

Available online at www.sciencedirect.com

# **ScienceDirect**

journal homepage: http://www.elsevier.com/locate/pjnns



# Original research article

# The assessment of risk factors for febrile seizures in children



Krystyna Gontko-Romanowska <sup>a,b,\*</sup>, Zbigniew Żaba <sup>b</sup>, Paweł Panieński <sup>a,b</sup>, Barbara Steinborn <sup>c</sup>, Michał Szemień <sup>a</sup>, Magdalena Łukasik-Głębocka <sup>a</sup>, Krystian Ratajczak <sup>a</sup>, Adrian Chrobak <sup>a</sup>, Joanna Mitkowska <sup>b</sup>, Jacek Górny <sup>a</sup>

#### ARTICLE INFO

Article history: Received 12 May 2016 Accepted 11 July 2017 Available online 31 July 2017

Keywords: Risk factors Children Febrile seizures

#### ABSTRACT

*Objective*: The aim of the paper was to assess the risk factors of febrile seizures in children. *Methods*: The paper presents an analysis of a group of 176 children aged 6 months to 5 years who were admitted to A&E because of febrile seizures.

Results: The analysed group of 176 children comprised 61.96% boys and 38.07% girls, and the average age equalled 23 months. Family history was significant in 9.66% of patients. A statistically significant difference was noticed between insignificant family history and the incidence of febrile seizures. In all the studied groups of children the factor that determined the incidence of febrile seizures was a sudden increase in the body temperature with an infection of the upper respiratory tract of several day's duration as another cause. Febrile seizure incident was most frequently associated with a sudden increase in the body temperature in 53.40% children. A statistically significant difference was observed between persisting fever and an increase thereof during the day. Yet another factor predisposing for febrile seizures incidence was an infection of the upper respiratory system that could be observed in 32.95% patients. The mean body temperature when the seizures occurred was 38.9 °C.

Conclusions: A sudden increase in the body temperature within the first day of pyrexia predisposes for the incidence of febrile seizures and it was proved that it depends on how long fever persists during the day. The other factor triggering the seizures was an infection of the upper respiratory tract of several days' duration.

© 2017 Published by Elsevier Sp. z o.o. on behalf of Polish Neurological Society.

E-mail address: gontko@ump.edu.pl (K. Gontko-Romanowska).

<sup>&</sup>lt;sup>a</sup> Department of Emergency Medicine, Poznan University of Medical Sciences, Poznan, Poland

<sup>&</sup>lt;sup>b</sup> Specialised Health Care Centre for Mother and Child, Poznan, Poland

<sup>&</sup>lt;sup>c</sup> Department of Developmental Neurology, Poznan University of Medical Sciences, Poznan, Poland

<sup>\*</sup> Corresponding author at: Heliodor Swiecicki Clinical Hospital at the Karol Marcinkowski Medical University in Poznan, Department of Emergency Medicine, Przybyszewskiego Street 49, 60-355 Poznań, Poland.

## 1. Introduction

Febrile seizures (FS) are the most common neurological disorder occurring in children and have been known since ancient times. Hippocrates described children with high fever who developed seizures that most often accompanied teething. There is the division of febrile seizures into 3 groups, as follows: simple febrile seizures (SFS), simple febrile seizures plus and complex febrile seizures (CFS). Duration of SFS in less than 15 min, seizures are described as generalised tonic clonic. Simple febrile seizures plus are characterised by more than 1 attack SFS, no neurological abnormalities are found. On the other side, we have got CFS with prolonged duration (over 15 min), focal symptoms or multiple seizures occur in close succession. FS should not be caused by meningitis, encephalitis, any other illness affecting the brain or electrolytes disorders. Recently the issue of febrile seizures has become an area of numerous research studies that allowed better understanding of the causes of the disorder and made it possible to devise the rules of medical proceedings [1-3]. The aim of the paper was to assess the risk factors of febrile seizures in children.

## 2. Materials and methods

The paper presents an analysis of a group of 176 children aged 6 months to 5 years who were admitted to Accident and Emergency Department (A&E) of Specialised Health Care Centre for Mother and Child in Poznan because of FS between 1st January 2008 and 31st December 2009.

The research was a retrospective one and the following factors were taken into consideration during medical records analysis: family history indicative of febrile seizures, if it was the first febrile seizure, body temperature during febrile seizures, the course of a convulsive fit (febrile seizure incidence time, level of child's alertness and consciousness during a convulsive seizure, the exact nature of febrile seizures, post-seizure symptoms), the incidence and character of infection symptoms.

The analysed group of patients was divided into three research subgroups according to age:

- group 1 (infancy) comprising 27 children aged 6–12 months (including 18 males and 9 females),
- group 2 (post-infancy) comprising 118 patients aged 13–36 months (including 73 males and 45 females),

 group 3 (kindergarten) comprising 31 children aged over 37 months and up to 60 months of age (including 18 males and 13 females).

The dependency between the studied characteristics was assessed using Spearman's rank correlation coefficient  $r_s$ . p < 0.05 value was considered statistically significant.

## 3. Results

The analysed group of 176 children comprised 61.96% (n = 109) boys and 38.07% (n = 67) girls, and the average age equalled 23 months  $\pm$  SD 13 months.

During the interview information on the past history of febrile seizures in first-degree relatives (siblings and parents) and second-degree ones (the remaining family members) was obtained. Family history was significant in 9.66% of patients with an incidence of febrile seizures in childhood present in 5.11% of parents, 3.41% of siblings and 1.14% in second-degree relatives of the studied group children (Table 1).

Insignificant family history for febrile seizures was observed as follows in all studied groups:  $group\ 1-96.30\%$ ,  $group\ 2-87.29\%$ , and  $group\ 3-100\%$ . A statistically significant difference was noticed between insignificant family history and the incidence of febrile seizures (p<0.0001).

In group 1 24 (88.89%) out of 27 children developed simple febrile seizures, the remaining part were patients with complex febrile seizures. In group 2 in 112 children (94.12%) there could be observed simple febrile seizures and 6 (5.08%) patients developed complex ones. In group 3 no complex febrile seizures were observed.

The first episode of febrile seizures was reported in 150 children (85.23%), the second one in 21 patients (11.93%), and remaining 5 patients related more than three incidents of febrile seizures.

In all the studied groups of children the factor that determined the incidence of febrile seizures was a sudden increase in the body temperature with an infection of the upper respiratory tract of several day's duration as another cause and gastroenteritis (Table 2). The history with the disease shows that three children (1.70%) had been preventively vaccinated a week before having an episode.

Febrile seizure incident was most frequently associated with a sudden increase in the body temperature in 94 children (53.40%) on the first day of fever and concerned 75 patients (42.62%) and with the body temperature increased above 39 °C in 35 (19.89%) children (Table 3).

Table 1 – Family history for the presence of febrile seizures in the studied age groups.										
	Group 1				Group 2			Group 3		
	n	%	% total	n	%	% total	n	%	% total	
Insignificant	26	96.30	14.77	103	87.29	58.52	31	100	17.61	
Febrile seizures in parents	0	0	0	9	7.63	5.11	0	0	0	
Febrile seizures in siblings	1	3.70	0.57	5	4.24	2.84	0	0	0	
Febrile seizures in distant family	0	0	0	2	1.69	1.14	0	0	0	

Table 2 – The cause of incidence of febrile seizures in children from the studied age groups.											
	Group 1				Group 2			Group 3			
	n	%	% total	n	%	% total	n	%	% total		
Upper respiratory tract infection of several day's duration	11	40.74	6.25	33	27.97	18.75	14	45.16	7.95		
Sudden increase in the body temperature	14	51.85	7.95	65	55.08	36.93	15	48.39	8.52		
Gastroenteritis	2	7.41	1.14	20	16.95	11.36	2	6.45	1.14		

Table 3 – Sudden increase in the body temperature associated with the incidence of febrile seizures in the studied age groups.

		Group 1			Group 2			Group 3	
	n	%	% total	n	%	% total	n	%	% total
Pyrexia									
Up to 24 h	7	25.93	3.98	55	46.61	31.25	13	41.94	7.39
1-2 days	3	11.11	1.70	8	6.78	4.55	1	3.23	0.7
Over 2 days	4	14.81	2.27	2	1.69	1.14	1	3.23	0.57
Body temperature									
Up to 38 °C	2	7.41	1.14	16	13.56	9.09	0	0	0
38–39 °C	5	18.52	2.84	22	18.64	12.50	6	19.35	3.41
Above 39 °C	5	18.52	2.84	23	19.49	13.07	7	22.58	3.98
No data	2	7.41	1.14	4	3.39	2.27	2	6.45	1.14

A sudden increase in the body temperature followed by febrile seizures in all studied children groups concerned the body temperature above 39  $^{\circ}$ C on the first day of fever (Table 3). A statistically significant difference was observed between persisting fever and an increase thereof during the day (p = 0.010).

Yet another factor predisposing for febrile seizures incidence was an infection of the upper respiratory system that could be observed in 58 patients (32.95%) with the body temperature increasing above 39  $^{\circ}$ C – 24 children (50.31%) usually within the first day since the onset of fever (Table 4).

In all children upper respiratory tract infection of several days' duration was most often associated with persisting over 24hr fever with the body temperature rising above 39 °C. Only in group 1 the body temperature was similar in all patients within the established fever range – every 3 children, and in group 2 it was equal within the temperature range between 38 °C and 39 °C and above 39 °C – 12 patients (Table 4). A significant difference was observed between persisting infection of the upper respiratory tract and the body temperature (p < 0.0001) and a sudden increase thereof during the day (p = 0.036).

Analysing medical records about the course of febrile seizures it could be observed that 165 children (93.75%) developed general tonic clonic seizures with a loss of consciousness (69.89%), eyeball movement disturbances (40.38%), skin cyanosis (19.89%) and accompanying trismus (9.66%), excessive salivation (10.22%) and apnoea (5.69%). In 167 children (94.89%) febrile seizures were simple and in the remaining 9 ones (5.11%) they were complex. 25 children (14.20%) developed vomiting after an episode of febrile seizures.

The body temperature that predisposed for the incidence of febrile seizures in the studied group of children was set on the basis of data obtained during interviews with parents or caregivers. In 92 children (52.27%) temperature was taken just before or during an incident of febrile seizures, and the mean

body temperature when the seizures occurred was 38.9  $^{\circ}\text{C}$   $\pm$  SD 0.8  $^{\circ}\text{C}.$ 

The mean body temperature that predisposed for the incidence of febrile seizures in children was as follows: in *group*  $1-38.8~C\pm SD~0.5~C$ ; in *group*  $2-38.9~C\pm SD~0.7~C$ , and in *group*  $3-39.0~C\pm SD~1.1~C$  (Fig. 1). A statistically significant difference between the body temperature and the incidence of febrile seizures in the studied groups was observed (p=0.028).

#### 4. Discussion

The paper was an attempt to assess risk factors of febrile seizures in children. One of the studied factors was family history significant for febrile seizures. In the studied population boys were more often exposed for FS (61.93% vs 38.07%). Differences may be caused by specific time, region, and small research group. Another reason could be delayed maturation of CNS and tendency to higher spontaneous bioelectric discharged in discussed age range in boys [2]. On the basis of the analysed material no dependency between the incidence of febrile seizures and positive family history was proved. It was negative in all studied groups and concerned 90.91% of patients. Only in 9.66% of patients there was a positive history of febrile seizures in first degree relatives, such as parents and siblings. Research by Strengell et al. proved that 28% of patients gave a family history of febrile seizures, which is almost three times more than in the current study [4]. Winkler et al., by contrast, declare a positive family history in 20% of children, and Ellatif et al. showed a dependency between the incidence of febrile seizures and a positive family history (p < 0.0001) [5,6]. In a study by Tosun et al. 57% of patients gave a negative family history [7]. Among Korean children the frequency of the incidence of febrile seizures in family encompassed 20.7% of siblings and 10.9% of parents [8] that in turn is more than threefold higher risk than it was

Table 4 – Upper respiratory tract infection associated with febrile seizures incidence in the studied age groups.											
		Group 1			Group 2			Group 3			
	n	%	% total	n	%	% total	n	%	% total		
Pyrexia											
Up to 24 h	8	29.63	4.55	22	18.64	12.50	11	35.48	6.25		
1–2 days	1	3.70	0.57	1	0.85	0.57	2	6.45	1.14		
Over 2 days	2	7.41	1.14	10	8.47	5.68	1	3.23	0.57		
Body temperatu	re										
Up to 38 °C	3	11.11	1.70	4	3.39	2.27	1	3.23	0.57		
38–39 °C	3	11.11	1.70	12	10.17	6.82	2	6.45	1.14		
Above 39 °C	3	11.11	1.70	12	10.17	6.82	9	29.03	5.11		
No data	2	7.41	1.14	5	4.24	2.84	2	6.45	1.14		

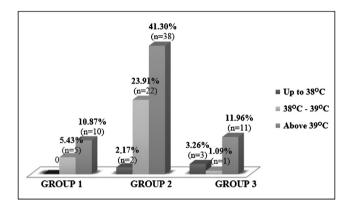


Fig. 1 – The body temperature predisposing for the incidence of febrile seizures in children based on body temperature taken by parents or caregivers in the studied age groups ( $\chi^2 = 10.90$ ; p = 0.028).

proved in the study. Varies between studies may be caused by fact that data was collected from the parents at the time of child A&E stay. They could not remember family past medical history. After improvement of child's status family past medical was not collected again.

The results of the analysed paper proved that 94.89% of children developed simple febrile seizures and only 5.11% of children suffered complex ones. As a comparison, among the population of Nigerian children simple febrile seizures were present in 32% of patients and complex ones occurred in as many as 62% of patients [9]. Yet research carried out in Iran by Gouurabi et al. shows the occurrence of simple seizures in 81.8% of children with the remaining percentage being complex febrile seizures that were present in patients up to 2 years of age. The results of their study proved no significant difference between sex and simple or complex seizures [10]. Studies by other researchers performed among Bedouin and Jewish children in Israel gave results similar to the ones obtained by Shimony et al. where 80.4% of Jewish children and 72.2% of Bedouin children developed simple febrile seizures [11]. Still in research by Strengell et al. performed on a population of Finnish children simple seizures were observed in 73% and complex ones in 27% of patients [4]. The differences may arise both from demographic, social, cultural or economic factors.

In the above study the incidence of febrile seizures in children was associated with a sudden increase in the body temperature on the first day of pyrexia. Results reveal that FS in children mostly occur on the first day of fever. Infection of the upper respiratory tract was yet another factor. Analysis shows that episode of FS during upper respiratory tract infections strictly depends of the body temperature value in the first day of fever. Considering the frequency of incidence, the third cause of febrile seizures was gastroenteritis and 1.7% of children had been preventively vaccinated within a week before the seizure. In their research performed among children in Iran Gouurabi et al. indicate an upper respiratory tract infection present in 72.29% of patients as the first cause of the incidence of febrile seizures and gastroenteritis present in 27.3% of children as the second one [10]. In their study Shimony et al., however, list otitis media as the first cause and then pneumonia in Bedouin and Jewish children [11]. Nevertheless Delpisheh et al. and Mahyar et al. in their research on an Iranian population of children give the causes of febrile seizures in the order as follows: upper respiratory tract infection, gastroenteritis, otitis media, and pneumonia [12,13]. Research carried out by Suga et al. in Tokyo proved that HHV-6 infection (roseola or sixth disease virus) is far more frequently associated with febrile seizures in infants and small children and often results in complex febrile seizures [14]. Yet they do not mention any relation between children being vaccinated and febrile seizures. By comparison, research performed in Great Britain and Denmark prove respectively that children vaccinated against flu face a higher risk of developing febrile seizures within 72 h after vaccination and that vaccination against measles, mumps and rubella increases the risk of developing febrile seizures within 2 weeks [15,16].

The most common type of seizures that was observed was a clonic tonic one with the loss of consciousness in 69.89% of patients with such accompanying symptoms as: eyeball movement disturbances, cyanosis, trismus, excessive salivation, and apnoea and 14.20% of children developed vomiting after febrile seizures. Delpisheh et al. in their research proved general clonic tonic seizures in 78.9% of children, who, according to the authors, are more prone to develop epilepsy [12].

One of the main causes of the incidence of febrile seizures in children is fever and the degree thereof is an idiosyncratic value and depends on an individual child's seizure threshold for fever [2]. In the studied group of children the mean body

temperature predisposing for the incidence of febrile seizures was defined on the basis of a measurement taken by parents or caregivers just before or during a fit and equalled 38.9 °C. The study proved a significant dependency between the incidence of febrile seizures and the body temperature in the studied groups. It was observed that the older the child, the higher the body temperature when febrile seizures occurred. By comparison, Mahyar et al. obtained similar mean body temperature when seizures occurred [13]. Yet Choi et al. mention that the mean body temperature in children is 39.0 °C, and Stuijvenberg et al. claim that among children in Holland mean temperature equals 39.3 °C during the first 2 h of fever [17,18]. By contrast, Hampers et al. noted that 91% of children treated in a Hospital Emergency Ward developed body temperature above 38 °C with the mean temperature 39.4 °C [19].

## Conflict of interest

None declared.

# Acknowledgement and financial support

None declared.

#### REFERENCES

- [1] Gryglewicz J. Fever in children. Warsaw: PZWL; 2009.
- [2] Wendorff J, Wiśniewska B, Piotrowicz M, Chamielec M. Febrile convulsions. Warsaw: PZWL; 2009.
- [3] Gontko-Romanowska K, Żaba Z, Steinborn B, Mitkowska J, Szemień M. Management of febrile seizures in children at the stage of prehospital and earlyhospital. Pediatr Med Stand 2016;13:639–45.
- [4] Strengell T, Uhari M, Tarkka R, Uusimaa J, Alen R, Lautala P, et al. Antipyretic agents for preventing recurrences of febrile seizures – randomized controlled trial. Arch Pediatr Adolesc Med 2009;163(September (9)):799–804.

- [5] Winkler AS, Tluway A, Schmutzhard E. Febrile seizures in rural Tanzania: hospital-based incidence and clinical characteristics. J Trop Pediatr 2013;59(4):298–304.
- [6] Ellatif F, El Garawany H. Risk factors of febrile seizures among preschool children in Alexandria. J Egypt Public Health Assoc 2002;77(1–2):159–72.
- [7] Tosun A, Koturoglu G, Serdaroglu G, Polat M, Kurugol Z, Gokben S, et al. Ratios of nine risk factors in children with recurrent febrile seizures. Pediatr Neurol 2010;43(September (3)):177–82.
- [8] Chung S. Febrile seizures. Korean J Pediatr 2014;57(9): 384–95.
- [9] Hoption Cann SA. Febrile seizures in young children: role of fluid intake and conservation. Med Sci Monit 2007;13 (September (9)):159–67.
- [10] Esmaili Gourabi H, Bidabadi E, Cheraghalipour F, Aarabi Y, Salamat F. Febrile seizure: demographic features and causative factors. Iran J Child Neurol 2012;6(4):33–7.
- [11] Shimony A, Afawi Z, Asher T, Mahajnah M, Shorer Z. Epidemiological characteristics of febrile seizures – comparing between Bedouin and Jews in the southern part of Israel. Seizure 2009;18(January (1)):26–9.
- [12] Delpisheh A, Veisani Y, Sayehmiri K, Fayyazi A. Febrile seizures: etiology, prevalence and geographical variation. Iran J Child Neurol 2014;8(3):30–7.
- [13] Mahyar A, Ayazi P, Fallahi M, Javadi A. Risk factors of the first febrile seizures in Iranian children. Int J Pediatr 2010; (June). <a href="http://dx.doi.org/10.1155/2010/862897">http://dx.doi.org/10.1155/2010/862897</a> [in press]
- [14] Suga S, Suzuki K, Ihira M, Yoshikawa T, Kajita Y, Ozaki T, et al. Clinical characteristics of febrile convulsions during primary HHV-6 infection. Arch Dis Child 2000;82(January (1)):62–6.
- [15] Jones T, Jacobsen S. Childhood febrile seizures overview and implications. Int J Med Sci 2007;4(2):110–4.
- [16] Vestergaard M, Christensen J. Register-based studies on febrile seizures in Denmark. Brain Dev 2009;31(May (5)): 372-7.
- [17] Choi J, Jin Min H, i Shin JS. Increased levels of HMGB1 and pro-inflammatory cytokines in children with febrile seizures. J Neuroinflammation 2011;8:135.
- [18] Kwinta P. The risk of recurrence of febrile seizures, depending on the body temperature and age. Med Pract Pediatr 2000;1:169–70.
- [19] Hampers LC, Thompson DA, Bajaj L, Tseng BS, Rudolph JR. Febrile seizures – measuring adherence to AAP guidelines among community ED physicians. Pediatr Emerg Care 2006;22(July (7)):465–9.