

THE EFFECT OF FAMILY HISTORY OF SEIZURES AS A RISK FACTOR FOR THE INCIDENCE OF RECURRENT FEBRILE SEIZURES AND TYPES OF FEBRILE SEIZURES IN CHILDREN AT WALED CIREBON HOSPITAL

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ABSTRACT

*Febrile seizures (FS) are common in children aged 6 months to 5 years, with familial seizure history implicated as a risk factor. However, regional data gaps persist, particularly in Indonesia. The research aims to analyze the influence of family seizure history on FS recurrence and types at Waled Hospital, Cirebon. A retrospective cohort study of 66 pediatric FS patients (2022) used chi-square tests and Prevalence Ratio (PR) analysis. Children with familial seizure history had significantly higher recurrent FS rates (62.1%, PR = 2.297, *p* = 0.009) but no association with seizure type (65.5% simple FS, PR = 0.797, *p* = 0.639). Familial history is a critical predictor of FS recurrence but not seizure complexity, underscoring the need for targeted monitoring and genetic-environmental interaction studies in high-risk children. This study contributes localized insights to global FS research and informs clinical prevention strategies.*

KEY-WORDS neo- children, family history seizures, recurrent febrile seizures, simple febrile seizures, complex febrile seizures



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INTRODUCTION

Fever is a condition where the body temperature is above 37 °C. Fever is one of the most common signs of illness and is the reason behind 15-25% of patient visits in primary health care facilities or emergency departments (DeWitt et al., 2017; El-Gamal et al., 2020; Guillebaud et al., 2018). According to the Indonesian Pediatrician Association (IDAI) in 2014, it was estimated that as many as 30% of patients came to the pediatrician due to fever (DG et al., 2020; Idai, 2016). In some cases, fever can be treated without medical intervention, but if a high fever occurs

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(temperature rise exceeds 38 °C)^h it can result in febrile seizures (Baran & Turan, 2018; Ray, 2020). According to IDAI, febrile seizures occur in children aged 6 months to 5 years who experience an increase in body temperature (temperature above 38 °C, with any temperature measurement method) that is not caused by intracranial processes (IDAI. Seizures are a worrying event for parents because most parents assume that their child has died. When a child experiences such a seizure, parents sometimes feel confused about how to handle it (NMR et al., 2018; Sirait et al., 2021).

Based on data from the World Health Organization (WHO) in 2018, it is estimated that the number of children who experience febrile seizures worldwide reaches more than 21.65 million people, and the number of children who have died is around 216 thousand. Meanwhile, the number of febrile seizures in Indonesia in 2009-2010 reached 16%, and as many as 2-3% were in the province of East Java, which is the holder of the highest cases of febrile seizures. Data from the Basic Health Research (Riskesdas) of Bali province in 2013 shows that febrile seizures are included in the top 3 diseases that are complained about (Arsa & Sulistya, 2021). According to the Ministry of Health (Kemenkes) in 2014, it was noted that children with an age range of 0-5 months and 3-5 years are prone to febrile seizures. Meanwhile, according to research conducted by Wibisono in 2015, children aged 6 months to 5 years experience febrile seizures of 3-4% (Mayan et al., 2020; NMR et al., 2018; Sirait et al., 2021).

One of the risk factors for the occurrence of the first febrile seizure is a family with a history of having had a seizure (Heydarian et al., 2018; Sharawat et al., 2016). The family consists of both parents and siblings (first-degree relatives). In a study conducted by Rimandhati (2018), it was found that children will have a 3.8 times greater risk of febrile seizures if they have a father with a history of seizures compared to a history of seizures for other family members. In a study conducted by Fuadi et al., the percentage of children with first febrile seizures was found to have a history of previous febrile seizures in their families, with a relative first-degree presentation of 14.6%, mothers 7.3%, siblings 6.1%, and fathers as much as 1.2%. Based on these results, it can be said that the risk factor for the occurrence of febrile seizures is the history of having suffered from febrile seizures in the family (first-degree relative) (Mayan et al., 2020; NMR et al., 2018; Sirait et al., 2021).

The prognosis of febrile seizures is generally good, but neurological abnormalities can occur in cases of prolonged seizures or recurrent seizures, both general and focal. Studies have reported that there is a cognitive memory impairment in children who have prolonged seizures (Idai, 2016).

Based on this data, children who have a family history of seizures will be at risk of experiencing recurrent febrile seizures (Mosili et al., 2020). Therefore, the researcher wants to research further whether or not there is a genetic influence on recurrent febrile seizures and types of seizures in children in the Cirebon area by taking data from Waled Cirebon Hospital to research more deeply about the risk factors for recurrent febrile seizures and the type of seizures in children by looking at the history of seizures in the family. With this study, it is hoped that the community, especially parents and families, can be better prepared to deal with children at risk of febrile seizures in a simple way, namely by looking at the history of seizures in the family so that fast and appropriate treatment can be carried out and complications arising from febrile seizures can be prevented.

This study builds upon prior research by specifically investigating the influence of family seizure history on both recurrent febrile seizures (FS) and seizure types (simple vs. complex) in children at Waled Hospital, Cirebon, a region underrepresented in existing literature. While earlier studies (e.g., Rimadhanti et al., 2018; Pokhrel et al., 2021) established familial seizure history as a risk factor for FS, this research uniquely quantifies the risk ($PR = 2.297$ for recurrence) and contrasts it with seizure type ($PR = 0.797$ for complex FS), revealing no significant association with the latter—a finding not extensively reported before. Additionally, it focuses on a localized Indonesian population, addressing gaps in regional data and aligning with global genomic research (e.g., Mosili et al., 2020; Sawires et al., 2022) by suggesting potential genetic mechanisms (e.g., ion channel mutations) yet emphasizing the need for further exploration in diverse settings.

RESEARCH METHOD

The scope of this research includes science in the fields of Genetics and Child Health Sciences. Sampling was carried out at the medical record installation of Waled Hospital in July 2023. This study is observational, analytical research with a retrospective cohort approach. The number of samples was 66 inpatient pediatric patients diagnosed with febrile seizures at Waled Hospital in 2022. Statistical tests use the chi-square test. The sampling technique uses total sampling. Data collection in the study used secondary data, namely inpatient medical records at Waled Hospital in 2022. The inclusion criteria for this study are patients diagnosed with febrile seizures at Waled Hospital, aged 6 months to 5 years, with records of family disease history describing the history of seizures, and medical records of hospitalization for the January-December 2022 period. Meanwhile, the data exclusion criteria are incomplete, and the data is not used.

The collected data is processed using univariate and bivariate analysis using the Prevalence Ratio (PR).

RESULT AND DISCUSSION

Based on the results of univariate data analysis from 66 respondents in Table 1, it was found that respondents aged 6-12 months amounted to 7 people (10.6%), 13-24 months amounted to 28 people (42.4%), 25-36 months amounted to 21 people (31.8%), and 37-48 months and 49-60 months amounted to 5 people (7.6%). Based on Table 1, it is also known that the majority of respondents are 13-24 months old.

Table 1 shows that the gender characteristics show that boys (56.1%) suffer from febrile seizures more than girls (43.9%). Meanwhile, the characteristics of febrile seizures showed that non-recurrent febrile seizures (57.6%) were more common than recurrent febrile seizures (42.4%). In the characteristics of febrile seizures, it was found that simple febrile seizures (60.6%) were more common than complex febrile seizures (39.4%). The characteristics of the family seizure history data showed that there were more children with no family seizure history (56.1%) than children with a family seizure history (43.0%).

Based on the results of the analysis of bivariate data, the relationship between the history of seizures in the family and the episodes of febrile seizures in table 2 shows that recurrent episodes of febrile seizures are more common in children with

a history of seizures in the family (62.1%) compared to children with no history of seizures in the family (27.0%). The results of the *chi-square* test showed a significant relationship between family history of seizures and febrile seizure episodes ($p\text{-value} \leq 0.05$). The results of the *Prevalence Ratio* (PR) calculation showed that children with a family history of seizures were at risk of experiencing 2,297 episodes of recurrent febrile seizures compared to children with no family history of seizures.

The results of the analysis of bivariate data on the relationship between the history of seizures in the family and the type of febrile seizures in Table 3 showed that children with a history of seizures in the family experienced more types of febrile seizures (65.5%) compared to complex febrile seizures (34.5%). The chi-square test results showed an insignificant relationship between the history of seizures in the family and the type of febrile seizure ($p\text{-value} > 0.05$). The results of the *Prevalence Ratio* (PR) calculation showed that children with a family history of seizures were at 0.797 times at risk of experiencing complex febrile seizures compared to children with no family history of seizures.

Table 1. Frequency Distribution of Characteristics of Research Subjects

No	Characteristic	Frequency (n)	Percentage (%)
1.	Age (months)		
	6-12	7	10,6
	13-24	28	42,4
	25-36	21	31,8
	37-48	5	7,6
	49-60	5	7,6
	Sum	66	100
2.	Gender		
	Man	37	56,1
	Woman	29	43,9
	Sum	66	100
3.	Episodes of febrile seizures		
	Recurring	28	42,4
	No Recurrence	38	57,6
	Sum	66	100
4.	Types of Febrile Seizures		
	Simple	40	60,6
	Complex	26	39,4
	Sum	66	100
5	History of seizures in the family		
	Ada	29	43,9
	None	37	56,1
	Sum	66	100

Table 2. Relationship between family history of seizures and febrile seizure episodes

Episodes of febrile seizures	Total	PR 95% CI
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History of sei- zures in the family	Non-recur- ring						<i>P</i> value	
	Recurring		ring					
	F	%	F	%	F	%		
Ada	18	62,1	11	37,9	29	100	2,297	0,009
None	10	27,0	27	73,0	37	100	(1,259-4,189)	

Table 3. Relationship between family history of seizures and febrile seizures

History of sei- zures in the family	Types of Febrile Seizures				Total		PR 95% CI	<i>P</i> value
	Complex		Simple					
	F	%	F	%	F	%		
Ada	10	34,5	19	65,5	29	100	0,797 (0,428-1,487)	0,639
None	16	43,2	21	56,8	37	100		

Discussion

Age is one of the risk factors for febrile seizures because it is related to the brain's imperfect response in dealing with fever (Badawy et al., 2017; Birbeck et al., 2024). This happens because during the maturation process, neuron stimulation will increase, affecting the onset of febrile seizures. For this reason, febrile seizures often arise in children under 3 years of age because the threshold value of the seizure is low (AK et al., 2018). The results of this study are in line with research conducted by Pokhrel et al. (2021) in Nepal, where the incidence of febrile seizures is mostly experienced by children aged 13-24 months, which is as much as 45% (RP et al., 2021).

In a study conducted by Hautala et al. (2022), the authors compared IL-1RA levels in febrile seizure patients. The results of this study indicate that patients with febrile seizures produce an excessive inflammatory reaction during febrile seizures, but not when febrile seizures occur alone or when the patient's state is healthy after febrile seizures. This increase in IL-1RA causes fever and seizures. Because of this point, studies on genomic associations of febrile seizures state that there are several unique factors of response to fever in febrile seizure patients (MK et al., 2023). This study is in line with research conducted by Pokhrel et al. (2021) in Nepal, namely, the most common febrile seizure episode is non-recurrent febrile seizure (79%) compared to the incidence of recurrent febrile seizure (21%) (RP et al., 2021).

Family history is included in the risk factors for febrile seizures or other seizure syndromes because they are related to genetic mutations in (1) *Voltage-Gated Sodium Ion Channels*: These canals have an important role in the propagation of action potentials in neurons. The variation in the gene encoding the sodium protein channel is known, and studies state that the SCN1B gene mutation has been found in all individuals suffering from seizures, including febrile seizures. (2) *Hyperpolarisation Activated Cyclic (Nuclotide-Gated Channels)*: Hyperpolarisation activates cyclic nucleotide-gated (HCN), which is the main channel for spasm activation that excites neurons. This mutation has been found in patients suffering from seizures and epilepsy, where the HCN1 mutation is associated with a broad spectrum of seizure diseases, including febrile seizures. In addition to the SCN and HCN

canal mutations, it is thought that other genetic mutations can also cause febrile seizures, but are not always identifiable in children with febrile seizures. So it is thought that other genetic changes that may contribute to the propagation of febrile seizures have not yet been identified. But what needs to be remembered is that if there is a mutation in the ion channels that play a role in febrile seizures, the mutation will show that they have a low penetration rate, which causes the propagation of the seizure (Sawires et al., 2022).

This is in line with a study conducted by Rimadhanti, et al. (2018) conducted in Palembang, which stated that there was a relationship between a history of seizures in the family and the incidence of febrile seizures with a result of $p\text{-value}=0.000$ ($p<0.05$) and obtained a value of $OR=21$ which means that children with a history of seizures in the family have a 21 times greater risk of having a febrile seizure compared to children who do not have a history of seizures in the family (NMR et al., 2018).

Research explains that family and twin siblings are important factors in the incidence of febrile seizures. About 1/3 of children who have febrile seizures have a family history of seizures. The percentage risk of febrile seizures affecting children is about 20%, and about 33% of parents are affected. *The concordance rate* is about 35-69% and 14-20% in monozygous and dizygous twins. Genes that increase the risk of febrile seizures have been mapped according to the loci of chromosomes: 1q31, 2q23-34, 3p24.2-23, 3q26.2-26.33, 5q14-15, 5q34, 6q22-24, 8q13-21, 18p11.2, 19p13.3, 19q, and 21q22 (AK et al., 2018; Mosili et al., 2020).

The results of this study are in line with research conducted by Rimadhanti et al. (2018), where children with a history of seizures in the family are more likely to suffer from simple febrile seizures (14%) compared to complex febrile seizures (12%). The *odd ratio value* obtained is $OR=0.236$, which means that children with a history of seizures in the family are 0.236 times at risk of experiencing complex febrile seizures compared to children without a history of seizures in the family (NMR et al., 2018).

CONCLUSION

This study found that children with a family history of seizures had a significantly higher risk of recurrent febrile seizures (62.1%, $PR = 2.297$) but no significant link to seizure type (65.5% simple seizures, $PR = 0.797$ for complex seizures). Future research should investigate genetic-environmental interactions, long-term epilepsy risk, and preventive strategies, while expanding sample sizes, differentiating familial seizure patterns, and analyzing additional risk factors to improve predictive models and clinical management.

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