

Predictors of Recurrent Febrile Seizures in Iranian Children

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Article information	Abstract
<p>Article history: Received: Accepted: Available online: 15 Jan 2013 ZJRMS 2013; X(X): XX-XX</p> <p>Keywords: Meta-analysis Recurrence Febrile seizure Iran</p> <p>*Corresponding author at: Department of Social Medicine, Prevention of Psychosocial Injuries Research Centre, Ilam University of Medical Sciences, Ilam, Iran. E-mail: sayehmiri@razi.tums.ac.ir</p>	<p>Background: A few factors appear to boost a child's risk of having recurrent febrile seizures, including young age during the first seizure, seizure type, and having immediate family members with a history of febrile seizures. The present study aimed to provide reliable information about recurrent febrile seizure in Iranian children.</p> <p>Materials and Methods: On the computerized literature valid on valid keyword with search in valid database PubMed, Scientific Information Databases (SID), Global medical article limberly (Medlib), Iranian Biomedical Journals (Iran Medex), Iranian Journal Database (Magiran), and Google Scholar recruited in different geographic areas. To explore heterogeneity in studies I² index was used. Meta-analysis used to data analysis with random effects model.</p> <p>Results: Hospital data of 4,599 children with febrile seizure. Overall, 21 studies met our inclusion criteria. Febrile seizure in 2 age groups (<2 and 2-6 years) were 55.8% (95% CI: 50.4-61.2) and 44.2% (95% CI: 38.8-61.2) respectively. Pooled recurrent rate of febrile seizure in Iran was 20.9% (95% CI: 12.3-29.5). In 28.8 (95% CI: 19.3-38.4), children there was positive family history. The mean prevalence of simple and complex seizures was 69.3% (95% CI: 59.5-79.0) and 28.3% (95% CI: 19.6-31.0) respectively. The rates in different geographical regions of central, east, and west of Iran, 25, 20.8 and 27.1% were estimated, respectively.</p> <p>Conclusion: According to the data the prevalence febrile seizure is higher in males and children under two years. Recurrence rate in Iran, similar to other studies performed in other regions of the world.</p> <p>Copyright © 2013 Zahedan University of Medical Sciences. All rights reserved.</p>

Introduction

Febrile seizures (FSs) are the most common seizure disorder in childhood, affecting 2-5% of children between the ages of 6 and 60 months [1, 2]. Prevalence of 4-6 cases per 1000 children in the population [3]. The International League Against Epilepsy (ILAE) has defined that seizure events in infancy or childhood is featured with temperatures over 38°C without evidence of acute electrolyte imbalances in CNS infection or history of FS [4].

The direct cause of FS is not known but the most important causes include fever, epilepsy, hypoglycemia, hypocalcaemia, head injury, poisoning and overuse drugs, respiratory infection or gastroenteritis [5]. Although FS may cause great fear and concern for parents, most FSs produce no lasting effects [6]. The odds that pediatrics will develop epilepsy after a febrile seizure are small; approximately 1% [7]. A few factors appear to boost a child's risk of having recurrent FSs, including young age (less than 15 months) during the first seizure, frequent fevers, and having immediate family members with a history of FSs [8]. If the seizure occurs soon after a fever has begun or when the temperature is relatively low, the risk of recurrence is higher [9]. A long initial FS does not substantially boost the risk of recurrent FS, either brief or

long [10]. Children rarely develop their first FS before the age of 6 months or after 3 years of age [11].

A large amount of studies have been done in the last decade on FS and its associated risk factors among Iranian children. However, many of them drew incompatible or even contradictory conclusion and the utilization of these statistics are therefore limited. This paper reviews on the available studies so as to provide comprehensive and reliable data about recurrent FS among pediatric age group in Iran, which is speculated to help make prevention strategies and guide further research.

Materials and Methods

Literatures on the febrile seizure among Iranian children were acquired through searching PubMed, Scientific Information Databases (SID), Medlib, Iran Medex, Google Scholar, and Mag Iran from 1997 to 2009. In order to search and include related studies as many as possible, we used combinations of various key words, including febrile seizure, convulsion, and Iran.

All the potentially relevant papers were reviewed independently by two investigators through assessing the

eligibility of each article and abstracting data with standardized data-abstraction forms.

In this stage all articles that title or abstracts febrile seizure had selected. Disagreements were resolved through discussion. Data-abstraction forms contains information author, title, year and place of study, methods of sample selection, sample size, study type, family history of febrile seizure, seizure type, age, and prevalence. Data-abstraction forms by researchers reviewed and ultimate papers were entered into the meta-analysis.

According to these procedures, 115 articles in basic search using key words was available, 56 duplicated articles were excluded, and 59 related articles enter a list of abstracts, afterward by review of abstracts, 20 articles that were irrelevant excluded thereafter the full text of residual articles reviewed and in the end, 21 article were entered into meta-analysis.

The inclusion criteria were: 1) studies in the mentioned databases with full text, despite the language of original text; 2) studies Hospital-based data; 3) reporting among Iranian children; 4) studies in children under 6 years. Exclusion criteria were: 1) studies without specific sample origins; 2) studies with overlapping time intervals of sample collection from the same origin; 3) studies of repetitive.

Statistical analysis: In our review, random effect models were used for meta-analysis, considering the possibility of significant heterogeneity between studies which was tested with the I^2 statistic (values of 25, 50 and 75% are

considered to represent low, medium and high heterogeneity respectively). Meta regression was introduced to explore and explain heterogeneity between studies in a Meta analysis. The Z or Chi-Square test was used to assess the differences among the subgroups. Data manipulation and statistical analyses were undertaken using the Statistical Software Package (STATA) 10.

Results

According to the literature search strategies, 115 studies (1 study in PubMed, 114 studies in other databases) were identified, but 94 studies were excluded based on the inclusion and exclusion criteria (Fig. 1).

There was 1 study in English [12] and 20 studies in Persian [13-32] of the finally adopted 21 studies. Looking for sample sizes, throughout the 21 selected studies, 4,599 children (219 samples on average) with febrile seizure including 2,734 males (59.5%) and 1865 females (40.5%) were studied. There was significant statistical difference between males and females ($Z=18.22$, $p=0.001$). The heterogeneity between studies was 91.5% with an I square (I^2) statistic ($p=0.001$) (Table 1).

Prevalence in children under two years and 2 to 6 years were 55.8% (95% CI: 50.4-61.2%) and 44.1% (95% CI: 38.8-62.2%) respectively. Prevalence of simple and complex febrile seizure were 69.3% (95% CI: 19.6-31.0) and 28.3% (95% CI: 59.5-79.0) respectively. Positive familial history of FS was observed in 28.8 children (95% CI: 19.3-38.4%) (Table 2).

Table 1. Feature of studies among children with febrile seizure at different regions

Study location (No. of Ref)	Study period	No. of patients	Gender, N(%)	
			Male	Female
Yazd (12)	2004-2005	139	63 (0.55)	76 (0.45)
Yazd (13)	2002-2005	100	59 (0.59)	41 (0.41)
Kerman (14)	2000-2002	115	68 (0.59)	47 (0.41)
Mashhad (15)	2001-2002	50	35 (0.70)	15 (0.30)
Zahedan (16)	2005-2006	178	94 (0.53)	84 (0.47)
Birjand (17)	2006-2007	145	84 (0.61)	76 (0.39)
Bandar Abbas (18)	2001-2002	181	112 (0.62)	69 (0.38)
Sanandaj (19)	2000-2001	115	70 (0.61)	45 (0.39)
Isfahan (20)	2005-2007	1486	892 (0.60)	594 (0.40)
Zanjan (21)	2000-2001	50	33 (0.66)	17 (0.34)
Kashan (22)	2001-2002	120	72 (0.60)	48 (0.40)
Tehran (23)	2007-2008	107	64 (0.60)	43 (0.40)
Tabriz (24)	2001-2003	582	321 (0.55)	261 (0.45)
Bushehr (25)	2005-2006	102	64 (0.65)	36 (0.35)
Bandar Abbas (26)	1996-1997	211	127 (0.60)	84 (0.40)
Tehran (27)	2003-2005	103	64 (0.62)	39 (0.38)
Babol (28)	1999-2000	230	138 (0.60)	92 (0.40)
Zanjan (29)	2005-2006	117	64 (0.55)	53 (0.45)
Tehran (30)	1997-2007	245	140 (0.57)	105 (0.43)
Ilam (31)	2007-2008	172	98 (0.57)	74 (0.43)
Ahwaz (32)	2003-2008	94	54 (0.57)	40 (0.43)

Table 2. Prevalence of febrile seizure among Iranian children through random effect models

Variables	No. of studies	No. of patients	Prevalence % (95% CI)	Heterogeneity	
				I^2 (%)	p -Value
Simple seizures	13	1859	69.3(59.5-79.0)	96.5	0.001
Complex seizures	12	1809	25.3(19.6-31.0)	88.8	0.001
Positive family history	9	1104	28.8(19.3-38.4)	93.2	0.001
Less than two years	9	1587	55.8(50.4-61.2)	77.0	0.001
More than two years	9	1456	44.2(38.8-49.6)	77.0	0.001

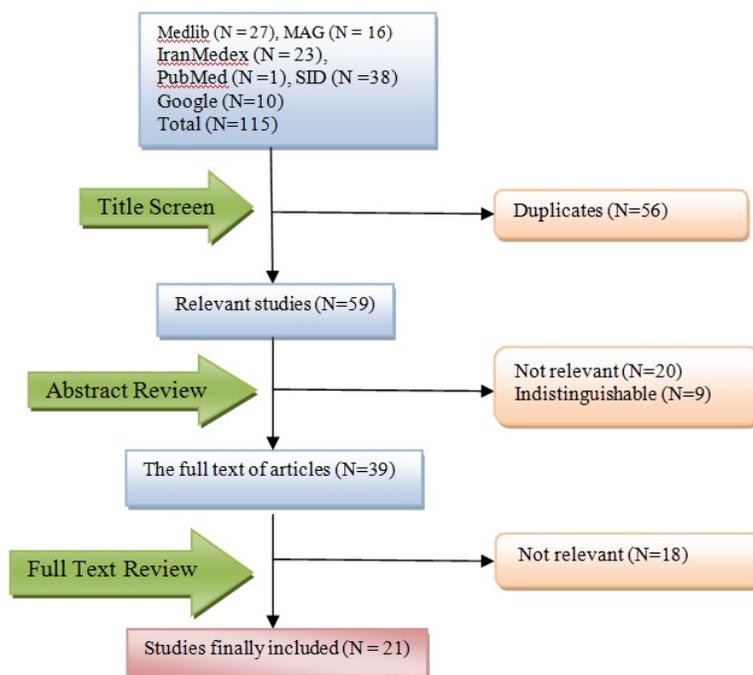


Figure 1. Results of the systematic literature search

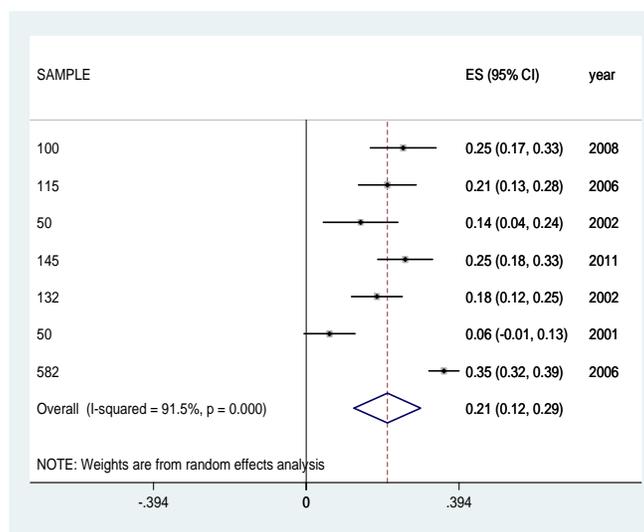


Figure 2. Forest plots for random effects meta-analyses. CI indicates confidence interval.

Discussion

The present study showed that prevalence of febrile seizure according two types of simple and complex seizures was 69.3% and 25.3% respectively. In children between the ages of 6 and 60 months, a simple febrile seizure is a benign and common event, and nearly all children have an excellent prognosis. Generalized seizure more associated with susceptibility to epilepsy [2]. Numerous researches have confirmed a significant

relationship between positive family histories and febrile seizure [33].

A few factors appear to boost a child's risk of having recurrent febrile seizures, including young age during the first seizure, seizure type, and having immediate family members with a history of FS [5, 9, 34] that is investigated in our study. According to the national epidemiological survey of seizures, FSs rate among the

general population decreased gradually with aging and the prevalence rate had significant difference between male and female [7]. The results of this study indicate that prevalence of FS according two types of simple and complex seizures was 69.3 and 25.3, respectively. This finding was consistent with the studies of Sampaio et al. [1].

Many researchers have showed that significant relationships between positive family histories are more likely to be febrile seizure [2, 34, 35]. A positive family history of febrile seizures points to the importance of genetic factors and common environmental exposures [10]. In the Berg study family history of febrile seizures was not consistently associated with an increased risk [2]. In our finding, 28.8% of the children had positive family history of FS. Tosun reported that was a family history of febrile seizures in 57% of children [34].

Several limitations in our study need to be addressed. First of all, the studies were observational and patients were not randomly chosen. Therefore selection bias and confounding seems inevitable. Secondly, many of our data were extracted from the internal databases in Iran. Thirdly, our ability to assess study quality was limited by the fact that many studies failed to offer detailed

information of selected subjects or valid data on important factors. Almost one-third of febrile seizures in Iranian children are related to a positive familial history which needs to be considered by parents and health policy makers.

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Authors' Contributions

Yousef Veisani: designed the study, collected data and participated in manuscript preparation. Dr. Ali Delpisheh prepared manuscript and helped study design. Dr. Kouroush Sayehmiri performed Meta analysis participated in manuscript preparation.

Conflict of Interest

The authors declare no conflict of interest.

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References

- Sampaio LP, Caboclo LO, Kuramoto K, et al. Prevalence of epilepsy in children from a Brazilian area of high deprivation. *Pediatr Neurol* 2010; 42(2): 111-7.
- Berg A, Shinnar S, Hauser W and Leventhal J. Predictors of recurrent febrile seizures: A metaanalytic review. *J Pediatr* 1990; 116(3): 329-37.
- Saz EU, Tekgul H, Serdaroglu G, et al. ECP01 Acute seizures in a pediatric emergency unit: Etiologic profiles and outcome. *Eur J Paediatr Neurol* 2007; 11(1): 98.
- Oka E, Ishida S, Ohtsuka Y and Ohtahara S. Neuroepidemiological study of childhood epilepsy by application of international classification of epilepsies and epileptic syndromes (ILAE, 1989). *Epilepsia* 1995; 36(7): 658-61.
- Pavlidou E, Tzitivridou M, Kontopoulos E and Panteliadis CP. Which factors determine febrile seizure recurrence? A prospective study. *Brain Dev* 2008; 30(1): 7-13.
- Watanabe T. Pros and cons of treatments and studies of recurrent febrile seizures. *J Pediatr* 1998; 133(5): 715.
- Baldin E, Ludvigsson P, Mixa O and Hesdorffer DC. Prevalence of recurrent symptoms and their association with epilepsy and febrile seizure in school-aged children: A community-based survey in Iceland. *Epilepsy Behav* 2012; 23(3): 315-9.
- Sugai K. Current management of febrile seizures in Japan: An overview. *Brain Dev* 2010; 32(1): 64-70.
- Bettis DB, Ater SB. Febrile seizures: Emergency department diagnosis and treatment. *J Emerg Med* 1985; 2(5): 341-8.
- Fukuyama Y, Seki T, Ohtsuka C, et al. Practical guidelines for physicians in the management of febrile seizures. *Brain Dev* 1996; 18(6): 479-84.
- van Zeijl JH, Mullaart RA, Borm GF and Galama JM. Recurrence of febrile seizures in the respiratory season is associated with influenza A. *J Pediatr* 2004; 145(6): 800-5.
- Fallah R, Karbasi S. Recurrence of febrile seizure in Yazd, Iran. *Turk J Pediatr* 2010; 52(6): 618-22.
- Barzegar M, Karegar M, Kivancheh N. Epidemiologic and clinical characteristics of seizures in children with first febrile attack. *J Tabriz Med Sci* 2006; 28(1): 17-21.
- Ahmadian M, Javadi N. Ethnologic factors and risk factors in 211 patients with seizure. *Hormozgan Med J* 1996; 12(2): 145-8.
- Ehsanipoor F, Gharouni M, Ardalan M, et al. Correlation between acetaminophen consumption and CSF glucose in febrile convulsion. *JK Science* 2011; 13(4): 176.
- Amini A, Kazemi A, Ghorbani A. Causes of seizures in children. *Iranian J Neurol* 2008; 7(24): 355-60.
- Ashrafzadeh F, Hashemzadeh A, Malek A. Febrile seizure in children six months to six years. *Iran J Otorhinolaryngol* 2001; (35): 33-9.
- Dehdashtian M, Momen AA, Ziaee T and Moradkhani S. Evaluation of seizure etiology in convulsive neonates admitted to Imam Khomeini and Abozar hospitals of Ahwaz 2004-2007. *J Med Sci* 2006; 8(2): 163-7.
- Ghotbi N, Soleimani S. Causes of seizures in children 1 month to 12 years. *J Med Sci Kurdistan* 2002; 7(25): 32-6.
- Golestani M, Fallah R, Akhavan-Krbasi S. Hundred cases of cerebrospinal fluid in children hospitalized due to febrile seizures. *J Yazd Med Sci* 2008; 16(5): 3-7.
- Hassanpoor H, Ghofrani M, Taheri N and Ziaee A. Risk factors in the recurrence of seizures with fever. *J Iran Med Sci* 2009; 16(65): 454-6.
- Hosseinasab A, Daiparizzi MH, Alidosti K. Demographic characteristics and risk factors of febrile seizure. *J Med Council* 2006; 24(2): 107-12.
- Kazemi A, Mousavi-Nasab N, Fatemi K. Cerebrospinal fluid examination in children hospitalized. *J Med Sci Zanjan* 2001; 9(35): 32-6.
- Khazai T, Hosseinzadeh A, Javadzadeh M. Causes of seizures in children. *J Birjand Med Sci* 2007; 14(4): 45-52.
- Khdapnahndh F. Studied 107 children with febrile seizures. *J Iran Med Sci* 2001; 8(25): 175-8.

26. Moayedi AR, Nazemi-Qshmy A, Safdarian F. Epidemiology and etiology of seizures and fever in children. *Hormozgan Med J* 2005; 9(3): 153-6.
27. Mohammadi J. Biochemical disorders in children with febrile seizure. *J Ilam Med Univ* 2008; 16(4): 1-6.
28. Namakin K, Shryfzadh G, Rezaei S. Demographic and clinical features febrile seizures. *J Birjand Med Sci* 2010; 17(4): 281-7.
29. Rasholi M, Moghimian A. Causes of fever in children with febrile seizures in children's hospital. *J Babol Univ Med Sci* 1999; 10(3): 131-7.
30. Sadeghzadeh M, Asl P, Mousavi-Nasab N, et al. Relationship between serum zinc levels and febrile seizure. *J Med Sci Zanjan* 2011; 19(74): 17-24.
31. Sanaidashti A, Karam A, Pazaki R. Risk factors for febrile seizures. *South Med Q* 2006; 9(2): 168-74.
32. Talebian A, Momtazmanesh N, Mousavi G and Khojasteh M. Relationship between febrile seizure and anemia. *Iran J Pediatr* 2006; 16(1): 79-86.
33. Offringa M, Bossuyt PMM, Lubsen J, et al. Risk factors for seizure recurrence in children with febrile seizures: A pooled analysis of individual patient data from five studies. *J Pediatr* 1994; 124(4): 574-84.
34. Tosun A, Koturoglu G, Serdaroglu G, et al. Ratios of nine risk factors in children with recurrent febrile seizures. *Pediatr Neurol* 2010; 43(3): 177-82.
35. Shi X, Lin Z, Ye X, et al. [An epidemiological survey of febrile convulsions among pupils in the Wenzhou region] Chinese [Abstract]. *Zhongguo Dang Dai Er Ke Za Zhi* 2012; 14(2): 128-30.

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