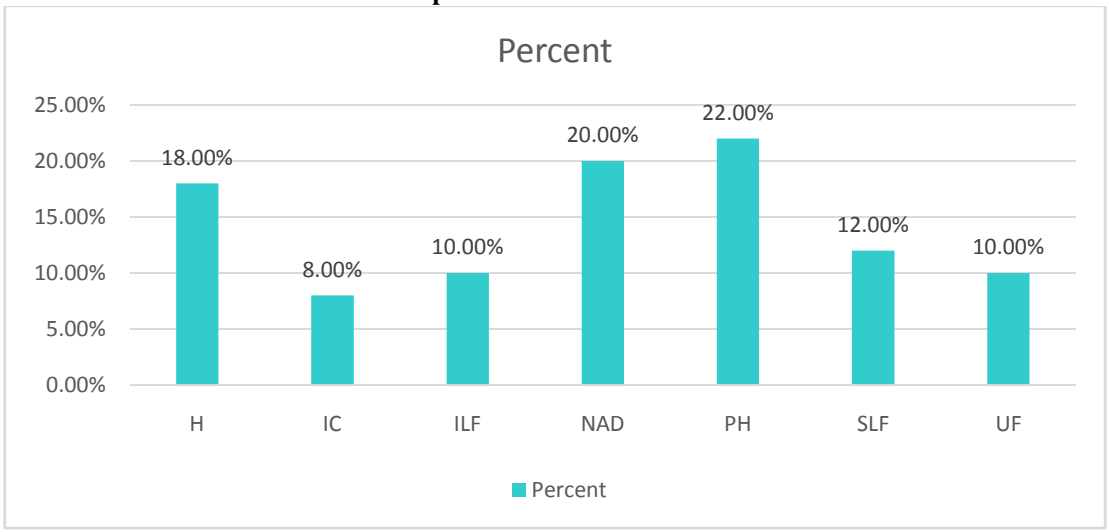
Mean FA- UF			
Region	Obs	Mean	Std Dev
NON UF	45.0000	0.7538	0.1263
UF	5.0000	0.2680	0.0743
	t Value	Pr> |t|	
	8.39	0.0000	

Graph 17: Mean FA – Uncinate Fasciculus



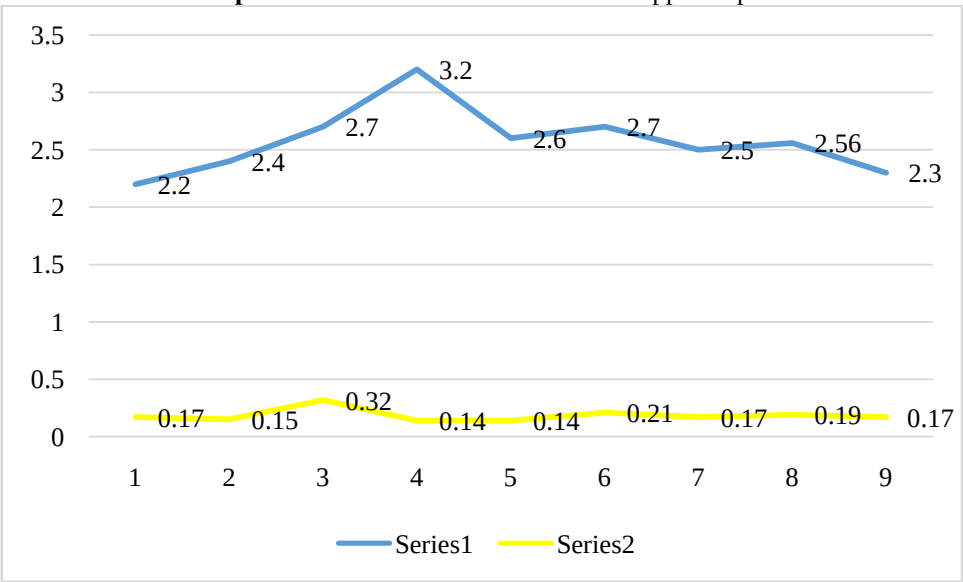
Seizure focus final MRI: Seizure foci in parahippocampal region was seen in 22% patients in final MRI, 18% in hippocampi, 12% in SLF region, 10% in uncinate fasciculus, 10% in ILF. No abnormalities were seen in 20% patients.

Graph 13: Seizure foci in MRI



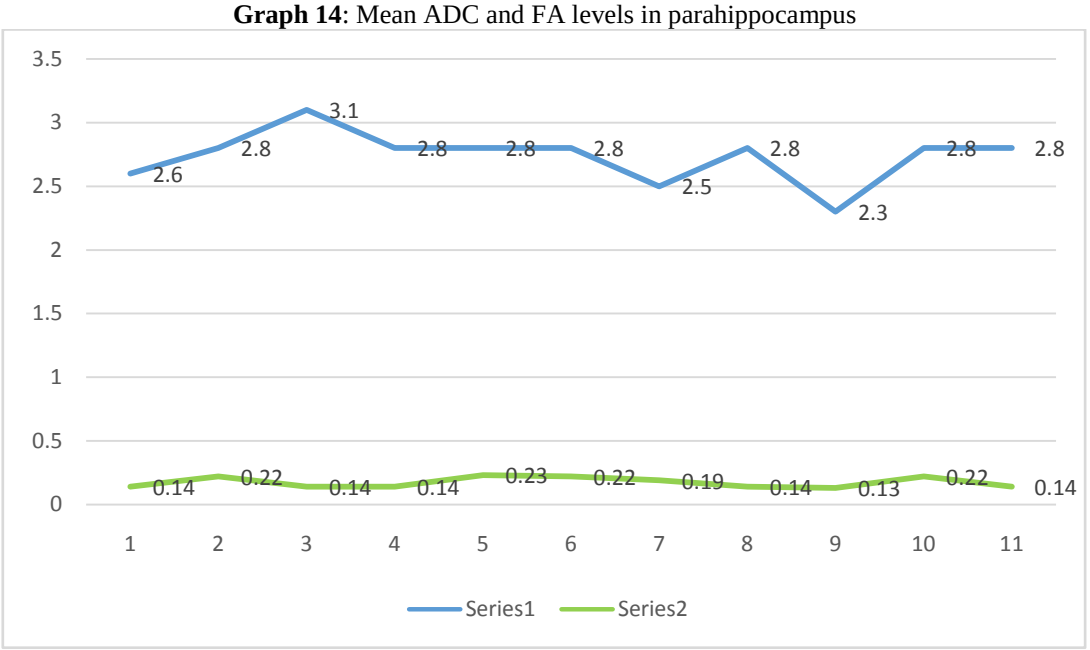
Mean ADC levels and FA levels in patients with seizure foci in hippocampus region:

Graph 19: Mean ADC and FA levels in Hippocampus



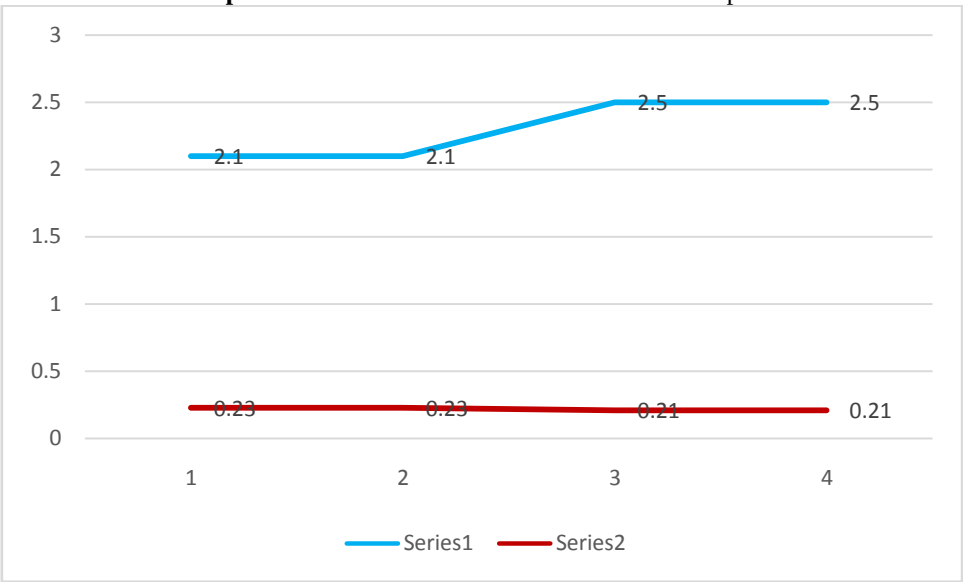
Mean ADC levels and FA levels in patients with seizure foci in parahippocampus region.

Graph 14: Mean ADC and FA levels in parahippocampus



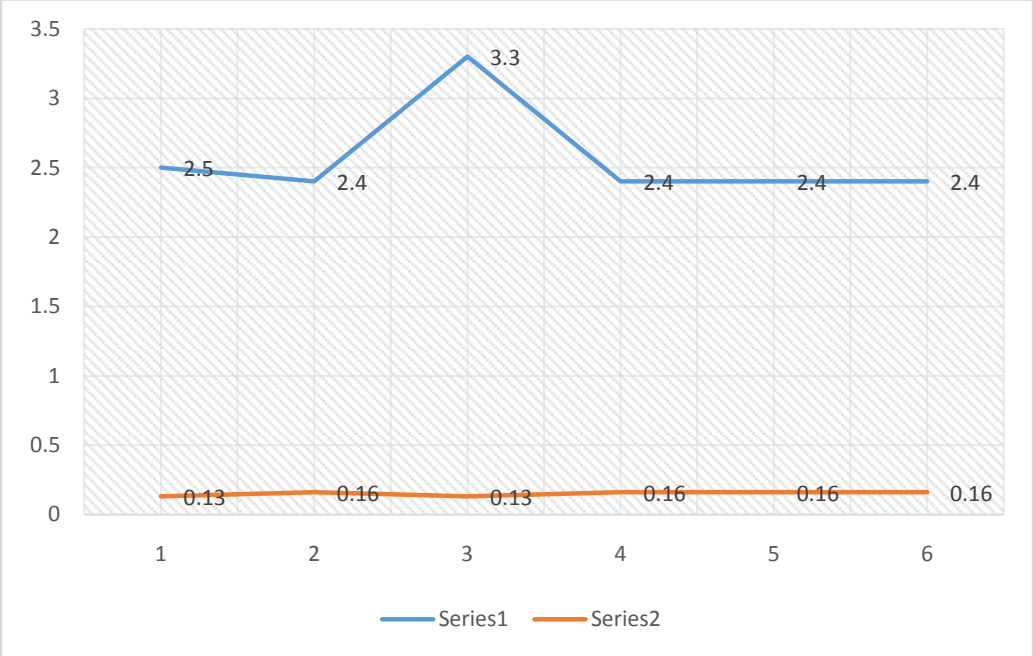
Mean ADC levels and FA levels in patients with seizure foci in the internal capsule region

Graph 21: Mean ADC and FA levels in internal capsule



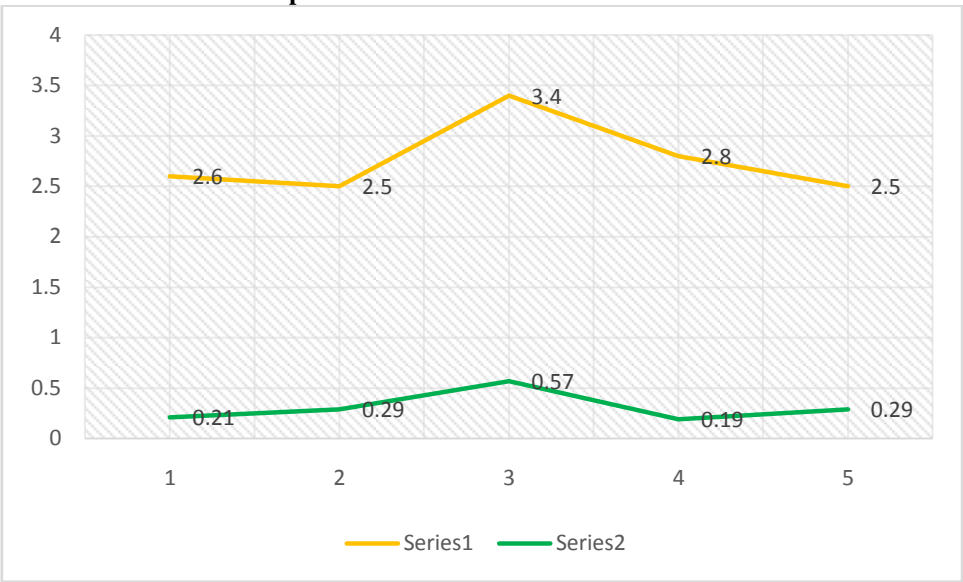
Mean ADC levels and FA levels in patients with seizure foci in SLF.

Graph 22: Mean ADC and FA levels in SLF



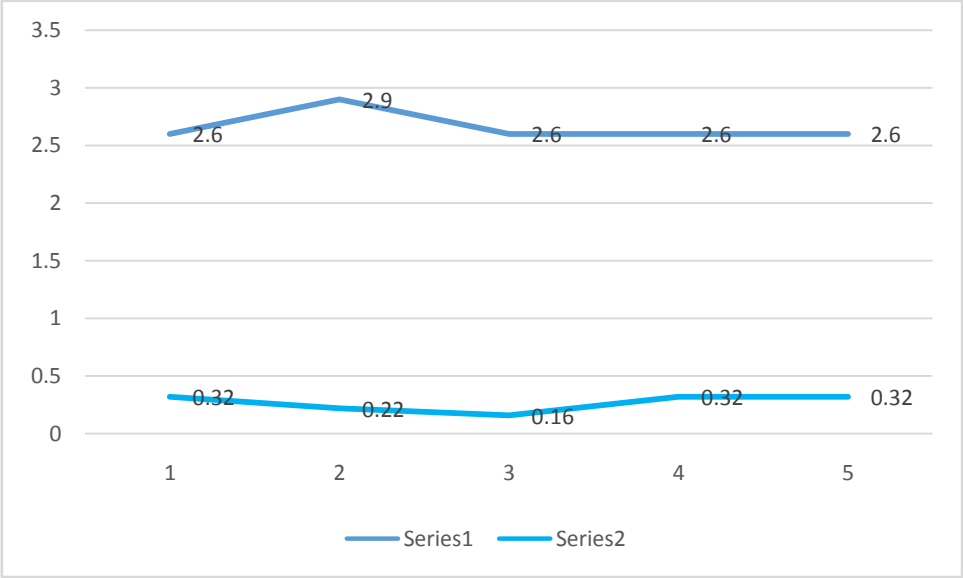
Mean ADC levels and FA levels in patients with seizure foci in ILF.

Graph 23: Mean ADC and FA levels in ILF



Mean ADC levels and FA levels in patients with seizure foci inuncinate fasciculus

Graph 24: Mean ADC and FA levels in UF



IV. Discussion

Seizures can be provoked or unprovoked. Provoked seizures, also known as acute symptomatic seizures, are caused by electrolyte imbalances, head injury, infections, vascular anomalies, tumours, and other factors. Epilepsy is a medical condition characterised by recurrent unprovoked seizures. It is critical for accurate diagnosis and treatment to know whether a first or recurring seizure is provoked or unprovoked. Other than seizures, idiopathic epilepsy has no symptoms. Seizures that are cryptogenic are those that are symptomatic of an underlying brain disorder but lack proper proof of the underlying cause [4]. Status epilepticus is an epileptic emergency. Status epilepticus is defined as a single generalised seizure lasting more than five minutes or a series of generalised seizures with no return of full consciousness.

DTI is a DWI variant that uses tissue water diffusion rate to generate images. DTI is being increasingly studied and used in clinical practise to assess various CNS disorders and brain lesions. DWI was first used on humans in 1986, and it has since become the gold standard in identifying acute strokes [5-7]. It is a relatively new method for detecting and examining the composition, orientation, and integrity of WM bundles, which cannot be determined optimally using conventional MRI [8–9]. It accomplishes this by quantifying the random motion of water molecules using Brownian motion and associating the degree of diffusion with different neural compartments.

FA is higher in white matter because water diffusion parallel to fibre tracts is less restricted than diffusion perpendicular to fibre tracts. The depiction of WM tracts is aided by brain fibre tractography (BFT) using FA and other diffusion data. The comparison of healthy and diseased fibre tracts aids in the quantification of white matter changes caused by damage[10-11]. DTI and tractography were now being used more frequently in the study of epilepsy, and they revealed various diffusion changes in grey and WM tissue [12–13]. Subcortical structures such as the amygdala, hippocampus, and thalamus have higher mean diffusivity and lower FA on the ipsilateral side of seizure focus.

The ultimate goal of epilepsy neuroimaging is not only to detect epileptogenic lesions, but also to confirm seizure lateralization and plan for surgery, as well as to provide information on cause and pathophysiology[14].

Nermeenet et al. [15] did a study to evaluate the role of DTI in diagnosing TLE. Their prospective study included 40 patients. TLE affected 20 patients, while the remaining 20 were normal. All patients underwent a traditional MRI examination followed by DTI and tractography. EEGs were taken from 36 patients in order to confirm the clinical diagnosis and determine seizure foci lateralization. Four patients were lost to follow-up. In our study, EEG assessment was not done as part of the study. EEG results were compared with MRI findings.
Taking a cutoff value of FA of 0.014, 28 patients with FA differences above 0.014 were considered DTI positive for abnormalities of the hippocampus, and 12 patients had a lower value and were considered DTI negative. The FA differences between both hippocampi were significantly greater compared to the control group. The authors concluded that DTI can identify hippocampal abnormalities even in subjects with normal conventional MR. It helps improve diagnostic accuracy before surgery for epilepsy.
Shaimaet al.[16] showed that there were abnormal DTI parameters (reduced FA and raised DC) detected in most of the WMT (p 0.001) among cases with epilepsy, similar to the current study findings.
In our study, seizure foci were found in 22% of patients in the parahippocampal region, 18% in the hippocampi, 12% in the SLF region, 10% in the uncinate fasciculus, and 10% in the ILF, according to our findings. No abnormalities were seen in 20% of patients.

V. Conclusion

DTI was discovered to be sensitive to various microstructural changes associated with epilepsy. DTI can easily detect white matter changes in patients with MR imaging-negative epilepsy. Advanced diffusion models have the potential to provide more quantitative information about crossing fibres and tissue microstructure, as well as strengthen microstructural associations with cognition in epilepsy. Because no single neuroimaging modality is without limitations, multimodal imaging studies that combine data from structural, functional, and diffusion imaging can provide a better understanding of network dysfunction in epileptic patients. We conclude that it is an important radiological tool in presurgical epilepsy evaluation and surgical planning.

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Dr. Husha Priya Laasya Bolla, et. al. "Localization of epileptogenic foci using diffusion tensor imaging (DTI)." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 22(2), 2023, pp. 14-36.