Role of Diffusion-Weighted and Contrast Enhanced MRI Brain in the Evaluation of Paediatric Epilepsy

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Abstract

Background: Epilepsy is a disease that is distinguished by enduring proclivity to produce epileptic seizures as well as neurobiological, cognitive, psychological, & social consequences of this situation.

Objectives: to identify & characterize lesions resulting epilepsy in children (zero-fifteen years) & to determine the frequency of etiological factors responsible for epilepsy in children (zero-fifteen years) using MRI brain.

Patients and methods: Qena University Hospital, South Valley University, Qena, Egypt, hosted this prospective cohort research. This research was shown on 50 children with Epilepsy in the duration between January 2021 till January 2022.

Results: Cortical malformation disorders were found in 11 patients (22%), infective and inflammatory lesions in 8 patients (16%), vascular lesions in 4 patients (8%), phakomatosis in 5 patients (10%), white matter disorders in 4 patients (8%), neoplastic lesions in 6 (12%). ADC significance was at a cutoff value of 2.23 x10-3 mm2/s for identifying abnormality, with a sensitivity of 95percent & precision of 98%, with PPV of 99.6percent & NPV of 78.9%,

Conclusion: There was an agreement between MRI and EEG findings. According to MRI, the most common findings were cortical malformation disorders followed by Infective and inflammatory lesions. Due to its high diagnostic yield in identifying epileptogenic substrates, multiplanar capability, & absence of ionizing radiation, MRI is indeed the initial examination of choice in seizure studied cases.

Keywords: Diffusion-Weighted; Contrast Enhanced; MRI; Brain; Epilepsy; Children.

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DOI: 10.21608/SVUIJM.2022.158921.1397

Received: 2 August, 2022.

Revised: 1 September, 2022.

Accepted: 6 September, 2022.

Published: 16 May, 2024

Cite this article as: Ghada M.Abdelrazek, Ali Helmi Bakri, Olivia Adel Melad Ebied.(2024). Role of Diffusion-Weighted and Contrast Enhanced MRI Brain in the Evaluation of Paediatric Epilepsy. *SVU-International Journal of Medical Sciences*. Vol.7, Issue 1, pp: 809-818.

Introduction

Epilepsy is characterized by at least 2 unprovoked seizures happening more than twenty-four hours apart, based on the International League against Epilepsy Classification of Epilepsies in 2017. **(Gastaut et al., 1964**)

International League against Epilepsy Categorization of Epilepsies has been revised to reflect our progress in knowledge of epilepsies & their underlying mechanisms in the years since the last ratified classification in 1989.

It introduces 3 levels, beginning with seizure type, which supposes the studied case is experiencing epileptic seizures as described by the new 2017 ILAE Seizure Classification. Following seizure type diagnosis, the next step is epilepsy type diagnosis, which includes focal epilepsy, generalized epilepsy, merged generalized & focal epilepsy, & unknown epilepsy group. 3rd level is epilepsy syndrome, which occurs when specific Syndromic diagnosis is possible. New classification combines etiology at each stage, emphasizing the importance of considering aetiology at each stage of diagnosis because it frequently has important cure effects **(Gastaut et al., 1969**).

Approximately five percent of children are at risk of having a seizure, & half of them have their first seizure in infancy. Incidence is higher during the neonatal period (nearly one percent in term & twenty percent in preterm). Epilepsy is a condition in which seizures occur on regular basis from within. The lifetime occurrence of epilepsy is three percent, with more than half of cases beginning in childhood **(Kalra et al., 2006**).For seizure activity, electroencephalogram & neurosonogram are frequently used as initial diagnostic workup. They are non-invasive & do not expose studied cases to radiation. Although computed tomography is useful in detecting calcific foci, it carries the risk of radiation exposure **(Gaillard et al., 2009**).

So, MRI is an important non-invasive tool for the evaluation of pediatrics with epilepsy that provides two pieces of critical information: a potentially epileptogenic brain abnormality and its surrounding anatomy. The soft tissue contrast provided by MRI makes it sensitive to small cortical lesions. In addition, the whole-brain coverage allows for the examination of lesion location in relationship to the eloquent cortex. It has more benefits in soft tissue characterization, excellent grey white matter diversity, the status of myelination & finding of focal structural brain lesions **(Scott et al., 2009**).

Basic MRI of the brain, when quickly available & in the context of clinical stability, can provide even more detail & adequately evaluate explained possible causative entities **(Gulati et al., 1991**).

Diffusion-weighted MRI (DWI) uses MRI sequences sensitive to the diffusion of water molecules in brain tissue and can be used to assess white matter architecture and microstructure. In the brain, the diffusion is restricted by intracellular and extracellular boundaries, with myelin being the main barrier. As such, the information contained in DWI images can guide algorithms that approximate and visualize white matter tracts in the brain by following pathways of unhindered water diffusion **(Levin et al., 2015**).

The addition of paramagnetic contrast agent gadopentetate dimeglumine enhanced the precision of cranial MRI diagnosis. It improves the recognition rate of certain intracranial lesions, particularly vascular lesions & those affecting meninges. It enhances radiologic specificity substantially, especially in identifying the extent & nature of certain neoplasms & distinguishing aggressive from benign procedures **(Cendes et al., 2013**).

The goals of the research are to identify & measure lesions resulting in epilepsy in children (zero-fifteen years old) & to determine the frequency of causes responsible for epilepsy in children. (0 - 15years) using MRI brain.

Patients and methods

This potential cohort research was shown in Qena university hospital, South Valley University, Qena, Egypt on a total of 50 children with Epileps the duration between January 2021 till January 2022.

Study subjects

The study included all pediatric studied cases (from zero-15 years) who existed with epilepsy

Methods

Studied cases were exposed to:

- Patient history & clinical test.
- brain MRI with diffusion-weighted and post-contrast imaging
- Investigations:
  Including
  1- CBC
  2- Random Blood Sugar
  3- Serum Na^+, K^+, calcium, Magnesium
  4- EEG
  5- initial metabolic screening according to clinical presentation +/- CSF

This study has been given approval by the Ethics Committee of Faculty Of Medicine, south valley University, Qena, Egypt. (**Ethical approval code is** SVU-MED-RAD028-1-21-3-154).

Statistical Analysis

All data were collected, tabulated, & statistically assessed using SPSS twenty-two for Windows (SPSS Inc., Chicago, IL, USA) & MedCalc thirteen for Windows (MedCalc Software bvba, Ostend, Belgium).

Every statistical comparison used a two-tailed significance test. P-values below 0.05 indicate a significant difference, those above 0.001 greater important variations , and those above 0.05 non-important variation. Statistical Package for Social Sciences version twenty-one will be used to analyze data just like follows:

• Quantitative data are described as average & range.

• Quantitative data is described as numbers & percentages.

• Chi-Square test compares qualitative parameters.

•Once suitable, data will be statistically presented in terms of mean standard deviation, median & range, & frequencies & percentages.

For associating categorical data, Chi-square (x2) test will be done.

Results

Patients aged between 0.17 to 15 years with a mean weight of 41.52 kg. 58% of the patients were males.(**Table.1)**

The mean duration of epilepsy is 1.36 years. 20% of the patients had a history of previous febrile convulsions, **(Table.2)**

38 patients (76%) had abnormal EEG and 22% had abnormal CSF,**(Table.3).**

The most prevent diagnosis was leukodystrophy (14%) followed by ventriculitis (10%). While normal was found in 18% of the patients,**(Table.4)**

This table shows that the majority of feastures on MRI was hypointense in T1(72%), hyperintense in T2/FLAIR(78%), non enhancing(74%) ,facilitated in DWIs(68%), **(Table.5)**

This table shows that cortical malformation disorders were found in 11 patients (22%), infective and inflammatory lesions in 8 patients (16%), vascular lesions in 4 patients (8%), phakomatosis in 5 patients (10%), white matter disorders in 4 patients (8%), neoplastic lesions in 6 (12%), **(Table .6)**

The mean ADC value was 2.63 x10-3 mm2/s among the studied patients, **(Table .7)**

ADC rate was minor in abnormalities associated with normal patients, **(Table .8)**

Table 1. Demographic characteristics of studied cases

Variables		***Patients (n=50)***
Years old *Mean± SD* *Range*		5.76 ± 4.82 0.17 – 15
Sex	*Male*	29 (58%)
	Female	21 (42%)
Weight *(kg)* *Mean± SD*		41.52 ± 15.94

Table 2. Clinical characteristics of studied patients

Variables	***Patients (n=50)***
Duration of epilepsy *(years)* *Mean± SD*	1.36 ± 0.967
History of previous	10 (20%)

Febrile convulsions	

Table 3. Clinical findings of studied patients

Variables	***Patients (n=50)***
EEG	
Normal	12 (24%)
Abnormal	38 (76%)
CSF	
Normal	39 (78%)
Abnormal	11 (22%)

Table 4. Diagnosis distribution between the studied patients

Diagnosis	***Patients (n=50)***	
	N	*%*
Normal findings	9	18%
ADEM	2	4%
Periventricular leukomalacia	4	8%
Subependymal heterotopia	2	4%
Leukodystrophy	6	14%
Tuberous sclerosis	2	4%
Ventriculitis	6	10%
Encephalitis	4	8%
AV malformation	2	4%
Focal cortical dysplasia	4	8%
Low-grade Glioma	2	4%
Lissencephaly	2	4%
Cavernoma	1	2%
Pilocytic astrocytoma	2	4%
Pleomorphic xanthoastrocytoma (PXA)	2	4%

Table 5. MRI features between studied cases

Variables	*Studied cases (n=50)*	
	N	*Percent*
T1		
Heterogenous	6	12
Hypo	36	72
Isogenous	8	16
T2/FLAIR		
Heterogenous	5	10
Hyper	39	78
Isogenous	6	12
Contrast		
Non	37	74
Enhancement	13	26
DWI		
Facilitated	34	68
Restricted	16	32

Table 6. MRI results between studied cases

MRI findings	***Studied cases (n=50)***	
	N	*%*
Normal findings	12	24%
Phakomatosis	5	10%
Cortical malformation disorders	11	22%
Neoplastic lesions	6	12%
Vascular lesions	4	8%
White matter disorders	4	8%
Infective and inflammatory lesions	8	16%

Table 7. ADC value of the studied patients

Variables	***Patients (n=50)***
ADC value *($x10^{-3}$ mm^2/s) Mean ± SD*	2.6 ± 0.871

Table 8. ADC rate of studied cases as MRI findings

	Normal *(n=12)*	***Abnormal*** *(n=38)*	***MW***	***P***
ADC rate *($x10^{-3}$ mm^2/s) Mean ± SD*	3.58 ± 0.432	2.19 ± 1.12	375	**.000**

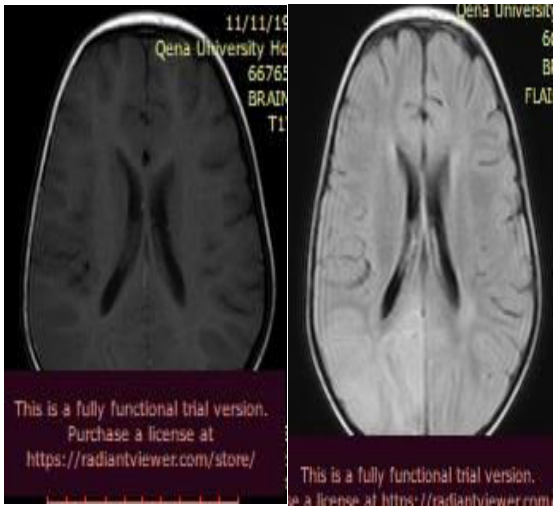
Case Presentation

Case 1.

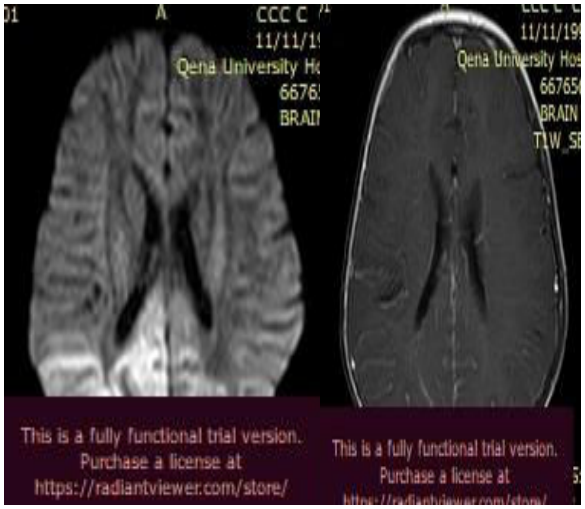
Male patient 1yrs old presented with convulsion post vaccination

MRI shows abnormal signal intensities at right temprooccipital region, being hypointense in T1(Fig 1A),hyperintense in T2 /FLAIR (Fig1B), restricted in DWI(Fig1C), no post-contrast enhancement (Fig1D)

Final diagnosis :ADEM (acute disseminated encephalomyelitis)



A B



C D

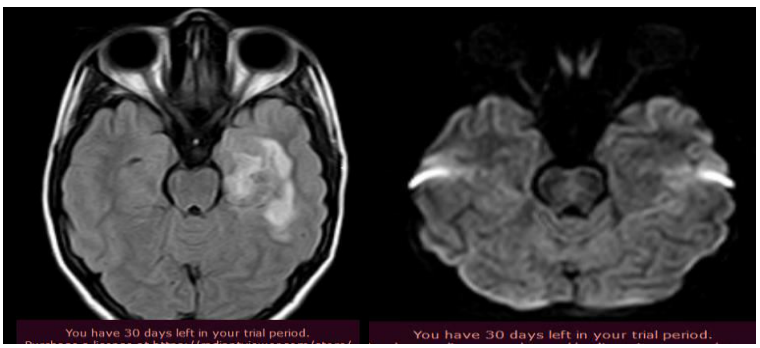
Fig. 1 A) Hypointense In T1 **B)** Hyperintense In T2/FlAIR **(C)** Restricted In DWIs **(D)** No Post Contrast Enhancement

Case 2.

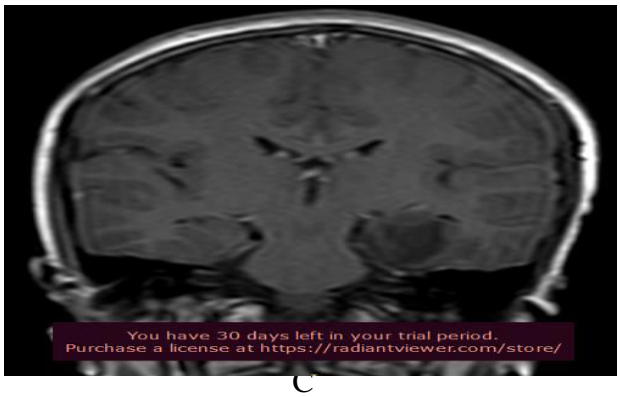
Female patient 14 yrs presented with generalized tonic-colonic convulsion

MRI shows abnormal signal intensity lesion seen involving the left temporal region reflects hyperintense signal on T2/FLAIR (Fig2A) , facilitated in DWIs(Fig2B), no post contrast enhancement (Fig2C)

Final diagnosis :Low-Grade Glioma



A B



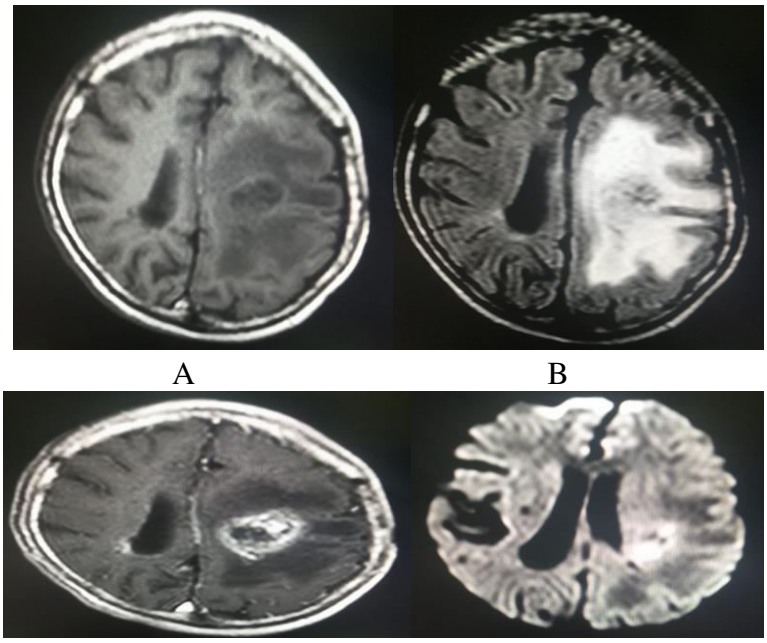
C

Fig. 2 (A) Hyperintense in T2/FLAIR **B)** Facilitated in DWIs.**(C)** No Post Contrast Enhancement

Case 3.

Female patient 13yrs presented with generalized tonic-colonic convulsion

MRI shows well-circumscribedpredominantly cystic lesion at the left temporal-parietal lobe which is hypointense in T1(Fig3A), hyperintense in T2/FLAIR (Fig3B), with enhancing solid nodule in post-contrast sequences(Fig3C),restricted diffusion in DWIs(Fig3D). **Final diagnosis** : Pleomorphic Xanthoastrocytoma



A B

C D

Fig.3 (A) Hypointense in T1 **(B)** Hyperintense in T2/FLAIR.**(C)** Enhancing Solid Nodule In Post-Contrast Sequences **(D)** Restricted diffusion in DWIs

Discussion

Epilepsy is a neurological disorder characterized by enduring proclivity to produce epileptic seizures as well as neurobiological, cognitive, psychological, & social consequences of this situation. An epileptic seizure is thought to be linked with abnormal neuronal activity caused by excessive & unsynchronized electrical discharge caused by abnormalities in the central nervous system's inhibitory & excitatory pathways. Epilepsy is a chronic situation characterized by recurrent, unprovoked seizures that impact one percent of the global population & have an annual incidence of 68/per 100,000 people. In 2015, 1.2percent of the US population had active epilepsy. This equates to approximately 3.4 million epileptics in the United States: 470,000 children & three million adults **(Fiest et al., 2017)**.

In inquiry of studied cases with seizures, MRI is the current imaging tool of choice. With the introduction of high-resolution MRI & committed epilepsy protocol, possibilities of recognizing reason have risen dramatically, causing positive clinical value in the treatment of these studied cases. MRI detects structural deficiencies that demand urgent therapies, like high-grade gliomas & arteriovenous malformations, as well as subtle structural abnormalities like Hippocampal sclerosis & cortical advancement malformations. Recognition of these situations has long-term therapeutic & prognostic consequences for cure options & likelihood of remission & inflexibility**(Kumari et al., 2017)**.

The main results of this study were as follows:

As regards Demographic characteristics of the studied patients, the present study showed that the mean age was 5.76 ± 4.82 years and ranged between 0.17 to 15 years with a mean weight of 41.52 kg. 58% of the patients were males.

The present study can be supported by **(Youssef et al., 2021)** who sought to assess the role of new magnetic resonance imaging technology in determining the reasons for epilepsy in children. There were forty studied cases in total, seventeen women & twenty-three men ranging in age from one to fifteen years.

Also, **(Shankar et al., 2022)** aimed to evaluate the role of brain MRI in the assessment of pediatric seizure disorder research including one hundred studied cases with seizures ranging in age from three months to eighteen years. According to this distribution, the greatest number of studied cases were in the age group two-six years, accompanied by twenty-seven percent in the age category two- twelve years. There were 59 males and 41 females.

As well, **(Moussa et al., 2021)** aimed to illustrate various reasons for epilepsy as well as to prove & emphasize the utility of MRI, the study enrolled 40 pediatric patients diagnosed with epilepsy whose ages ranged between 3 months and 17 years. A total of 22 (55%) children were male and 18 (45%) were female.

Furthermore, **(Kumari et al., 2017)** research included seventy-three studied cases with clinical signs of epilepsy who had undergone MRI imaging, with forty-five men & twenty-eight women ranging in age from zero to sixteen years.

Also, **(Samia et al., 2021)** aimed to evaluate the role of MRI in pediatric seizure disorder. The research included 288 children with a declared epilepsy diagnosis, with a median age of six years. Moreover, five years was found to be significantly linked to abnormal imaging results in research. As well, **(Umap et al., 2020)** aimed to identify & characterize epileptic lesions as well as the frequency of etiological factors responsible for epilepsy in the pediatric age group (zero - twelve years). The study comprised 100 cases of pediatric patients. The majority of studied cases (sixty percent) were between the ages of zero & three years. Men (sixty-five percent) were more impacted than women (thirty-five percent).

In addition, **(Anand et al., 2017)** MRI was used to identify & measure various lesions resulting in epilepsy in children aged zero to twelve years, as well as to determine the frequency with which they took place. The research included ninety-five children under the age of twelve years. The majority of studied

cases in the research were aged zero-three years, followed by ten-twelve years. Males outnumbered females by a ratio of 2.1:1.

Also, **(Shreyas et al., 2020)** sought to identify the spectrum of Paediatric Epilepsy MRI results. The research included one hundred participants. The average age was seven years, & median age was eight years. Men made up 58.7percent of the group, while women made up 41.3percent.

The current study showed that the mean duration of epilepsy was 1.36 years. 20% of the patients had a history of previous febrile convulsions.

However, **(Youssf et al., 2021)** period of disease illness at the time of MRI research ranged from one year to thirteen years (Mean 6.2 ± 3.17 years).

While, to **(Kumari et al., 2017)** More than half of the studied cases (44/73, & 60.27percent) had a disease period of more than three months. There had been no previous febrile convulsions in any of the studied cases.

The present study showed that there were 38 patients (76%) who had abnormal Electroencephalogram (EEG) and 22% had abnormal Cerebrospinal fluid (CSF).

This can be supported by **(Shankar et al., 2022)** who reported that eighty-two percent of studied cases, EEG results were abnormal. MRI results were normal in forty-five (forty-five percent) of studied cases & abnormal in fifty-five (fifty-five percent). It was discovered that EEG & MRI have a positive relationship.

Also, **(Kumari et al., 2017)** reported that EEG findings were abnormal in 65.5% of patients.

As well, **(Shreyas et al., 2020)** reported that EEG findings were abnormal in 52.5 % of patients.

In research shown by **(Khodapanhandeh et al., 2006),** EEG abnormalities were found in seventy-one percent of children. It was discovered that EEG & MRI had a positive relationship, i.e., children who had EEG abnormalities during seizures had MRI abnormalities. MRI abnormalities were discovered in approximately 58.5 percent of children with EEG abnormalities, which is consistent with previous studies indicating that MRI abnormalities are commonly linked with abnormal EEG **(Doescher et al., 2006)** EEG can be used to diagnose seizures, recognize syndromes, & predict prognosis **(Jallon et al., 2001).** Unusual EEG in studied cases may expect positive MRI conclusions, but normal EEG does not rule out brain abnormalities. This indicates that MRI has a better likelihood of sensing seizure concentration than EEG alone, which is in line with previous research by **(Kuzniecky et al., 2002).** EEG may be useful in some cases, but not in all.

The current study showed that the most prevent diagnosis was leukodystrophy (14%) followed by ventriculitis (10%). While normal was found in 18% of the patients.

In agreement with our findings the systematic review by **(Sumayo & Sirven, 2018)** reveal that the most common diagnosis was leukodystrophy.

However, **(Youssf et al., 2021)** reported that According to the Etiology of epileptic focus according to EEG Right temporal lobe epilepsy was found in 10 (25%) patients, while left temporal lobe epilepsy was found in 7 (17.5%) patients, Bilateral temporal lobe epilepsy was found in 9 (22.5%) patients, right frontal lobe epilepsy was found in 6 (15%) patients, left frontal lobe epilepsy was found in 3 (7.5%) patient, Bilateral frontal lobe epilepsy was found in 5 (12.5%) patients.

Furthermore, **(Samia et al., 2021)** As per EEG, thirty-two percent (n = 46) had generalized (twenty-two percent) & focal (seventy-eight percent) interictal epileptiform discharges. There was focal & diffuse slowing in seventeen (six percent) children, with fifty-three percent of them being independent of inter-ictal epileptiform activity. Asymmetrical backgrounds were noted in only 7 children (five percent).

Regarding MRI findings between the studied patients the present study showed that cortical malformation disorders were found in 11 patients (22%), infective and inflammatory

lesions in 8 patients (16%), vascular lesions in 4 patients (8%), phakomatosis in 5 patients (10%), white matter disorders in 4 patients (8%), neoplastic lesions in 6 (12%).

In line with our results, **(Youssf et al., 2021)** reported that according to pathological findings by MRI Cortical dysplasia had been found in 9 (22.5%) patients, Polymicrogyria had been found in 4 (10%) patients, Sturge Weber disease had been found in 3 (7.5%) patients, Gliosis from acquired insult had been found in 11 (27.5%) patients, Hippocampal sclerosis had been found in 3 (7.5%) patients; Brain tumors had been found in 10 (25%) patients.

However, **(Shankar et al., 2022)** According to study, the most common abnormalities were gliosis (45.4percent), periventricular leukomalacia (12.7percent), & neurodegenerative modifications in white/grey matter (7.3percent), focal cortical dysplasia (7.3percent), arteriovenous malformations (7.3percent), polymicrogyria (5.5percent), mesial temporal sclerosis (5.5percent), and abnormal spectroscopy (3.6 percent).

Also, **(Moussa et al., 2021)** revealed that the three most common causes of epilepsy in the study were cortical malformation disorders, accounting for 35% (14 patients), followed by Neurocutaneous disorder & mesial temporal lobe lesions each accounted for twenty-five percent (ten studied cases), accompanied by other causes such as brain tumors & vascular malformations, accounting for 15% (six patients).

Furthermore, **(Samia et al., 2021)** most common results were encephalomalacia (n = 18: 6.3percent), cerebral atrophy (n = 11: 3.8percent), neuronal migration disorders (n = 11: 3.8percent), periventricular leukomalacia (n = 9: 3.1percent), & hippocampal sclerosis (n = 8: 2.8percent). Only 4 children had outcomes concerning infectious etiology.

Also, **(Umap et al., 2020)** majority of studied cases (eighty-nine percent) had abnormal MRI outcomes. Hypoxic ischemic encephalopathy (31.5percent) was the most common cause of epilepsy, accompanied by infection (25.8percent) & developmental malformations (13.5percent).

In addition, **(Anand et al., 2017)** Infection was reported in twenty-five studied cases, accompanied by anoxia & hypoxic-ischemic encephalopathy in twenty-one studied cases (twenty-five percent). Following that, twelve studied cases had cortical advancement malformations. Phakomatoses & vascular induces each had five studied cases. MTS & other induces each had four studied cases. Demyelinating diseases & neoplasms were observed in three studied cases. Inherited metabolic disorders were the least common, accounting for two studied cases. Infection was the most common aetiology in this research, accompanied by anoxia & HIE.

As well, **(Shreyas et al., 2020)** Magnetic Resonance Imaging abnormalities were found to be more common in epileptic children with abnormal neurological examinations. Malformations of Cortical Development were the most common abnormalities discovered.

The current study showed that the mean isotropic apparent diffusion coefficient rate was 2.63 x10-3 mm2/s among the studied patients. ADC rate was minor in studied cases with abnormalities associated with normal patients. This can be explained as during status epilepticus, sodium-calcium pumps on brain cell membranes fail, causing rapid uptake of water intracellularly & cellular swelling **(Rosenberg et al., 1999)**. In dispersion MRI, cellular swelling is reflected as a decrease in ADC parameters. Following cytotoxic edoema, vasogenic edoema enables fluid & proteins to enter interstitial extracellular space, increasing extracellular volume &, as result, ADC **(Vulliémoz et al., 2007)**.

Wieshmann & colleagues' 1997 study on women studied cases with focal motor SE was one of the first to look at DWI in SE. When likened to the contralateral hemisphere, their dispersion results reveal a twenty-seven percent reduction in ADC in the left motor cortex & thirty-one percent rise in ADC in subcortical white matter **(Wieshmann et al., 1997)**.

2 years later, Diehl & colleagues & Lansberg & associates reached similar conclusions **(Diehl et al., 1999, Lansberg et al., 1999)**. Diehl's group specifically

explored the diffusion of ADC in thirty-five studied cases with focal motor SE & discovered a twenty-three percent reduction in ADC in the frontal region of interest. Furthermore, based on intraoperative EEG, the region of maximal reduction corresponded with the area of seizure activity **(Diehl et al., 1999).** Lansberg & colleagues discovered cortical hyperintensity on T2 images, & their ADC assessments revealed a thirty-six percent decrease in the impacted hemisphere when likened to the unharmed one **(Lansberg et al., 1999).**

To our knowledge, the present study was the first to assess the diagnostic accuracy of ADC in Pediatric Epilepsy.

The current study showed that ADC can be used as a marker of the presence of Epilepsy.

Conclusion

There was an agreement between MRI and EEG findings. According to MRI, the most common findings were cortical malformation disorders followed by Infective and inflammatory lesions. Due to its high diagnostic produce in identifying epileptogenic substrates, multiplanar potential, & absence of ionizing radiation, MRI is the initial examination of choice in seizure studied cases.

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