ORIGINAL ARTICLE

Annals of Agricultural and Environmental Medicine
www.aaem.pl

Clinical and electroencephalographic characteristics of febrile seizures – a retrospective cohort study

Jolanta Strzelecka[1,A-F], Tymon Skadorwa[2,3,A-F], Paweł Dryżałowski[1,B,D,F]

[1] *Department of Paediatric Neurology, Medical University, Warsaw, Poland*
[2] *Department of Paediatric Neurosurgery, Bogdanowicz Memorial Hospital for Children, Warsaw, Poland*
[3] *Department of Descriptive and Clinical Anatomy, Medical University, Warsaw, Poland*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Strzelecka J, Skadorwa T, Dryżałowski P. Clinical and electroencephalographic characteristics of febrile seizures – a retrospective cohort study. Ann Agric Environ Med. doi: 10.26444/aaem/146895

Abstract

Introduction and Objective. Febrile seizures (FS) are the most common type of seizures in childhood. Depending on focality, duration and possible recurrence FS are divided into simple (SFS), complex (CFS) and simple plus (SFS+). Simple FS are considered not to require detailed diagnostics nor electroencephalographic (EEG) studies, even though some cases present EEG abnormalities that may affect the initial diagnosis and long-term prognosis. The aim of the study was to assess the usefulness of EEG as a potential prognostic neuromarker of FS.

Materials and method. 103 FS children aged 5–55 months (SFS – 62 cases (60%); SFS+ – 15 cases (15%); CFS – 26 cases (25%) were retrospectively analyzed. EEG was performed in all cases after the resolution of fever (3rd-7th day). The clinical characteristics (seizure morphology, episode duration and recurrence) were confronted with EEG findings (normal vs. epileptiform pattern: generalized or focal). The results were analyzed statistically to look for prognostically useful correlations.

Results. Abnormal EEG pattern was recorded in 29% of patients (SFS 27%; SFS+ 40%; CFS 27%). Generalized epileptiform discharges were noted in 18 cases (SFS 21%; SFS+ 27%; CFS 4%) while focal EEG discharges were seen in 12 cases (SFS 6%; SFS+ 13%; CFS 23%). Generalized FS in 30% were associated with generalized (19%) or focal (11%) EEG discharges.

Conclusions. The current protocol of FS management does not warrant further diagnostics in 27–40% of FS children with abnormal EEG. SFS+ children are be the most underdiagnosed group, with a greater number of EEG abnormalities compared to SFS and CFS. It seems reasonable to extend the routine EEG diagnostics into this group of FS patients.

Key words

adolescent, fever, infant, electroencephalography, seizures, epilepsy, status epilepticus

INTRODUCTION AND OBJECTIVE

Febrile seizures are often described as occurring between the 6th – 60th month of age. They are associated with an increase in body temperature of over 38°C (fever), but without infection of the central nervous system, acute electrolyte imbalance, metabolic disease, or any other defined cause [1]. Febrile seizures can be divided into simple and complex, with the predominance of simple seizures of 65–75% [2]. Simple febrile seizures (SFS) are featured with generalized tonic/tonic-clonic convulsions, lasting less than 10 minutes, occuring once in 24h (non-recurrent), and are present in a neurologically and developmentally normal child. In contrast, complex febrile seizures (CFS) include focal convulsions, last more than 10 minutes, occur more than once in 24h (recurrent), and may have a history of a pre-existing neurological disorder [3]. The most severe variant of CFS is 'febrile status epilepticus' (FSE). According to the results of an FEBSTAT study, in the course of FSE a number of abnormalities can be detected in cerebrospinal fluid, imaging and EEG examinations, but e mortality and complications are extremely rare [4, 5].

Address for correspondence: Tymon Skadorwa, Department of Peadiatric Neurosurgery, Bogdanowicz Memorial Hospital for Children, Nieklanska 4/24, 03-924 Warsaw, Poland
E-mail: tskadorwa@wum.edu.pl

Received: 01.07.2021; accepted: 22.02.2022; *first published: 04.04.2022*

The traditional FS classification does not cover all groups of patients. In 2015, the American Academy of Pediatrics added a new category – 'simple febrile seizures plus' (SFS+), including patients with recurrent generalized seizures within 24h, with no abnormalities in neurological examination during the inter-ictal period [6, 7]. This category should not be confused with genetic epilepsy and febrile seizures plus (GEFS+), a complex epileptic encephalopathy associated with repeated multiform seizures and impairment of motor and mental development, atactic gait and spasticity. This separate, often drug-resistant epileptic syndrome is associated with mutations in the SCN1A gene and commonly diagnosed in children outside the typical age range [7]. Two other recently identified mutations in sodium channel genes in children with GEFS+ revealed a benign course of this disease [8]. Another category that should be included in the differential diagnosis of febrile seizures is 'febrile infection-related epilepsy syndrome' (FIRES), a catastrophic epileptic encephalopathy, developing as a consequence of a febrile episode in early childhood (4–9 years) [5, 9, 10]. FS are defined as recurrent when another set of seizures is observed within 24h with a new episode of fever in a child who previously experienced FS. The risk of FS recurrence is estimated for approximately 40% [11]. The most common risk factors for recurrence of both simple and complex FS include the age of onset lower than 15 months, a positive family history for FS

or epilepsy in first-degree relative, a maternal preponderance in the positive family history for FS, an episode of complex FS at onset, previous multiple episodes within the same febrile illness and a gradual rise in temperature prior to the initial onset of seizures [12]. The recurrence of FS is still a discussed factor influencing the management of FS. Along with the presence of bacterial infection it was recently investigated as a reason for hospital admission. In the study by Kannikeswaran et al., the rate of seizure recurrence and serious bacterial infection in children with CFS was relatively low (5.1% and 6.7%, respectively) [13]. According to a 2021 Japanese study, the body temperature may be another independent predictor of FS recurrence during a febrile illness [14]. Prophylaxis in recurrent FS may be achieved with the use of antiepileptic and antipyretic drugs, such as intermittent diazepam and continuous phenobarbital. Although effective, this therapy brings a risk of adverse effects (reported in up to 30% of patients). The benefit of other therapies, e.g. with clobazam or levetiracetam, need further validation studies [15]. Febrile seizures are currently conceptualized as a disturbance of the neuronal networks, and may be a precursor of lifelong epilepsy. The risk of subsequent epilepsy after simple FS is comparable to the general population (less than 2%) [12]. However, the risk is notably higher after complex FS episode, and is considereto be around 4–7% [16, 17, 18]. Risk factors for epilepsy development in FS children include developmental delay, abnormal neurological status, a history of complex FS (and FS status epilepticus, with low morbidity and mortality), epilepsy and prolonged FS in a first-degree relative, higher age at the time of complex FS, multiple FS episodes within 24h, FS episode duration over 10 minutes and the presence of focal epileptiform discharges [19, 20]. Subsequent unprovoked seizures may be also prognostically related with a low parental educational status [21]. Considering these factors, in most of the institutions a long-lasting medical care is offered to FS patients in order to monitor the potential epileptic sequelae. Another reason for close follow-up is the anxiety of families related to a first-time seizure [22]. Apart from epilepsy concerns, there is also evidence of mild cognitive deficits in higher-order functions in preschool and school-age children with CFS, which are observed just a few months after the first episode of FS. The development of these symptoms may be prevented by using various behavioural methods, such as neurobiofeedback [23].

Nevertheless, in a complex diagnostics of FS a reliable predictive biomarker is still a matter of hypotheses. Neuromarkers represent objective measurements of brain anatomy or physiology that can be obtained in clinical practice by applying neuroscientific methods. This term is applied to any neuropsychological parameter of behaviour or a structural or functional indicator of the brain. Although to-date no reliable studies on FS-related neuromarkers have been published, some papers suggest that such a role may be attributed to an electrophysiologic variety observed among FS patients [24]. According to Thébault-Dagher et al., a better understanding of the role of EEG in the characteristics of FS and related prognosis may lead to the introduction of early clinical care [25, 26]. Other papers postulate the inclusion of other techniques in diagnostics, such as quantitative EEG (QEEG) or event-related de/synchronization (ERD/ERS) assessing cognitive and memory functions in response to the auditory stimulus, and event-related potentials (ERPs).

As all these papers highlight the role of EEG, the aim of this study was a direct comparison of the clinical characteristics of FS with their EEG appearance in order to find any matches of predictive or diagnostic value. This assumption may seem controversial, as the papers on EEG in febrile seizures have not proved a clear benefit from its use in this group of patients [27, 32]. The American Academy of Pediatrics does not recommend EEG after SFS as a part of routine investigation, as the majority of patients with this disorder have good prognosis and do not develop epilepsy [28]. However, the risk of developing epilepsy is higher when seizures are focal or complex, and when EEG displays focal discharges [29, 30, 31]. Therefore, patients after CFS are examined with EEG as a routine part of diagnostics [32], although according to a recently published review (Cochrane Library, 2020 update), the usefulness of EEG in CFS still remains debatable since no randomised controlled trials were found to support its use and timing [33].

Considering these facts and knowing that EEG can be of the utmost importance for the prognosis of epilepsy, and that the overall risk for epilepsy development is higher in people with a history of FS, the aim of this study was to confront the clinical picture of febrile seizures in children with their EEG records.

MATERIALS AND METHOD

This is a retrospective cohort study, conducted between March – September 2020 (duration: 6 months). The studied group consisted of 103 paediatric patients from the authors' clinical practice, aged from 5 – 55 months. The group consisted of 54 boys (52%) and 49 girls (48%). All patients were admitted to the hospital due to the first or another episode of a febrile seizure. In all cases, the history of FS was taken and included the seizure morphology (generalized tonic or tonic-clonic vs. focal), the number of lifetime and daily episodes, and the duration of a single episode. All patients were treated according to current protocol [6].

EEG was performed in all cases after the resolution of fever, typically between the 3rd – 7th day. The parents or caregivers of all patients consented to the examination. Children burdened with neurological disorders (such as cerebral palsy or developmental delay) or patients with a previous diagnosis of epilepsy, were not enrolled to the study. EEG recordings were performed during 60 minutes of spontaneous sleep with the use of a 16-channel Elmico EEG DigiTrack device, according to the international 10–20 superficial electrode placing system. Activation procedures (hiperventilation, photostimulation) were not used. The EEG records were classified either as normal or abnormal, with generalized or focal discharges. The protocol of the study was approved by the local Bioethics Committee (Ref. No. AKBE/2/2020).

Obtained data were analyzed statistically with Statistica 13.6PL software (StatSoft Poland). The differences between the variables were assessed with the chi-squared test. Effect sizes were measured with Pearson's C or Cramer's V coefficients. Probability values below 0.05 were considered statistically significant.

RESULTS

The average age at the time of FS was 27±13 months. Generalized seizures were observed in 96 patients (93%), simple febrile seizures were noted in 62 patients (60%), simple febrile seizures plus presented in 15 patients (15%) and 26 patients had complex febrile seizures (25%). In 59 patients (57%), the episode of FS occurred for the first time, 34 patients presented with a second episode (33%), and 16 patients experienced their third or further episode of FS (16%). The duration of an episode was less than 10 minutes in 82 patients (80%), and longer in 21 patients (20%), of whom 2 (1.9%) were documented as febrile status epilepticus (FSE). The majority of patients (84 cases, 82%) reported one episode per day, 19 patients (18%) had at least one recurrence in 24h. Of all patients, 73 children (71%) had normal EEG and 30 presented epileptiform discharges (29%): generalized in 18 cases (17%) and focal in 12 (12%). Detailed results are included in Tables 1–3.

Table 1. Relation of episode duration to clinical features and recurrence

Clinical characteristics	Type of FS			Statistics used	
	SFS	SFS+	CFS	difference	correlation
duration <10 min	62 (76%)	15 (18%)	5 (6%)	p<0.05; χ^2 test	Cramer's V; V=0.87, p<0.05
duration >10 min	0 (0%)	0 (0%)	21 (100%)		
non-recurrent FS	62 (74%)	0 (0%)	22 (26%)	p<0.05; χ^2 test	Cramer's V; V=0.88, p<0.05
recurrent FS	0 (0%)	15 (79%)	4 (21%)		

FS – febrile seizures.

Table 2. Relation of the type of FS to episode duration and recurrence

Clinical characteristics	Episode duration		Statistics used	
	<10 min	>10 min	difference	correlation
generalized seizures	77 (80%)	19 (20%)	p>0.05; χ^2 test	Pearson's C; C=0.05, p>0.05
focal seizures	5 (71%)	2 (29%)		
non-recurrent FS	67 (80%)	17 (20%)	p>0.05; χ^2 test	Pearson's C; C=0.07, p>0.05
recurrent FS	15 (79%)	4 (21%)		

Table 3. Relation between clinical and electroencephalographic characteristics of febrile seizures

	EEG characteristics			
Clinical characteristics	normal	generalized	focal	correlation
SFS (n=62)	45 (72.6%)	13 (20.9%)	4 (6.4%)	Cramer's V; V=0.20, p>0.05
SFS+ (n=15)	9 (60.0%)	4 (26.7%)	2 (13.3%)	
CFS (n=26)	19 (73.1%)	1 (3.8%)	6 (23.1%)	
generalized seizures (n=96)	67 (69.8%)	18 (18.7%)	11 (11.5%)	Cramer's V; V=0.12, p>0.05
focal seizures (n=7)	6 (85.7%)	0 (0.0%)	1 (14.3%)	
non-recurrent FS (n=84)	61 (72.6%)	14 (16.6%)	9 (10.8%)	Cramer's V; V=0.08, p>0.05
recurrent FS (n=19)	12 (63.2%)	4 (21.0%)	3 (15.8%)	
duration <10 min (n=82)	59 (71.9%)	17 (20.7%)	6 (7.3%)	Cramer's V; V=0.29, p<0.05

FS – febrile seizures, *SFS* – simple febrile seizures, *SFS+* – simple febrile seizures plus, *CFS* – complex febrile seizures

The clinical presentation of FS did not correlate with the duration of seizures. Most of the generalized FS were short-lasting seizures, but in on-fifth of the cases the episodes lasted longer. Shorter episodes also dominated in focal FS, but the percentage of episodes exceeding 10 minutes duration in this group was up to 30%. Differences between the groups were not statistically significant (Tab. 1). However, the episode duration strongly corresponded to the type of FS (Tab. 2). None of the SFS and SFS+ patients by definition had seizures lasting more than 10 minutes, but among CFS patients, 21/26 (81%) presented long-lasting seizures and 5/26 (19%) had exclusively short episodes of FS.

The episode duration correlated neither with the recurrence of FS and in children nor with recurrent FS the prolongation of seizures was observed with the same frequency as in children without recurrence (Tab. 1). Nevertheless, in relation to the type of FS, recurrence was observed in SFS+ (by definition) and CFS patients; in the latter group only 4/26 (15%) patients revealed recurrent seizures. The correlation between these two factors was strong and statistically significant (Tab. 2).

A similitude analysis of clinical and electroencephalographic characteristics of FS showed that, regardless, the seizures lasted less or more than 10 minutes, and at least 66% of patients had normal EEG. This ratio was higher in patients presenting short-lasting episodes (non-significant, Tab. 3). However, a weak correlation existed between the EEG abnormalities and duration of seizures: generalized EEG discharges were found four times more frequently in short-lasting episodes, while patients manifesting long-lasting seizures had focal EEG discharges recorded about three times more often than patients with short FS episodes (Tab. 3).

Another interesting finding is the observation that almost 70% of children presenting generalized FS had a normal EEG. Generalized EEG discharges were seen in less than one-fifth of patients manifesting generalized seizures. In addition, focal EEG discharges were recorded with comparable frequency in patients presenting generalized and focal FS (Tab. 3). The relation between the type of FS with EEG revealed a non-significant tendency that the occurrence of focal EEG discharges rises with the complexity of FS (Tab. 3). Generalized EEG discharges were observed most commonly in the group of SFS+. This group was also characterized by the smallest number of normal EEG compared to the SFS and CFS groups (Tab. 3).

DISCUSSION

Febrile seizures constitute a multidisciplinary problem. In many countries they are in the domain of paediatric management and are also an area of interest for paediatric neurologists. Although the treatment protocol has been established and validated by international paediatric and neurologic societies, the phenomenon still raises some concerns about its mechanism and prognosis. Despite well-based clinical classificatio, only a few papers focus on the correlation between EEG and clinical characteristics in particular categories of FS. The presented study seems to be the first combining such observations in a large group of children.

The literature data indicate that FS occur at a similar frequency in both genders, with a slight tendency toward male individuals (54–58%) [27]. The findings of the current

study are consistent with this result – the prevalence of males in the presented group was not significant and amounted to 52%.

The common opinion is that the complexity of FS and possible recurrence and duration of a single episode are the most important clinical features, as they bring specific issues about the management and subsequent prognosis. The complexity determines further diagnostic work-up, the recurrence makes a distinction between SFS and SFS+, and the episode duration is directly related to therapeutic procedures. The combination of these three factors not only determines the type of FS, but also promotes (or not) the need for further neurologic care (Tab. 4).

Table 4. Combinations of clinical factors determining the type of febrile seizures

Clinical factors of FS	non-recurrent	recurrent
generalized seizures AND duration <10 min	SFS	SFS+
generalized seizures AND duration >10 min	CFS	CFS
focal seizures AND duration <10 min	CFS	CFS
focal seizures AND duration >10 min	CFS	CFS

FS – febrile seizures, *SFS* – simple febrile seizures, *SFS+* – simple febrile seizures plus, *CFS* – complex febrile seizures

According to literature data, most patients have simple seizures [32]. SFS are believed not to be burdened with electroencephalographic abnormalities and therefore to carry a good prognosis [28, 34]. CFS carry a higher risk of subsequent epilepsy, but in the mentioned study of Kannikeswaran et al. the EEG abnormalities were observed only in 4.4% of CFS cases [13]. Results of the current study showed that in simple FS, both types of EEG abnormalities could be recorded, with the expected predominance of generalized discharges. In SFS+ patients, the percentage of focal discharges was higher than in SFS. In CFS cases, it reached the greatest amount of 23%. Besides, normal EEG was recorded in only 60% of all SFS+ patients. This distribution does not reflect the popular belief in maintaining the extant protocol of management. According to the American Academy of Pediatrics, SFS patients do not require routine EEG [28], and its implementation in CFS is also debatable [33]. On the other hand, the risk of developing epilepsy rises in abnormal EEG and complex FS [29, 30, 31], which indicates the need for these patients to be guided by a neurologist. The results obtained in the current study showed that 29.1% of FS patients had abnormal EEG and at least 47.5% would need subsequent neurologic care (Tab. 5).

Table 5. Distribution of normal and abnormal EEG in the studied population

	normal EEG [%]	abnormal EEG [%]
SFS	43.7	16.5*
SFS+	8.7	5.8*
CFS	18.4*	6.8*

Asterisk (*) – patients requiring further neurologic care due to abnormal EEG or complex FS. *SFS* – simple febrile seizures, *SFS+* – simple febrile seizures plus, *CFS* – complex febrile seizures

Translating the percentages into the number of patients reveals interesting therapeutic scenarios. Of 96 patients in this study who presented with generalized seizures, 29 had abnormal EEG. Of these, 17 were initially classified as SFS, 6 as SFS+ and 6 as CFS (Fig. 1). According to the guidelines, the EEG should not have been routinely performed in 23 children. This finding shows that subjective assessment of the type of FS is not always confirmed in the EEG, and in some cases it may prevent a necessary diagnostics.

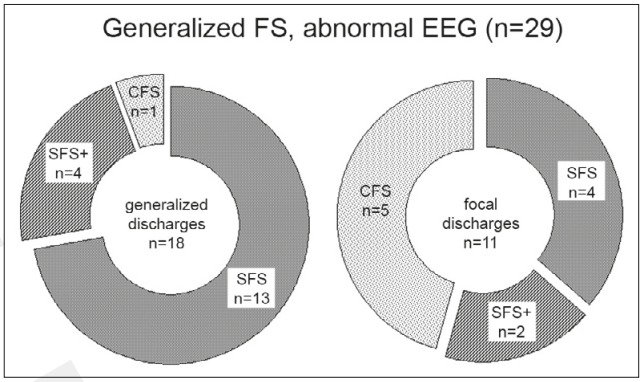

Figure 1. Distribution of types of FS among children with generalized FS and EEG abnormalities

The second area of analysis covered a potential link between the recurrence of FS episodes and EEG normality. Data obtained in the current study revealed that EEG abnormalities were recorded in 37% of patients with recurrent FS, and in 27% non-recurrent individuals. This factor also influences the decision making process. Of 84 non-recurrent FS patients, 23 had abnormal EEG and 17 were classified on admission as SFS. In the group of recurrent FS patients (19 cases) the EEG abnormalities were detected in seven children (six cases of SFS+ and one case of CFS). Taking the guidelines into account, additional diagnostics and subsequent neurologic care would then be offered to only one child in this group (Fig. 2).

The last analyzed parameter was the duration of FS episode. The distribution of EEG findings showed that regardless of the episode duration, at least 66% of patients presented normal EEG. Among 29% of the remaining patients, in those with short-lasting episodes generalized discharges were recorded more frequently than focal. In contrast, children

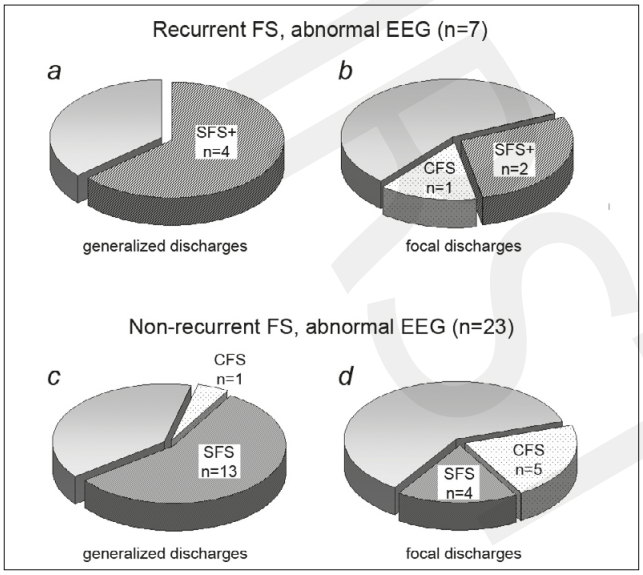

Figure 2. Distribution of types of FS among children with abnormal EEG and recurrent FS (a, b) or non-recurrent FS (c, d)

with abnormal EEG and episodes longer than 10 minutes revealed rather focal EEG discharges (Tab. 3). This finding shows an interesting observation regarding the relation between FS episode duration and EEG abnormalities: focal EEG discharges were recorded more often in long-lasting FS episodes. The relation between these two factors was not very strong, but statistically significant, and corresponded to a trend observed between the EEG and the type of FS, where focal EEG discharges appeared more often in complex FS. These two effects may suggest that focal discharges tend to occur more likely in complex and long-lasting seizures.

The episode duration alone also has therapeutic importance. The duration of five minutes for a seizure has been recently suggested as the limit for an active therapeutic intervention [35]. This instruction was supported by an observation that seizures lasting more than five minutes rarely stop spontaneously, and have a higher potential to induce permanent neuronal injury and drug resistance, which may lead to FSE [36]. Distinguishing between the prolongation of FS or status epilepticus caused by an infection, and acute encephalopathy, may clinically not always be straightforward. This is especially in the first stage of the disease, which, as a common complication of viral infection (rarely bacterial), mostly affects young children and is related to a high mortality and morbidity. Acute encephalopathies with convulsions, impaired consciousness and fever may be provoked by bacterial meningitis, viral encephalitis, or other severe infections [37, 38].

The presented data show the diagnostic pitfalls associated with the rigid use of the FS treatment protocol. The question is whether the FS classification should be based only on the clinical factors (episode duration, clinical picture, recurrence), or whether the EEG may play the role of a fourth, independent factor. The weakness of the original hypothesis that EEG could be a prognostic biomarker of FS is in the fact that no clinically significant correlation was found between the results of EEG and the type of FS. It should be noted, however, that the results of statistical analysis were very close to the significance (p=0.07), which allows them to be interpreted as an interesting trend. In the authors' opinion, the analysis of a larger number of cases could verify this result.

Analysis of the correlation between the EEG result and individual factors revealed very interesting relationships that contribute a great deal to the perception of FS as an independent entity. It seems that the prognostic value is not only in the FS type itself, but also in the combination of discussed factors. This indicates that while SFS and SFS + arise as single variants, CFS is a multivariate type and individual combinations may be associated with a different prognosis. The inclusion of EEG as an independent prognostic factor could help avoid the pitfall associated with the current protocol, that a child with abnormal EEG would not receive neurologic care.

According to literature data, an abnormal EEG may be found in up to 10% of healthy individuals [39], but all of them are advised to be guided by a neurologist, at least until the causes of abnormalities requiring any type of treatment are excluded [40]. A straightforward diagnosis of a focal seizure in a small child is extremely difficult and in most of the cases a generalized seizure is diagnosed which, in turn, increases the chance of diagnosing simple FS. The current analysis shows that abnormal EEG is involved in

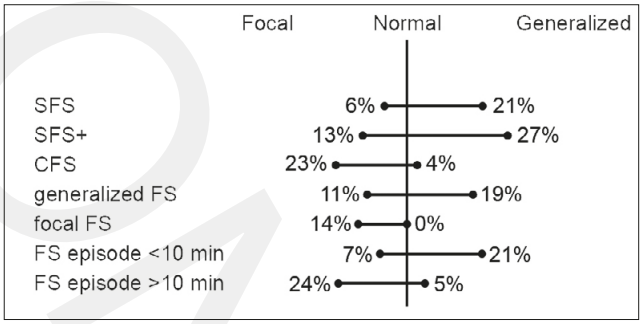

Figure 3. EEG deviations in FS children by clinical categories

all types of FS (Fig. 3), but only in CFS an EEG exam is routinely recommended. Focal EEG discharges, in turn, direct the diagnostics towards imaging, which means that about 11% of patients have serious reasons for concern. While the diagnosis of focal seizure (and thus CFS) immediately indicates the need to extend the diagnostic work-up, the more commonly diagnosed generalized seizures more likely lead to the diagnosis of SFS or SFS+. In these cases, the recurrence becomes a differentiating element as it indicates that children with SFS+ may be the most underdiagnosed group, with the greatest number of detected EEG abnormalities. While simple FS do not exceed the populational risk of having an abnormal EEG, the group of patients with SFS+ does. Therefore, it may seem reasonable to routinely perform an EEG examination in this group, and based on the result, to refer the patients for subsequent diagnostics.

CONCLUSIONS

1. Most of FS (71–80%) are short-lasting seizures (less than 10 minutes).
2. The episode duration of FS does not correlate with its recurrence, but reveals a weak correlation with EEG abnormalities: short-lasting FS are more often generalized in EEG, while long-lasting FS more likely tend to be focal discharges.
3. Most of FS patients have normal EEG, regardless of the type of FS and clinical picture (generalization or focality).
4. EEG abnormalities appear in 30% of FS patients:
   a. generalized EEG discharges are present in 19% of generalized FS;
   b. abnormal EEG discharges are observed in 40% of SFS+ patients;
   c. focal EEG discharges occur more often in CFS than in SFS or SFS+.
5. Although the status of EEG and its timing after FS has not been validated, the authors consider that the group of SFS+ patients would benefit from medical care after the FS episode. Considering the presented data, it is the authors' opinion that the usefulness of EEG in FS patients should be investigated in subsequent studies.

Acknowledgements
The authors would like to acknowledge Dr. Adam Zieliński and Dr. Małgorzata Paciorkowska from Bogdanowicz Memorial Hospital for Children, Warsaw, who contributed to the collection of clinical data.

REFERENCES

1. Leung AK, Hon KL, Leung TN. Febrile seizures: An overview. Drugs Context. 2018; 7: 1–12. https://doi.org/10.7573/dic.212536
2. Harini C, Nagarajan E, Kimia AA, et al. Utility of initial EEG in first complex febrile seizure. Epilepsy Behav. 2015; 52: 200–204. https://doi.org/10.1016/j.yebeh.2015.09.003
3. Gupta A. Febrile seizures. Continuum (Minneap Minn). 2016; 22(1): 51–59. https://doi.org/10.1212/CON.0000000000000274
4. Hesdorffer DC, Shinnar S, Lax DN, et al. Risk factors for subsequent febrile seizures in the FEBSTAT study. Epilepsia. 2016; 57(7): 1042–1047. https://doi.org/10.1111/epi.13418
5. Cross JH. Fever and fever-related epilepsies. Epilepsia. 2012; 53: 3–8. https://doi.org/10.1111/j.1528-1167.2012.03608.x
6. Mastrangelo M, Midulla F, Moretti C. Actual insights into the clinical management of febrile seizures. Eur J Pediatr. 2014; 173(8): 977–982. https://doi.org/10.1007/s00431-014-2269-7
7. Ma QL, Wang B, Chen GF, et al. Association between SCN1A rs3812718 polymorphism and generalized epilepsy with febrile seizures plus. Zhongguo Dang Dai Er Ke Za Zhi. 2018; 20(2): 130–133. https://doi.org/10.7499/j.issn.1008-8830.2018.02.010
8. Ma H, Guo Y, Chen Z, et al. Mutations in the sodium channel genes SCN1A, SCN3A, and SCN9A in children with epilepsy with febrile seizures plus (EFS+). Seizure. 2021; 88: 146–152. https://doi.org/10.1016/J.SEIZURE.2021.04.006
9. Fox K, Wells ME, Tennison M, et al. Febrile Infection-Related Epilepsy Syndrome (FIRES): A Literature Review and Case Study. Neurodiagn J. 2017; 57(3): 224–233. https://doi.org/10.1080/21646821.2017.1355181
10. Culleton S, Talenti G, Kaliakatsos M, et al. The spectrum of neuroimaging findings in febrile infection-related epilepsy syndrome (FIRES): A literature review. Epilepsia. 2019; 60(4): 585–592. https://doi.org/10.1111/epi.14684
11. Cappellari AM, Brizio C, Mazzoni MB, et al. Predictive value of EEG for febrile seizure recurrence. Brain Dev. 2018; 40(4): 311–315. https://doi.org/10.1016/j.braindev. 2017.12.004
12. Wilmshurst JM, Gaillard WD, Vinayan KP, et al. Summary of recommendations for the management of infantile seizures: Task Force Report for the ILAE Commission of Pediatrics. Epilepsia. 2015; 56(8): 1185–1197. https://doi.org/10.1111/epi.13057
13. Kannikeswaran N, Sivaswamy L, Farooqi A, et al. Children With Complex Febrile Seizures: Is Hospital Admission Necessary? Clin Pediatr (Phila). 2021; 60(8): 363–369. https://doi.org/10.1177/00099228211017702
14. Kubota J, Higurashi N, Hirano D, et al. Body temperature predicts recurrent febrile seizures in the same febrile illness. Brain Dev. 2021; 43(7): 768–774. https://doi.org/10.1016/J.BRAINDEV.2021.03.002
15. Offringa M, Newton R, Nevitt SJ, et al. Prophylactic drug management for febrile seizures in children. Cochrane Database Syst Rev. 2021; 6(6) https://doi.org/10.1002/14651858.CD003031.PUB4
16. Patel N, Ram D, Swiderska N, et al. Febrile seizures. BMJ. 2015; 351: h4240. https://doi.org/10.1136/bmj.h4240
17. Patterson JL, Carapetian SA, Hageman JR, et al. Febrile seizures. Pediatr Ann. 2013; 42(12): e258–e263. https://doi.org/10.3928/00904481-20131122-09
18. Jain A, Tiwari S, Padickaparambil S. Cross-disciplinary appraisal of knowledge and beliefs regarding the diagnosis of autism spectrum disorders in India: A cross-sectional survey. Indian J Psychol Med. 2020; 42(3): 219–224. https://doi.org/10.4103/IJPSYM.IJPSYM_163_19.
19. Gencpinar P, Yavuz H, Bozkurt Ö, et al. The risk of subsequent epilepsy in children with febrile seizure after 5 years of age. Seizure. 2017; 53: 62–65. https://doi.org/10.1016/j.seizure.2017.11.005
20. Kim H, Byun SH, Kim JS, et al. Clinical and EEG risk factors for subsequent epilepsy in patients with complex febrile seizures. Epilepsy Res. 2013; 105(1–2): 158–163. https://doi.org/10.1016/j.eplepsyres.2013.02.006
21. Hwang G, Kang H, Park SY, et al. Predictors of unprovoked seizure after febrile seizure: short-term outcomes. Brain Dev. 2015; 37(3); 315–321. https://doi.org/10.1016/J.BRAINDEV.2014.06.003
22. Klotz KA, Özcan J, Sag Y, et al. Anxiety of families after first unprovoked or first febrile seizure – A prospective, randomized pilot study. Epilepsy Behav. 2021; 122. https://doi.org/10.1016/J.YEBEH.2021.108120
23. Mirski A, Pachalska M, Mirska N, et al. An evaluation of personalized neurofeedback training for rolandic epilepsy: a case study. Acta Neuropsychologica 2014; 12(3): 271–287. https://doi.org/10.13140/2.1.4321.4724
24. Kropotov JD. Functional neuromarkers for neuropsychology. Acta Neuropsychologica 2018; 16(1): 1–7. https://doi.org/10.5604/01.3001.0011.6504
25. Thébault-Dagher F, Deguire F, Knoth IS, et al. Prolonged and unprolonged complex febrile seizures differently affect frontal theta brain activity. Epilepsy Res. 2020; 159: 106217. https://doi.org/10.1016/j.eplepsyres.2019.106217
26. Billstedt E, Nilsson, G, Leffler L, et al. Cognitive functioning in a representative cohort of preschool children with febrile seizures. Acta Paediatr. 2020; 109(5): 989–994. https://doi:10.1111/apa.15059
27. Gradisnik P, Zagradisnik B, Palfy M, et al. Predictive value of paroxysmal EEG abnormalities for future epilepsy in focal febrile seizures. Brain Dev. 2015; 37(9): 868–873. https://doi.org/10.1016/j.braindev.2015.02.005
28. Duffner PK, Berman PH, Baumann RJ, et al. Clinical practice guideline – Neurodiagnostic evaluation of the child with a simple febrile seizure. Pediatrics. 2011; 127(2): 389–394. https://doi.org/10.1542/peds.2010-3318
29. Lee SH, Byeon JH, Kim GH, et al. Epilepsy in children with a history of febrile seizures. Korean J Pediatr. 2016; 59(2): 74–79. https://doi.org/10.3345/kjp.2016.59.2.74
30. Seinfeld SA, Pellock JM, Kjeldsen MJ, et al. Epilepsy after Febrile Seizures: Twins Suggest Genetic Influence. Pediatr Neurol. 2016; 55: 14–16. https://doi.org/10.1016/j.pediatrneurol.2015.10.008
31. Tsai JD, Mou CH, Chang HY, et al. Trend of subsequent epilepsy in children with recurrent febrile seizures: A retrospective matched cohort study. Seizure. 2018; 61: 164–169. https://doi.org/10.1016/j.seizure.2018.08.019
32. Laino D, Mencaroni E, Esposito S. Management of pediatric febrile seizures. Int J Environ Res Public Health. 2018; 15(10): 2232. https://doi.org/10.3390/ijerph15102232
33. Shah PB, James S, Elayaraja S. EEG for children with complex febrile seizures. Cochrane Database Syst Rev. 2020; 4(4): 1–23. https://doi.org/10.1002/14651858.CD009196.PUB5
34. Pavlidou E, Panteliadis C. Prognostic factors for subsequent epilepsy in children with febrile seizures. Epilepsia. 2013; 54(12): 2101–2107. https://doi.org/10.1111/epi.12429
35. Natsume J, Hamano SI, Iyoda K, et al. New guidelines for management of febrile seizures in Japan. Brain Dev. 2017; 39(1): 2–9. https://doi.org/10.1016/j.braindev.2016.06.003
36. Prosad S. Management of febrile convulsion in children. Emerg Nurse. 2015; 23(2): 18–25. https://doi.org/10.7748/en.23.2.18.e1431
37. Sooyoung L. Electroencephalographic Approach for Early Diagnosis of Acute Encephalopathy and Encephalitis. Hideo Yamanouchi, Solomon L. Moshé, Akihisa Okumura, editors. Acute Encephalopathy and Encephalitis in Infancy and Its Related Disorders. Elsevier; 2018. p. 71–76.
38. Oguri M, Saito Y, Fukuda C, et al. Distinguishing Acute Encephalopathy with Biphasic Seizures and Late Reduced Diffusion from Prolonged Febrile Seizures by Acute Phase EEG Spectrum Analysis. Yonago Acta Med. 2016; 59(1): 1–14.
39. Tashkandi M, Baarma D, Tricco AC, et al. EEG of asymptomatic first-degree relatives of patients with juvenile myoclonic, childhood absence and rolandic epilepsy: a systematic review and meta-analysis. Epileptic Disord. 2019; 21(1): 30–41. https://doi.org/10.1684/epd.2019.1024
40. Jeong KA, Han MH, Lee EH, et al. Early postictal electroencephalography and correlation with clinical findings in children with febrile seizures. Korean J Pediatr. 2013; 56(12): 534–539. https://doi.org/10.3345/kjp.2013.56.12.534