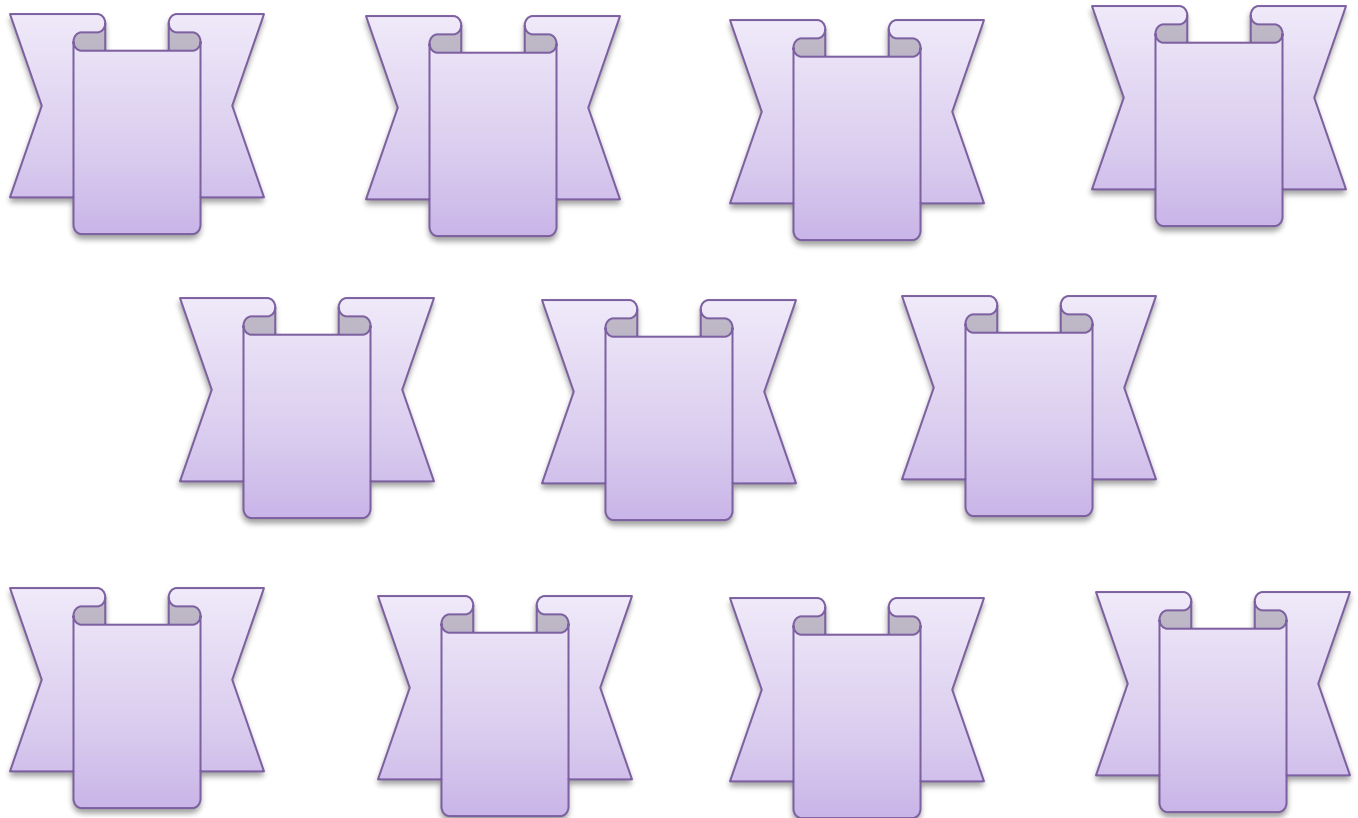


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Original Article

Reflex Epilepsy in Children: Clinical, Electroencephalographic and Brain Magnetic Resonance Imaging Findings

Abdeltief Shaker Abdeltief *, Shora Yussef Mostafa, Mohie-eldin Tharwat
 Mohamed

Department of Neurology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

ABSTRACT

Article information

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*Corresponding author

Email: abdelatif2018@gmail.com

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Background: Reflex epilepsy is an epileptic event precipitated by external stimuli such as flashes of light or internal mental process like thinking or calculation and/or associated with photo-paroxysmal response on electroencephalogram [EEG].

The Aim of the work: To identify clinical, neuroradiological and EEG findings of children with reflex epilepsy.

Patients and Methods: The study included children with reflex epilepsy who attended the outpatient Pediatric Clinics of Neurology Department at Al-Azhar University hospitals in the period between the starting of June 2022 and the end of march 2023, We conducted a hospital-based study. Reflex epilepsy in children younger than 18 years old is necessary of inclusion. These cases underwent complete neurological history, examination, electro-encephalogram and brain magnetic resonance imaging.

Results: Twenty of 400 patients had reflex epilepsy and 16 of these patients the most frequent stimuli of seizures were photosensitivity while, one patient had seizures precipitated by hot water, one patient had seizures precipitated by visual stimuli and startle response, one patient had startle epilepsy and one patient had musicogenic epilepsy. Clinical neurological examination was normal in 85% while magnetic resonance imaging of the brain was normal in 80% of patients. 12 out of 20 patients had abnormal EEGs discharges. The most frequent prescribed drug was sodium valproate followed by levetiracetam.

Conclusion: The frequency of reflex epilepsy was 5%, the family history of epilepsy was quite common, head trauma and history of febrile convulsion was significant predisposing factors, most of patients had normal neurological examination, MRI findings and EEG abnormality were detected in 60% of patients.

Keywords: Reflex epilepsy; Generalized epilepsy; Photo sensitive epilepsy.



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INTRODUCTION

Reflex epilepsies are a class of epilepsy syndromes in which a particular stimulus or trigger can cause a seizure to occur. The trigger could be as simple as a tactile sensation or as sophisticated as reading, writing, or even thinking about a particular topic. Photosensitive epilepsy is the most frequent form of reflex epilepsy [1]. Reflex epilepsy comes in various forms. For example, seizures induced by somatosensory stimuli frequently occur in response to specific stimulations such as cleaning teeth or stimulating the external ear [1,2].

Bathing with hot water that is typically over 37 degrees or pouring it over the head might cause hot water or bathing epilepsy [2]. Startle epilepsy is a rare form of reflex epilepsy in which loud noises or unexpected surprises cause seizures [3]. An abnormal visual sensitivity response of the brain to light stimuli, sporadic light sources or more complex stimuli like television [TV], video games and visual patterns is known as photosensitive epilepsy [1]. Different types of musical stimuli have the potential to cause musicogenic epilepsy to varying degrees and extents. Epileptic seizures occurred by eating are quite rare. Seizures that are extremely rarely caused by reading are known as reading epilepsy [1].

Seizures that are self-inflicted by the movement of the extremities are known as proprioceptive-induced seizures [4]. Specific cognitive activities including math, picture-drawing, card games, chess, making judgements and thinking, may cause thinking epilepsy [3, 4]. In the study of **Gürsoy et al.** the frequency of reflex epilepsy was 5% and the most common type was photosensitive epilepsy. The positive family history of seizures, positive consanguinity and past history of febrile convulsions were the most common significant risk factors [2]. The objective of this study was to identify clinical, neuroradiological and EEG findings of children with reflex epilepsy.

PATIENTS AND METHODS

The current study is a hospital-based study done on epileptic children with reflex epilepsy who attended the outpatient Pediatric Clinics of Neurology Department at Al-Azhar University hospitals in the period between the starting of June 2022 and the end of march 2023. The study was approved by ethical committee of Al-

Azhar faculty of medicine, Cairo, Egypt. We obtained written informed consent from parents/ caregiver before enrollment in this study.

All the patients with Reflex epilepsy younger than 18 years were included in the study, patients with comorbid medical condition or MRI findings suggestive of space occupying lesion were excluded. The diagnosis of epilepsy was consistent with the diagnostic criteria of International League Against Epilepsy [ILAE] 2017.

In this study, all epileptic children with reflex epilepsy underwent the followings; demographic data [age-sex], perinatal and developmental history, family history of epilepsy, age of onset of seizures, types of seizures, frequency of seizures, previous history of status epilepsy, history suggestive of CNS infection, history of head trauma with unconscious, history of febrile convulsion, types of reflex epilepsy, frequency of stimuli and anti-seizure medications used [name, number, dose and duration]. Full general and neurological examination, EEG and MRI brain.

Neuro-physiological evaluation: It was carried out using a conventional electroencephalogram [EEG]. The EEG results encompassed various findings, including normal readings, generalized epileptiform discharges, focal epileptiform discharges, photo-paroxysmal response, slow wave paroxysm, and disorganized background activity. The EEG was categorized based on the coherence and balance of frequencies and amplitudes in the background activity, as well as the existence of seizures, into the following classifications: [1] Normal - characterized by a continuous and symmetrical background activity with no presence of epileptiform discharges, [2] Normal background with the presence of epileptiform discharges, either unilaterally or bilaterally, [3] Abnormal background - indicated by a disrupted or asymmetrical pattern - but without epileptiform discharges, and [4] Abnormal background with the presence of epileptiform discharges.

Brain magnetic resonance imaging [MRI]: The MRI was performed using a 1.5 T Siemens scanner and followed a well-established epilepsy protocol. A high-resolution coronal oblique T2-weighted image with a slice thickness of 2-3 mm and no gaps between slices was obtained along a plane that is perpendicular to the long axis of the hippocampus. This imaging technique allows for the identification of

temporal lobe encephaloceles, which are often missed or not detected using other methods. The combination of coronal FLAIR [fluid-attenuated inversion recovery] and coronal 3D inversion recovery [IR] sequences provides clear visualization of subtle focal abnormalities. This is particularly useful in identifying conditions like bottom-of-sulcus dysplasia.

Statistical analysis: All data were collected, presented and analyzed by using an appropriate statistical package program [Statistical Package for Social Science [SPSS], version, 20]. All Data were qualitative and presented by number and percentage.

RESULTS

In the present study, reflex epilepsy was detected in 20 out of 400 patients, the frequency of reflex epilepsy was [5%] [Figure 1]. 16 [80%] of patients had photosensitive seizures, regarding other causes, hot water epilepsy was detected in one [5%] case, musicogenic epilepsy was detected in one [5%] case also, startle epilepsy was detected in one [5%] case, while mixed startle and photosensitive epilepsy were detected in another case [5%] [Figure 3].

In the current study, there were 12 [60%] females and 8 [40%] males. The age of onset of seizures spanned from 4 to 18 years ,the most common age group was between 11-14 years in 14 [70%] of patients [figure 2], 11 [55%] of patients had positive consanguinity, 2 [10%] of patients were complicated by obstructed labour

and only one [5%] patient was reported delayed global developmental milestones.

In the current study, history of febrile convulsion was determined in 9 [45%] of patients, positive family history of epilepsy was determined in 12 [60%] of patients, 3 [15%] of patients had history of significant head trauma, significant post-natal infections were determined in 2 [10%] of patients and 3 [15%] had previous history of status epilepticus [Table 1].

In the current study, the types of seizures were generalized tonic clonic seizures in 7 [35%] of patients, myoclonic seizures were in 2 [10%] of patients, while mixed generalized tonic clonic seizures and myoclonic seizures were in 2 [10%] of patients and generalized tonic clonic with focal to bilateral seizures were in 2 [10%] of patients. Clinical neurological examination was normal in 17 [85%] of patients [Figure 4] and MRI of the brain was normal in 16 [80%] of the patients. EEG abnormality was detected in 12 [60%] of patients as described in [Table 2]. The sodium valproate was the most frequent drug used in 5 [25%] and levetiracetam in 4 [20%] of patients.

16 [80%] of cases had normal MRI results, 4 [20%] of patients had abnormal MRI findings which were distributed as follow, 2 [10%] of patients had multiple brain patches [post-encephalitic], one [5%] patient had encephalomalacia in the left tempo-parietal cortical and subcortical area and one [5%] patient had an arachnoid cyst.

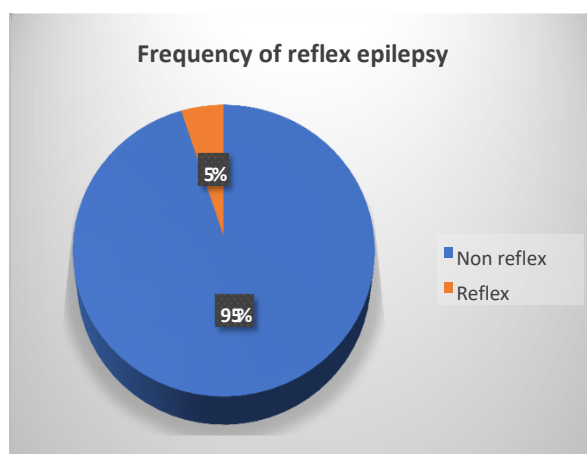


Figure [1]: Frequency of reflex epilepsy

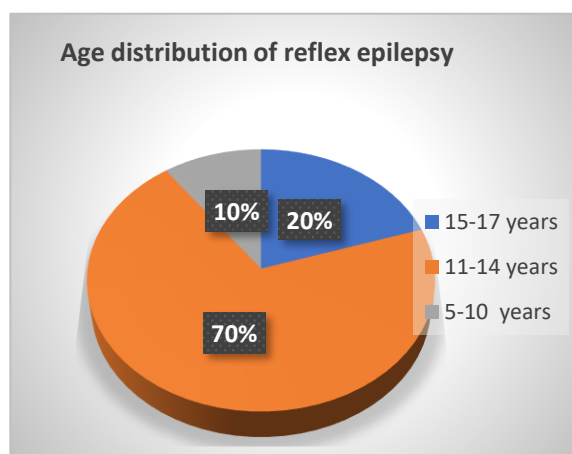


Figure [2]: Age distribution of reflex epilepsy

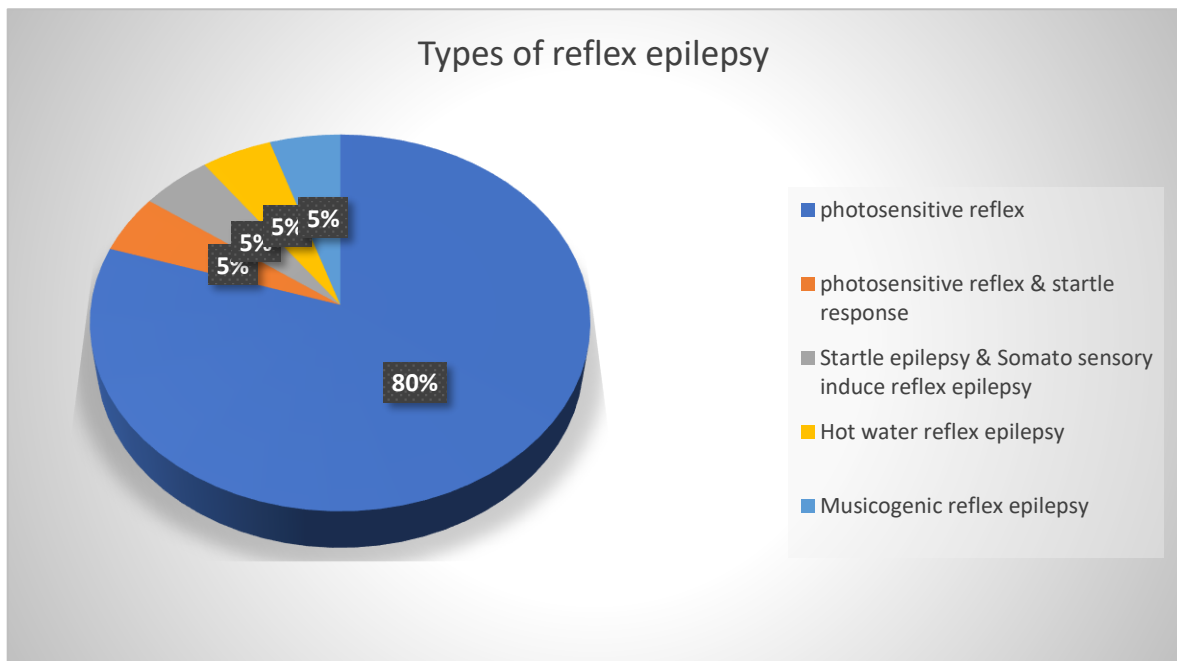


Figure [3]: Types of reflex epilepsy

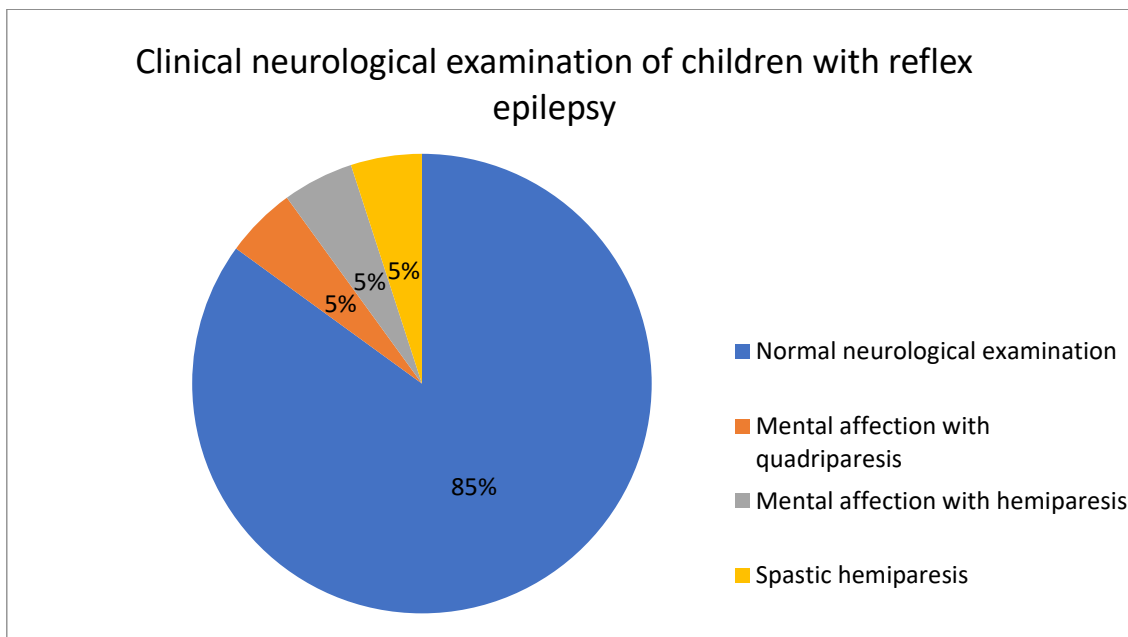


Figure [4]: Clinical neurological examination of children with reflex epilepsy

Table [1]: Risk factors of patients with reflex epilepsy

	Number of positive [affected] cases and their percentage	Number of negative [not affected] cases and their percentage
Consanguinity	11 [55%]	9 [45%]
History of birth asphyxia	2 [10%]	18 [90%]
Family history of epilepsy	12 [60%]	8 [40%]
History of febrile seizures	9 [45%]	11 [55%]
History of post-natal infection	2 [10%]	18 [90%]
History of head trauma	3 [15%]	17 [85%]
History of status epilepticus	3 [15%]	17 [85%]

Table [2]: EEG findings of patients with reflex epilepsy

	Normal	Generalized epileptiform discharges	Right fronto parietal epileptiform discharges with secondary generalization	Photo paroxysmal response	Left frontal epileptiform discharges	Bi frontal epileptiform discharges with secondary generalization
Photosensitive reflex	7	4	1	3	1	
Photosensitive reflex & startle response		1				
Hot water induces reflex epilepsy	1					
Musicogenic reflex epilepsy		1				
Startle epilepsy & Somato sensory induce reflex epilepsy						1
Total	8	6	1	3	1	1

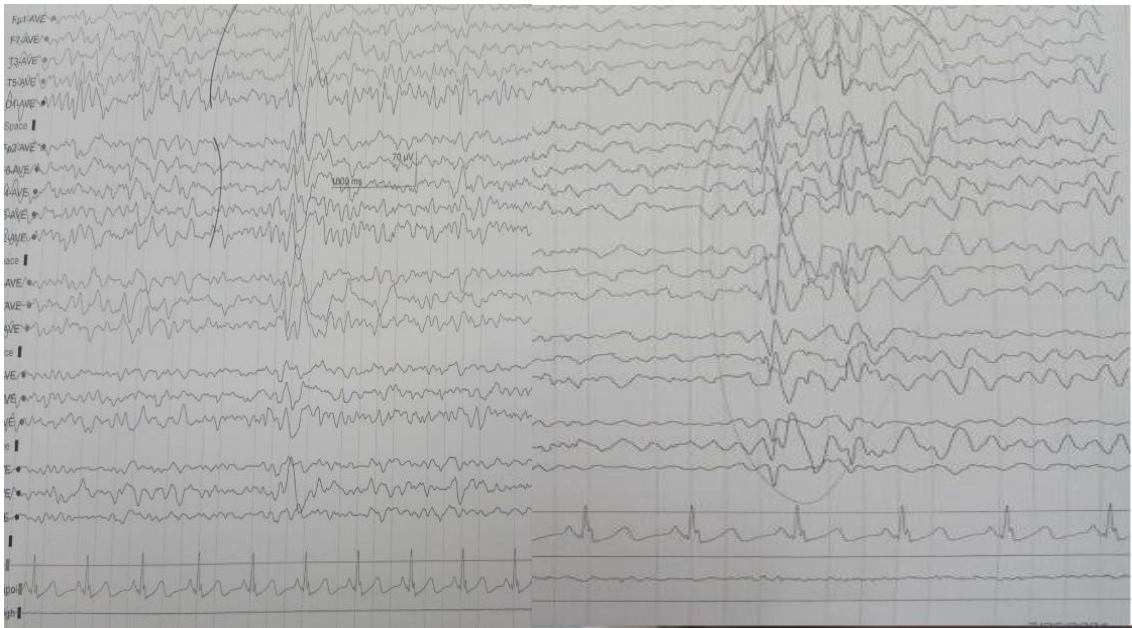


Figure [5]: EEG finding of a 15 years old girl presented with startle epilepsy showed bi-frontal epileptiform discharges activity with secondary generalization

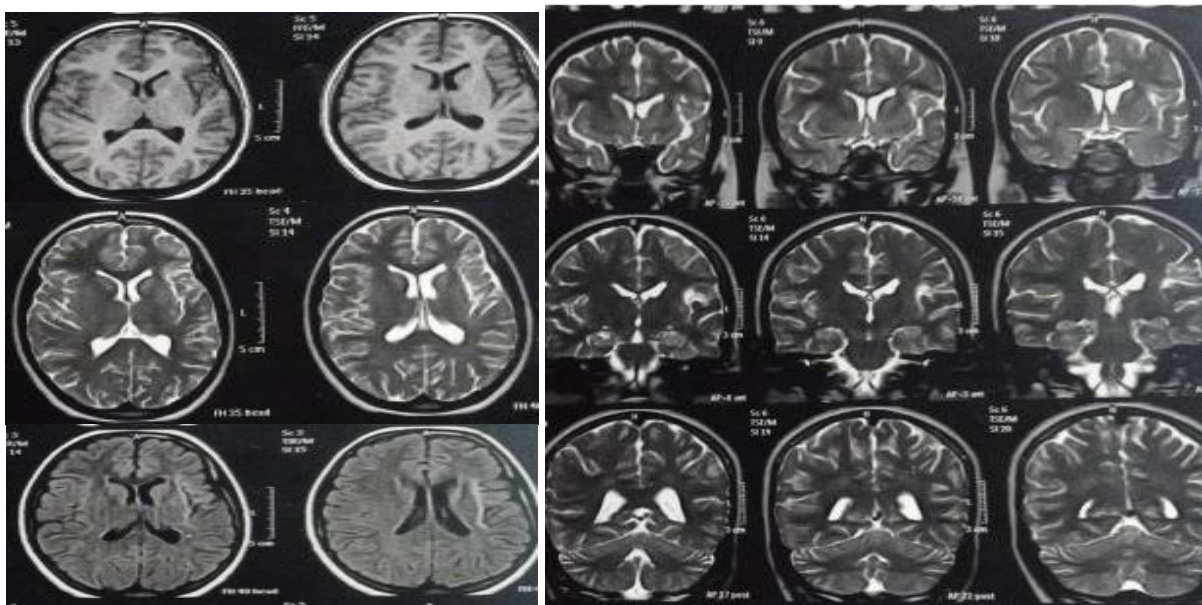


Figure [6]: MRI brain showed left cortical and subcortical area of encephalomalacia of a 15 years old female patient presented with startle epilepsy

DISCUSSION

Reflex seizures are events that are induced by a certain stimulus or trigger, making them specific from other epileptic seizures ^[1]. The frequency of reflex epilepsy in the current study was 5%, and the most common triggering factor was photosensitivity in 16 [80%] of patients. This is quite similar to the study by **Gürsoy et al.** ^[2], which showed that the prevalence of photosensitive epilepsy was 90% in relation to the categories of reflex seizures.

Reflex epilepsy is quite uncommon. The possible explanations of these results are as follows: The presence of reflex seizures requires a complex genetic inheritance pattern involving multiple genes ^[3]. Most cases of reflex epilepsy were misdiagnosed as psychiatric disorders. To confirm the diagnosis of reflex epilepsy, expert pediatric neurology is needed to ask relevant questions about reflex epilepsy. We collected data from a tertiary healthcare institution, which made it difficult for people living in rural areas to access.

In the current study, the most typical age spanned from 11 to 14 years. The average age of seizure beginning was documented in earlier research to be 15.4 years, however the age of seizure onset in the literature has been reported to range from 2 months to 58 years ^[4]. Reflex epilepsy was more common in females [60%] than in males [40%] according to the current study's demographic data. Numerous studies, such as the one by **Savic and Engel** ^[5], revealed that girls were more significantly impacted than males. Other studies showed that males were affected more than females ^[6], while other studies showed no significant differences ^[7]. Sex hormones may play a role in this situation, as they have the potential to change seizure activity, as steroid hormones have the potential to affect brain excitability ^[8].

Children born from consanguineous marriages made up 11 [55%] of patients in the current study, indicating a higher frequency of reflex epilepsy. This matched a study conducted by **Gürsoy et al.** ^[2], which showed that 45% of reflex epilepsy patients were the offspring of consanguineous marriages. The familial photo paroxysmal response [PPR] pattern suggests a complex method of inheritance involving multiple genes is considered a potential explanation for these findings ^[9]. According to the current study's risk factors: 12 [60%] of the patients had a

positive family history of epilepsy, 9 [45%] had a history of febrile convulsions, 3[15%] had significant head trauma, 2 [10%] had birth asphyxia due to obstructed labor, 2 [10%] had significant postnatal infection [encephalitis], and 3 [15%] of patients had a prior history of status epilepticus. Complex febrile seizures cause long-term functional alterations in the hippocampal circuitry as well as short-term anatomical abnormalities to some hippocampal pyramidal neurons ^[10].

Most children with reflex epilepsy reported normal developmental milestones in 17 [85%] of patients, as supported by neurological examination. The most frequent seizure semiology was generalized tonic-clonic seizures. These results can be explained by the presence of complex stimuli and activities in combination with cognitive processes, which can increase the probability of a generalized seizure. These stimuli and activities may lead to generalized seizures ^[11].

In the current study, we have identified one case [5%] of hot water epilepsy, which is characterized by focal to bilateral seizures when the patient's body temperature rises above 40 degrees Celsius. Both the patient's EEG and brain MRI results were normal, and they were being treated with carbamazepine for seizure control. The exact pathophysiological mechanism of hot water epilepsy remains unknown. Several explanations can be considered for this result: First, the patient's response to hyperthermia may have been provoked by high-temperature stimuli during bathing ^[12]. Secondly, variations in the thermoregulatory systems of hot water epilepsy patients may be genetically based, making them more sensitive to sudden temperature increases ^[13]. Additionally, channelopathies, such as SCN1A mutations seen in Dravet syndrome, have been implicated in the triggering of hot water epilepsy. In fact, in Japan, a screening test for Dravet syndrome is performed on patients with hot water-induced seizures as a predictive factor ^[14].

We had one [5%] case of startle epilepsy, which is very rare, presented by tonic contraction of both upper limbs. Both EEG and MRI brain were abnormal and the case was resistant to anti-seizure medications. Although the exact pathophysiology of startle epilepsy is unknown, the seizure semiology may indicate that the motor and supplementary motor regions are involved ^[15].

EEG findings were normal in 8 [40%] of patients, 6 [30%] of patients had generalized epileptiform discharges, 3 [15%] of patients had photoparoxysmal response, and 3 [15%] had focal epileptiform discharges.

In the current study, the majority of reflex epilepsy cases are idiopathic, occurring as a result of genetic disorders that alter brain excitability without structural lesions [16]. Various studies using functional MRI have demonstrated changes in metabolism in specific regions related to each type of reflex epilepsy [17], which may be the cause of this result.

The following guiding principles have been used to manage patients with reflex epilepsy: avoiding provocative stimuli, using medication therapy, and using certain technology to draw attention away from stimuli [18]. Most patients in the current study were using a single medication, such as valproate in 5 [25%] of patients and levetiracetam in 4 [20%] of patients. The most frequent combined medications were valproate and levetiracetam in 4 [20%] of cases, while valproate and carbamazepine were combined in 2 [10%] of cases.

Numerous case studies have demonstrated the impact of sodium valproate on photosensitive epilepsy, providing support for this study. For example, **Fisher et al.** [19] conducted a study that revealed the effectiveness of valproate in 78% of photosensitive patients. Complete control of seizures was achieved in 54% of cases, and there was a significant reduction in photosensitivity in 24% of patients.

There is no obvious cause for why sodium valproate is the most effective medication for treating photosensitive reflex epilepsy, but numerous studies have shown that it lowers the photoparoxysmal response of the EEG and improves the prognosis for seizures [20].

Conclusion: In this hospital-based study, the frequency of reflex epilepsy was found to be 5%. The most common age observed in children with reflex epilepsy was between 11 and 14 years. A family history of epilepsy was quite common in children with reflex epilepsies. The most common type of reflex epilepsy was the photosensitive type. Most children with reflex epilepsy had a normal neurological examination. Abnormal EEG findings were detected in 60% of children with reflex epilepsy. Most children with reflex epilepsy had normal brain MRI

findings. The identification of the pattern of reflex seizures is important in the selection of anti-seizure medications, such as sodium valproate for photosensitive epilepsy, levetiracetam for musicogenic epilepsy, and carbamazepine for hot water epilepsy.

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