# Clinical and Electrographic parameters as predictors of outcome of patients with Childhood Absence seizures

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## Abstract

*        **Background:** Childhood absence epilepsy (CAE) accounts for 10% to 17% of childhood epilepsy. Most of the available evidence is inconclusive regarding evolution and prognosis of CAE because of the wide range of diagnostic criteria used. This retrospective study was done to assess clinical and EEG parameters as outcome predictors of patients with CAE.*

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***Methodology***: *In this study, we reviewed the data of 45 patients with a clinical diagnosis of Absence epilepsy who presented to the outpatient Neurology clinic at Tripoli Children Hospital in the period from January 2008 to June 2019, medical records were reviewed for sex, age at absent Seizure onset, additional seizure types, previous febrile seizures , first-degree family history of epilepsy, neurological examination, EEG findings, medications, response to medication ( required that all seizures remained under full control for at least 1 year after drug withdrawal and at least one year seizure freedom for patients with ongoing treatment at time of study data collection).*

***Results:*** *Study group of 45 patients consisted of 25 male (55.6%) and 20 (44.4%) female. (6.7%) have early onset absence. 15.6% have a history of generalized tonic clonic seizures after the onset of the absence attacks. history of febrile seizures were present in11.1%. 82.2% of patients have typical EEG findings with generalized synchronous and symmetrical 3-4 Hz spike-and-wave discharges. Na Valoproate was the initial treatment for all patients, 93.3% treated with monotherapy. Remission were achieved in 88.9% of patients.*

***Conclusion***: *The study findings suggest that early onset of absence seizures, GTCSs during the active stage of the disease and EEG features atypical for CAE are the most important predictive factors for an unfavorable prognosis of CAE.*

*    **Keywords:** Absence seizures, childhood absence epilepsy( CAE**),** typical CAE and early-onset CAE*

## 1   Introduction

Childhood absence epilepsy (CAE) accounts for 10% to 17% of childhood epilepsy with an annual incidence of 6.3 to 8/100,000 in children < 15 years[1,2]  and is clearly more frequent in girls, with some exceptions[3]. The definition of CAE is based on the frequency of absences or patterns of recurrence, and on age of seizure onset [4]. It is characterized by multiple typical absences (TAs) per day [5]. Absence seizures may be classified as typical or atypical according to their electroclinical characteristics. Typical absence seizures characteristically start and end abruptly and usually last 5-15 seconds. Ictal EEG shows generalized synchronous and symmetrical 3-Hz spike-and-wave discharges[6]. A majority of children with typical absence seizures have normal findings on neurologic examination and  have normal or mildly low intelligence Compared with age-matched controls. Typical absence seizures may be associated with generalized tonic-clonic seizures in 40–60 percent of patients. In most children, the generalized tonic-clonic seizures occur after onset of the absence seizures. Although atypical absence seizures form a separate category of absences, overlap between the two seizure types is considerable, and they appear to represent a clinical continuum. Diminished postural tone, or tonic or myoclonic activity, is significantly more likely to be the initial clinical feature in atypical than in typical absences. Automatisms are less likely in atypical absences than in typical absences. Like typical absences, atypical absences have a distinct onset and ending, without auras or postictal symptoms. Although atypical absences usually are of longer duration than typical absences[7]. Typical absence seizures are included in numerous epileptic syndromes listed in the International League Against Epilepsy classification of epilepsies and epileptic syndromes, which is included in

the group of idiopathic generalized epilepsies such as childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME), and epilepsy with myoclonic absences[8] as well as in the newly described syndromes of eyelid myoclonia with absences and perioral myoclonia with absences. Because these syndromes have different prognoses and outcomes, it is important to define the syndromic classification for every patient rigorously[9]. In this context, the literature regarding the evolution and prognosis of patients with CAE is considerable but still inconclusive because of the wide range of diagnostic criteria used [10]. These syndromes have different prognoses and outcomes. Unfavorable prognostic factors have been considered to be age at onset, nonpyknoleptic absence seizure patterns, later development of myoclonic attacks or GTCs, atypical EEG features, psychiatric comorbidities, and side effects of AEDs [4,11,12,13,14].

**Objectives:** To evaluate remission rates in patients with CAE in relation to different diagnostic criteria and to assess clinical and EEG parameters as predictors of outcome of patients with CAE.

**Methodology:** Descriptive case series study where clinical records for all patients with a clinical diagnosis of Absence epilepsy who presented to the outpatient Neurology clinic at Tripoli Children Hospital in the period from January 2008 to June 2019 have been reviewed to obtain the relevant information. which include sex, age at absent Seizure onset we considered the age of onset at four years or earlier as early-onset and above four years as typical CAE, additional seizure types (myoclonic attacks and/or generalized tonic–clonic seizures), previous febrile seizures (FS), first-degree family history of epilepsy, neurologic examination, EEG findings, medications, and response to medications (required that all seizures have stopped after a reasonable titration period

and any needed further adjustments, and that seizures remained under full control for at least 1 year for patients who are still ongoing treatment at time of study data collection and at least one year off seizures and off treatment for patients who have drug withdrawal).

The data coded and analyzed by SPSS software. Frequency , percentage, mean and standard deviation used to describe the data. Chi – square used to find the significant level of difference between categorized data, P value < 0.05 considered significant.

**Results:** 45 patients records have diagnosis of absence epilepsy were reviewed 25 were male (55.6%) and 20 (44.4%) were female **figure 1**. Most of them 42 patients (93.3%) they have absence seizure onset at age above four years and only three (6.7%) have early onset absence **figure 2**. 34 (75.6%) of the patients have only absence seizures at the time of presentation to our clinic, ten patients (22.2%) were have a history of generalized tonic clonic seizures after the onset of the absence attacks, one patient (2.2%) the absence was accompanied with eyelid myoclonia. Only five patients (11.1%) were have history of febrile seizures. 11 patients(24.4%) were have first degree relative has been diagnosed as epilepsy. Regarding EEG findings 37(82.2%) of patients have typical EEG findings with generalized synchronous and symmetrical 3-4 Hz spike-and-wave discharges. **Table 1** demonstrate the clinical and EEG findings. Na Valoproate was the initial treatment for all patients, 39 (86.7%) treated with VPA as monotherapy three patients because of poor response Lamotrigine were added on, other two patients were switched to Ethosuximide one of them because of poor seizure control and the other because of VPA side effect (significant hair loss) and one patient was switched to Lamotrigine because of developing of secondary nocturnal enuresis as side effect of VPA. 88.9% of patients have good

seizure control and achieved remission. Only 33.3% of patients with early onset absence achieved good seizure control **figure 3**. Remission rate for patients with accompanied GTC seizures was 60%.  **Table 2** demonstrate the relation of seizure control and other variables.

**Discussion:** Childhood absence epilepsy(CAE) accounts for 10% to 17% of  all cases of childhood-onset epilepsy making it the most common form of pediatric epilepsy[1,2]. In our study it represented 7.5% of patients with epilepsy. Most of the available evidence is inconclusive regarding evolution and prognosis of CAE and a wide range of remission rates (33%–79%) have been reported in the literature . This is because of the different classification criteria adopted in the studies and because of diverse follow-up periods[10]. There is however a period of overlap between CAE and JME. In a retrospective study 18% of patients diagnosed with JME evolved from CAE [15]. Jallon and Latour in their comprehensive review  mentioned that with some exceptions a two- to five-fold preponderance of CAE in girls was usually reported[16]. In our study was a slight male preponderance 1.25 :1 this difference could be biological (e.g., genetic variations among different populations). But the sex ratio was not significantly different in early-onset CAE compared to typical CAE. Other seizure types are sometimes observed in patients with CAE. Generalized tonic-clonic seizures were reported in 30–60% of the patients with CAE in the literature[7,17] the true proportion is likely much lower when stringent diagnostic criteria for CAE are used. In two contemporary long-term follow studies of children with CAE, only 12 to 13 percent of children with CAE developed GTCS [18,19]. in current study only 22.2% were develop GTC seizures after the onset of the absence attacks and in 2.2% of patients the absence was accompanied with eyelid myoclonia. This is in contrast to previous studies that reported

an evolution of generalized tonic-clonic seizures between 30% and 60% **[7,20,21].** This discrepancy might be due to our relatively short average follow-up period of 3-4 years, because there is a second manifestation peak of generalized tonic-clonic seizures usually 5 to 10 years after onset.The interesting and statically significant finding in this study that the patients with early onset absence have higher rate of developing GTC than patients with typical CAE onset (66.7% versus 21%). Family history of generalized seizures seem to predict development of generalized tonic–clonic seizures but it did not influence the final outcome (P =.391) these results corroborate the findings of a prospective study by Callenbach et al. 2009 **[18].** In our study history of febrile convulsion was reported in 11.1% of the patients and with higher incidence in the patients with early-onset CAE 33.3% as compared to those with typical CAE 9.5% (P = 0.2) and these consistent with data obtained in Marini C et al study where 10–15% of the patients with CAE have a history of earlier febrile seizures**[21].** The interictal EEG in CAE shows normal background activity although it is common to see occasional generalized spike wave discharges or focal abnormalities. In a review 445 pre-treatment EEGs, occipital intermittent rhythmic delta activity (OIRDA) was noted in 21 percent, focal sharp waves in 2.5 percent, and focal slowing in 0.7 percent **[22].** In another study, interictal focal intermittent paroxysmal activity was noted in 38 percent of 29 children with CAE, consisting in most cases of frontal spike wave or polyspike and wave discharges **[23].** In current study 82.2% of patients have typical interictal EEG findings of normal background activity with generalized synchronous and symmetrical 3-4 Hz spike-and-wave discharges and 97.3% of them good seizures control, while 8.9% of patients have accompanied polyspike and wave discharges and only

2.2% of patients have frontal focal slow wave discharges and both groups have poor seizure control(3.3% & 0% respectively). Focal interictal spikes are not related to an unfavorable outcome **[24]** but the prognostic value of the fixed frontal "lead in" anomaly is inconclusive. Indeed patients with ictal EEGs showing this feature have been considered to belong to the "frontal absence group," with a higher incidence of learning problems and less controllable absences **[25]** In our study we found 40 of 45 patients achieved remission ( 88.9%), the seizures were uncontrolled in 11.1 % of patients. VPA as monotherapy was started at the time of initiation for all patients, remission rate difference between patients with typical CAE and those with early onset absence (92.8% versus 33.3%). lower percentage (2.4% ) of typical CAE patients receiving combined therapy when compared with those with early onset absence 66.6%. Many other studies have found that the absence of a clinical seizure within 6 months of taking AEDs or those who need monotherapy tend to have a better outcome than do those whose disease remains uncontrolled for >1 year [**4,12,13,14,26**]

**Limitations of the study:** This was a retrospective clinic-based series and may not represent the full spectrum of childhood absence epilepsies. One possible clinical difference between typical CAE and early onset CAE is worse cognitive function in the latter group. However we did not examine the cognition of the patients with detailed neuropsychological testing in this study

**Conclusion**: Although the current study is based on a small sample populations the findings suggest that early onset of absence seizures, GTCSs during the active stage of the disease, abnormal neurodevelopmental status and EEG features atypical for CAE are the most important predictive factors for an unfavorable prognosis of CAE.

While sex , family history of generalized epilepsy; and personal history of febrile convulsions are not predictors for CAE outcome.

    **Recommendations:** Large prospective multicentric studies would be necessary to investigate the possible cognitive function difference between typical CAE and early-onset CAE.
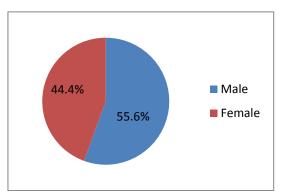


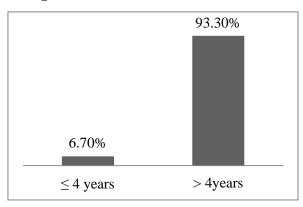**Figure 2: Male to female distribution**
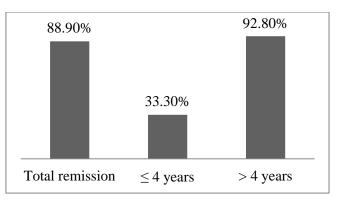


**Figure 2: Age of absence seizure onset distribution**

**Figure 3: Remission rate distribution**

**Table 1: Frequency of clinical characters**

| Character | Frequency (%) |
|---|---|
| Other seizure types | |
| Only absence | 34  (75.6%) |
| GTC | 10  (22.2%) |
| Eyelid myoclonia | 1     (2.2%) |
| History of febrile seizures | |
| Positive | 5    (11.1%) |
| Negative | 40  (88.9%) |
| Family history IGE | |
| Positive | 11 (24%) |
| Negative | 34  (75.6%) |
| EEG findings | |
| 3-4 GSW/sec | 37 (82.2%) |
| Focalslowdischarges+3GSW/sec | 1  (2.2%) |
| 2.5 GSW/sec +polyspikes | 4   (8.9%) |
| Not available | 3    (6.7%) |
| Monotherapy | |
| Na Valoproate | 39  (86.7%) |
| Ethosuximide | 2    (4..4%) |
| Lamotrigine | 1    (2.2%) |
| Companied therapy | |
| Na Valoproate + Lamotrigine | 3    (6.7%) |
| Seizure control | |
| Remission | 40   (88.9%) |
| Uncontrolled | 5    (11.1%) |

**Table 2: Relation of seizure control with other characters**

| Character | | Seizure control | | P Value |
|---|---|---|---|---|
| | | Remission | Uncontrolled | |
| Sex | | | | 0.243 |
| | Male | 21 (84%) | 4 (16%) | |
| | Female | 19 (95%) | 1 (5%) | |
| Age of seizure onset | | | | 0.002 |
| | ≤4 years | 1 (33.3%) | 2 (66.7%) | |
| | > 4years | 39 (92.8%) | 3 (7.1%) | |
| History of febrile seizures | | | | 0.502 |
| | Positive | 4 (80%) | 1 (20%) | |
| | Negative | 36 (90%) | 4 (10%) | |
| Other seizure type | | | | 0.004 |
| | Only absence | 33 (97.0%) | 1 (2.9%) | |
| | GTC | 6 (60%) | 4 (40%) | |
| | Eyelid myoclonia | 1 (100%) | 0 | |
| Neurodevelopmental status | | | | 0.002 |
| | Normal | 30 (90.9%) | 3 (9.09%) | |
| | Motor delay | 0 | 1 (100%) | |
| | Learning disabilities | 0 | 1 (100%) | |
| Family H/O of epilepsy | | | | 0.391 |
| | Positive | 9 (81.8%) | 2 (18.1%) | |
| | negative | 31(93.9%) | 3 (8.8%) | |
| EEG findings | | | | 0.0001 |
| | 3-4GSW/sec | 36 (97.3%) | 1 (2.7%) | |
| | 3GSW/sec +Focal slow w | 0 | 1 (100%) | |
| | 2.5 GSW/sec +polyspikes | 1 (25%) | 3 (75%) | |
| | Not available | 3(100%) | 0 | |
| Treatment | | | | 0.0001 |
| | Na Valoproate | 37 (94.9%) | 2 (5.1%) | |
| | Ethosuximide | 2 (100%) | 0 | |
| | Lamotrigine | 1 (100%) | 0 | |
| | Na. Valoproate + Lamotrigine | 0 | 3 (100%) | |

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