Prognosis of Epilepsies and Epileptic syndromes in Children

**Abstract**

Epilepsies and epileptic syndromes are among the most frequent chronic neurologic disorders in neonates, infants, and children. Seventy percent of children with epilepsy will enter remission but the rest will suffer from frequent seizures and will become refractory to various treating modalities. Such refractory seizures have a huge negative impact on the quality of life of children and their families. Prognosis of epilepsies is defined by the recurrence risk of the seizures or convulsions. Among the risk factors for recurrence, the most important are the age of seizure presentation, the neurodevelopment of the child, the etiology of seizures, the seizure frequency before anticonvulsant withdrawal, response to antiepileptic medications, the type of epileptic syndrome, and the electroencephalography of the patient. Knowing about the risk factors of recurrence could help us to optimally manage our treatment protocols and finally could reduce the negative impact of seizures on the patient and their families. In this paper, two child neurologists who are expert in the field will review in a narrative manner the most important risk factors for the recurrence of epilepsies in children.

**Keywords**; Epilepsy, Children, Recurrence, Prognosis

## Introduction

Epilepsies and epileptic syndromes are common neurologic disorders in children. (1) These neurologic disorders could occur from birth and during the whole life. Fortunately, 70% of these disorders are responsive to usual anticonvulsive medications but about 25% to 30% of the epilepsies are reluctant to various treatment modalities and have a huge negative impact on the quality of life of children and their families. (2) Prognosis of epilepsies and epileptic syndromes is defined by the recurrence risk of seizures or convulsions and the risk of sudden death. (3) The most important aim of treating seizures is the prevention of recurrence, therefore, knowing about the different risk factors of recurrence and the impact of them could help us optimally manage our treatment protocols in our patients and finally improve their quality of life.

Among the different risk factors for recurrence the most important that have critically been studied by the previous works are the etiology of seizures, the age of onset of seizures, the initial response to appropriately chosen anticonvulsive agents, the neurodevelopment of the patient, the epileptic syndrome, the electroencephalography (EEG) of the patient, and the frequency of seizures before anticonvulsive medication withdrawal. (4-8)

In this paper, we will review in a narrative manner, the different risk factors of recurrence based on an age approach and will discuss the most important risks of recurrence in different age groups in children from birth to adolescence.

## Literature review

Two experts in the field of child neurology decided to search the literature to answer this question; what is the main prognostic factors in children with epilepsy? Our aim was to write a review in a narrative manner, therefore, based on our experience in the field we select the most important articles of the field to answer this question. In addition, this review is not a systematic

or meta-analysis and the main audience of this review will be the general adult neurologists and child neurologists who are relatively familiar with this issue.

**The neonatal period**

Seizures are the most neurologic disorders in neonates. The brain of the term and preterm neonates is very vulnerable to different insults and seizures are the most prevalent manifestation of different insults to the brain in this age group. (9-12) The main risk factor for recurrence of seizures in term and preterm neonates is etiology of the seizures. The etiologies of seizures in neonates are very different including etiologies with excellent prognosis such as hypocalcemia and hypoglycemia and etiologies with poor prognosis such as Early Infantile Epileptic Encephalopathy with Burst-Suppression which is also known as Ohtahara syndrome. (13-18) Hypocalcemia and Hypoglycemia are very common in neonates especially among neonates of the diabetic mothers. Fortunately, both of these etiologies of neonatal seizures have an excellent prognosis and after treatment of hypocalcemia and hypoglycemia, no further anticonvulsive prophylaxis is needed. Unfortunately, profound and prolonged neonatal hypoglycemia leads to severe insult to the brain of the neonate and results in severe and reluctant seizures in the neonate. This type of hypoglycemia almost always develops refractory seizures in neonates and infants. (11)

Structural brain disorders in neonates are among important causes of seizures. Seizures in neonates with structural brain disorders such as pachygyria and lissencephaly almost always are reluctant to anticonvulsive agents and need long prophylactic treatments after seizure control albeit if successfully stopped by conventional anticonvulsive medications. Many of these neonates with complex structural brain disorders need other seizure-controlling modalities such as ketogenic diet. They also have limited life expectancy and many of them will die during infancy because of other complications such as frequent pneumonia.(11, 12)

Epileptic syndromes, both with excellent and poor prognosis, are common in neonates. Among the epileptic syndromes with the poorest prognosis are Ohtahara syndrome and early myoclonic encephalopathy (EME). These two syndromes present by short tonic spasms and myoclonic seizures which, are very reluctant to anticonvulsive medications even ACTH (Adrenocorticotropic hormone). These neonates have poor neurologic development and many of them if survive will develop other refractory epileptic syndromes such as West syndrome. (13, 19-24)

Epileptic syndromes with excellent prognosis are benign familial and benign idiopathic neonatal seizures. The mothers of these neonates almost always have had an unremarkable pregnancy and delivery. The neonates develop different types of seizures especially focal clonic and tonic seizures and have electroencephalography with normal developmental indicators. Their seizures respond to anticonvulsant medications very well and long-term prognosis is excellent but a small number of these neonates develop seizures during infancy and childhood. (25-28)

In the neonatal period, other etiologies are existed with different impacts on the prognosis of epilepsies and seizures. One of the main etiologies is the hypoxic-ischemic encephalopathy (HIE) which have different stages including mild, moderate, and severe. Neonates with mild and moderate HIE almost always have a relatively good prognosis but neonates with severe HIE always developed severe cerebral palsy and refractory seizures. (9-12, 29)

Neonatal sepsis and meningitis are among the etiologies for developing epilepsies in children. In the literature of child neurology and epilepsy the neonatal meningitis has called remote symptomatic etiology which means that these neonates have risk for developing epilepsies in the future but the prognosis is related to the extent of the damage to the brain. (9-12, 29)

One of the etiologies of epilepsy and epileptic spasms in neonates is pyridoxine deficiency and pyridoxine decency. These neonates show severe seizures such as epileptic spasms from birth through the infancy. If the diagnosis and treatment with high doses of pyridoxine is made early these neonates and infants developed normally and the prognosis for epilepsy might be acceptable but without treatment the prognosis is poor, therefore, the early diagnosis is important. (9-12, 29)

**Infancy**

The risk factors for the recurrence of seizures in infancy are very similar to neonatal period and should be considered when approaching to an infant with seizures but some especial epileptic syndromes typically begin in this period and the most important of them is febrile seizures and febrile convulsions. (29, 30)

Febrile convulsions are the most frequent seizures in children and almost always have an excellent prognosis. Their clinical course is fully studied and many authorities believe that these seizures are benign and no prolonged prophylaxis is needed. (31-34) But this reality should be considered that different types of epileptic syndromes both with excellent and poor prognosis such as Dravet syndrome could begin as febrile seizures. Therefore, febrile seizures especially prolonged ones that persist more than 15 minutes before stopping need especial attention. (35, 36)

The best approach in infants and children with seizures and epilepsies is the syndromic approach. In this approach, based on the age of the patient, seizure semiology, seizures etiology, and electroencephalography an epileptic syndrome could be diagnosed. Many of the epileptic syndromes have defined clinical course and prognosis, therefore, based on this approach, the clinician could understand the clinical course of the patient and could develop the best managing plan. (37-41)

One of the most important epileptic syndromes with poor prognosis is epileptic spasms (West syndrome). This syndrome is characterized by epileptic spasms, developmental regression or retardation, and an interictal EEG of hypsarrhythmia. This syndrome is reluctant to many conventional anticonvulsive agents and in the majority of infants is refractory to even three appropriately selected anticonvulsive medications. Many of these infants with the west syndrome will need a ketogenic diet for seizure control and finally will develop poorly. Many of these infants will become autistic even after seizure control. Unfortunately, many of these infants develop another refractory epileptic syndrome after infancy and will show the characteristic seizures of Lennox-Gastaut syndrome. (42-46)

Fortunately, all of the epileptic syndromes in infancy have not a poor prognosis. Benign myoclonic epilepsy of infancy is an epileptic syndrome characterized by frequent myoclonic jerks during infancy and generalized multiple spikes in EEG. These infants develop normally and show an excellent response to valproate. (40, 41)

**Childhood**

Like infancy, epileptic syndromes with poor and excellent prognosis have described that begin in childhood. Rolandic epilepsy or Benign partial epilepsy of childhood, the main syndrome with an excellent prognosis, begins in this age period. (40, 41) This syndrome is characterized by focal seizures of the lip especially during sleep, normal development, and characteristic EEG with Centrotemporal spikes (Rolandic spikes). Many authors believe that these type of seizures do not need any treatment and many of these children had no frequent seizures and finally will develop complete remission even without treatment. (47-49)

A subgroup of children with Rolandic epilepsy develops cognitive decline during the course of epilepsy. These children have CSWS (Continuous Spike Wave Discharges in Slow-Wave

Sleep) during sleep EEG. Unfortunately, these patient have a poor prognosis but a high index of suspicion and early treatment with appropriate agents could improve outcome. (50).

Lennox-Gastaut syndrome develops during this age period and have a poor prognosis and is very reluctant to anticonvulsive medications. This syndrome is defined by multiple types of seizures (atypical absences, focal seizures, sleep tonic seizure, and atonic), a characteristic EEG, and developmental delay. Many of these children will develop poorly and will become debilitated. Prognosis for seizure remission is extremely poor. (42, 43, 45)

**Adolescence**

In adolescence, juvenile absence epilepsy and juvenile myoclonic epilepsy are the main epileptic syndromes with an excellent prognosis. Children with these syndromes almost always develop normally, have an acceptable response to appropriately selected anticonvulsive medications, and have acceptable cognitive abilities after seizure control. In juvenile absence epilepsy anticonvulsive medications could withdraw successfully but in juvenile myoclonic epilepsy, patients will need lifelong treatment for seizure remission. Unfortunately, a number of patients with juvenile myoclonic epilepsy develop CSWS and will need especial treatment.

**Other aspects of prognosis**

Besides approaching the patients with epilepsies while epileptic syndromes in mind, other aspects of the recurrence risk should be considered when dealing with these patients. In the following, some of these aspects will be reviewed in brief.

**Age of onset**

Studies showed that onset of seizures during adolescence have a negative impact on the prognosis and these patients will develop more relapses after drug withdrawal. (51, 52)

**Idiopathic versus symptomatic**

Children with idiopathic epilepsies have an excellent prognosis versus children with lesional epilepsy and developmental delay. (53)

**Seizure type**

Some studies showed that focal seizures have poor prognosis while other studies had different results and showed that generalized seizures have a poor prognosis. (54, 55) But almost all studies showed that patients with multiple types of seizures have a poor prognosis. (56, 57)

**Response to Anticonvulsants (AEDs)**

Studies showed that children with a cluster of seizure after anticonvulsant initiation and children who continued to have weekly seizures during the first year of treatment have a poor prognosis (58).

**Early versus late treatment**

Many clinicians believe that early treatment could improve the prognosis but one study showed that early treatment versus treatment only after a further seizure has a comparable impact on the long-term prognosis (59).

**EEG and recurrence after AED withdrawal**

One study in children investigated the effects of EEG before drug withdrawal in children with epilepsy. The results of this study showed that a normal EEG without epileptiform discharges is an excellent prognostic factor before the withdrawal of medications but the presence of irregular generalized spike waves is a poor prognostic factor. Children with normal EEG before withdrawal had 33% relapse rate versus 67% of the children with abnormal EEG with irregular generalized spike waves. (60)

**Prognosis following epilepsy surgery**

Studies showed that in patients with epilepsy who had been selected appropriately for surgery, more than 60% of them became seizure free and their quality of life was also improved significantly. (61-63)

## Conclusion

In conclusion, the prognosis of epilepsies in children and the recurrence of seizures depend on many factors. Among these risk factors, the most important are the etiology of seizures, the neurodevelopment of the patient, and the epileptic syndrome. Knowing about these risk factor of recurrence could help clinicians to optimally manage the treatment plan of their patients.

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