

INFORMASI ARTIKEL

Received: September, 24, 2025

Revised: November, 25, 2025

Available online: November, 30, 2025

at : <https://e-jurnal.iphorr.com/index.php/mchc>

Risk factors for recurrent seizures in children with febrile seizures

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Abstract

Background: Febrile seizure is defined as a seizure occurring in children aged 6–60 months with fever $\geq 38^{\circ}\text{C}$ without intracranial infection. It is most common in children under three years, with a global prevalence of 2–5% and up to 12% in Asia. Although generally benign, recurrent febrile seizures may increase the risk of epilepsy later in life.

Purpose: This study aimed to determine the risk factors associated with recurrent febrile seizures in children.

Method: An analytical observational study with a cross-sectional approach was conducted using medical records of children diagnosed with febrile seizures. Bivariate analysis with chi-square test was applied to examine the association between risk factors and recurrence.

Results: Children aged <2 years had a 2.5-fold higher risk of recurrence. Low birth weight (<2500 g) increased the risk by 2.5 times. A family history of febrile seizures was identified as a strong predictor of recurrence. Additionally, seizure onset with body temperature $>39^{\circ}\text{C}$ raised the risk by 4.5-fold.

Conclusion: Age, low birth weight, family history, and high fever at seizure onset were significantly associated with recurrent febrile seizures. Early identification of these risk factors is essential for prevention and parental education to minimize recurrence and long-term complications.

Keywords: Children; Febrile Seizure; Recurrence; Risk Factors.

INTRODUCTION

Febrile seizures are seizure condition simultaneously with an increase in body temperature, which is clinically characterized by a rectal temperature exceeding 38°C , and occurs due to an extracranial process. According to experts, febrile seizures are commonly experienced by children aged 6 months to 5 years. The prevalence of febrile seizures in children under 5 years of age is estimated to be between 2-5%. The highest incidence of febrile seizures is found in children aged 6-22 months, with the peak incidence at 18 months (Maghfirah & Namira, 2022). Febrile seizures are seizures that occur in children aged 6-60 months accompanied by a fever of $\geq 38^{\circ}\text{C}$ without intracranial infection/invasion, most often at an age of <3 years. This range consists of clinical guidelines and reviews (Hasibuan & Dimiyati, 2020).

The prevalence of febrile seizures in children ranges from 2% to 5% in Western countries and reaches 12% in some parts of Asia. Basic competence is usually found in children aged 6 months to 5 years without central nervous system (CNS) infection, metabolic problems, or a history of epilepsy (Corsello, Marangoni, Macchi, Cozzi, Agostoni, Milani, & Dilella, 2024). However, higher incidences have been reported in Japan (7-10%) and Guam (14%). Incidence does not appear to be influenced by gender. While febrile seizures are most common between 6 months and 5 years of age, there have been reports of first febrile seizures in children up to 7 years of age, and as young as 3 months. The highest incident occurs in children between 12 and 18 months of age. Febrile seizures are most often reported in winter, which corresponds to the peak

incidence of fever in children (Sawires, Buttery, & Fahey, 2022). The incidence of febrile seizures in Indonesia in 2016 reached 2-5%, with 85% caused by respiratory tract infections. As many as 17.4% of children experienced febrile seizures in 2017, then increased to 22.2% in 2018 (Angelia, 2019). Meanwhile, in Lampung Province, the prevalence of fever in children reached 36% in 2019 (Sari, Hasan, & Rahman, 2022).

Seizures that occur simultaneously with fever in children who have a history of seizures without fever are not categorized as febrile seizures. According to the International League Against Epilepsy Commission on Epidemiology and Prognosis (ILAECEP), febrile seizures are seizures experienced by children older than 1 month of age, associated with fever and non-infectious central nervous system diseases, without a history of neonatal seizures or previous seizure problems. Febrile seizures most often occur within the first 24 hours of an infectious disease, particularly acute respiratory infections such as pharyngitis and otitis media, pneumonia, urinary tract infections, and gastroenteritis. Viral infections are a more dominant cause than bacterial infections (Widiyastuti, Elda, & Handayani, 2025). Febrile seizures can be triggered by various factors, such as genetic factors or a family history of seizures, immaturity of the brain's nervous system, and infection. This condition is caused by the multifactorial nature of febrile seizures. Among these various factors, heredity is known to play a major role. This is supported by previous studies showing that about one-third of people with febrile seizures have a family history of seizures. In addition, there are still various factors that can trigger recurrent febrile seizures, but studies discussing these risk factors, including the link between family history of seizures and recurrence of febrile seizures, are still limited (Widyawati, Febrianti, Rabiah, & Ponulele, 2022).

Statistical analysis using the chi-square test and odds ratio proves a clear correlation between risk factors and the occurrence of febrile seizures. For the < 24-month age group, the p-value was 0.003 ($P < 0.05$) and OR=3.215. For the group with a body temperature $> 38.5^{\circ}\text{C}$, the p-value was 0.025 ($p < 0.05$) and OR = -1.214. These findings confirm that age under 24 months and high body temperature are considered triggering factors for febrile seizures

(Yasmin, Maulanza, & Patricia, 2022). Confirmed that young age, below-normal body temperature, and a family history of seizures are risk factors for Febrile Status Epilepticus (FSE) (Sharafi, Rad, & Aminzadeh, 2019). In addition, anemia and developmental delays have also been shown to contribute to the risk of FSE (Mosili, Maikoo, Mabandla, & Qulu, 2020).

Children with a history of recurrent febrile seizures have been found to have relatively lower non-verbal intelligence than children in general. Febrile seizures can also increase the risk of epilepsy by 57% if they occur repeatedly and persistently. Recurrent febrile seizures can cause damage to the nervous system, causing children to experience behavioral and intellectual disorders. Therefore, appropriate first aid for children with febrile seizures is essential (Nurwijayanti, 2022).

RESEARCH METHOD

This quantitative research employed analytical methods. The study was conducted at Dr. H. Abdul Moeloek Regional General Hospital from January to December 2024. The study design employed a case-control approach, an observational analytic study with a case-control design. This study aimed to determine the relationship between risk factors and the incidence of febrile seizures.

The population and sample consisted of all 116 patients diagnosed with febrile seizures and had medical records. Fifty-eight patients had recurrent febrile seizures, and 58 patients had non-seizure fevers. The independent variables were age, sex, birth weight, family history of febrile seizures, and body temperature. The dependent variable in this study was febrile seizures. The tool used to collect secondary data was medical records.

Inclusion criteria for children aged 6 months to 6 years experiencing febrile seizures where there has been a history of febrile seizures in different episodes, children diagnosed with febrile seizures (simple or complex) based on medical records. Have complete medical record data that can be accessed by researchers, while exclusion criteria are children with a history of seizures without fever (epilepsy or other afebrile seizures), children with central nervous system infections (eg meningitis, encephalitis) and incomplete or unavailable medical record data.

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DOI: 10.56922/mchc.v4i8.1806

RESEARCH RESULTS

Table Frequency Distribution of Respondents (N=116)

Table	Results	OR Value (95% CI)	P-Value
Age (Mean±SD) (Range) (Year)	(2.51±1.796) (0-6)		
>2	57/37.3	2.490 (1.180-5256)	0.016
<2	59/62.7		
Gender (n/%)			
Men	48/41.4	6.273 (2.742-14.351)	0.000
Women	68/58.6		
Birth Weight (n/%)			
<2500	61/52.6	4.496 (1.181-5.275)	0.016
>2500	55/47.2		
History Of Febrile Seizures in the Family (n/%)			
No history of febrile Seizures in the family	50/43.1	4.500 (1.658-12.213)	0.002
Having a family history of seizures	66/56.9	7.283 (3.161-16.782)	0.000
Temperature (n/%)			
<39°C	55/47.4	4.582 (2.095-10.025)	0.000
>39°C	61/52.6		

Based on the table, the results of bivariate analysis show the relationship between several risk factors and the occurrence of recurrent febrile seizures in children. Five variables were analyzed, namely the child's age, gender, birth weight, family history of febrile seizures, and body temperature during seizures. The child's age was found to be significantly associated with the occurrence of recurrent febrile seizures. Children aged < 2 years had a risk approximately 2.5 times greater of experiencing recurrent febrile seizures compared to children aged > 2 years (OR 2.490; 95% CI: 1.180-5.256; p = 0.016). This shows that the younger the child, the higher their susceptibility to recurrent febrile seizures. Gender also showed a significant association with recurrent febrile seizures. Girls were recorded to have more experienced recurrent seizures (79.3%) compared to boys (20.7%), with an odds ratio of 6.273 (95% CI: 2.742-14.351; p < 0.001). This means that girls have a much higher risk of experiencing recurrent febrile seizures than boys.

Based on birth weight, birth weight was also significantly associated with recurrent febrile seizures. Children with birth weight < 2500 grams had a 2.5 times higher risk of experiencing recurrent febrile seizures compared to children with a normal birth weight (> 2500 grams) (OR 2.496; 95% CI: 1.181-5.275; p = 0.016). This indicates that nutritional status at birth influences a child's susceptibility to recurrent seizures.

A family history of febrile seizures is one of the strongest risk factors. Children with a family history of febrile seizures are 4.5 times more likely to experience recurrent febrile seizures (OR 4.500; 95% CI: 1.658-12.213; p = 0.002). In fact, specifically, children with a positive family history show a more than 7-fold risk compared to those without a history (OR 7.283; 95% CI: 3.161-16.782; p < 0.001). This confirms the role of genetic factors or family predisposition in the occurrence of recurrent febrile seizures. Body temperature during seizures also had a significant effect. Children who experienced

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seizures at temperatures $> 39^{\circ}\text{C}$ had a 4.5 times greater risk of experiencing recurrent seizures compared to children with seizure temperatures $< 39^{\circ}\text{C}$ (OR 4.582; 95% CI: 2.095-10.025; $p < 0.001$). This indicates that the higher the body temperature during a seizure, the greater the likelihood of a child experiencing recurrent febrile seizures.

DISCUSSION

The results showed that age was significantly associated with recurrent febrile seizures. Children younger than 2 years of age had a 2.5 times greater risk of recurrent febrile seizures than children older than 2 years (OR 2.490; 95% CI: 1.180-5.256; $p = 0.016$). This indicates that the younger the child, the higher their susceptibility to recurrent febrile seizures. This finding is interesting because many large studies have reported that the risk of recurrent febrile seizures tends to decrease with age; for example, the risk of recurrence is reported to be higher in infants and very young children (especially < 12 -18 months) and decreases after 1-2 years of age. This places your results as a finding that differs slightly from the general trend reported in several large studies (Papež, Labounek, Jabandžiev, Česká, Slabá, Ošlejšková, & Nestršil, 2023).

This is supported by previous research, which shows that younger age is a major factor that increases the risk of recurrent febrile seizures. The OR value for young age is 0.61 (95% CI: 0.46-0.80; $p < 0.001$), which means that as the child gets older, the risk of recurrence decreases. Biologically, this is as they grow. In younger children (especially those under 18-24 months of age), the nervous system is not yet mature, so the seizure threshold is lower, and they are more prone to febrile seizures. Therefore, children who experience their first seizure at an earlier age (e.g., < 18 months) tend to have a higher risk of recurrence (Shen, Lu, Wu, Suo, Zheng, Zhong, & Li, 2024). Previous research has shown that the peak incidence of febrile seizures occurs at 12–18 months of age, and many studies have shown that younger age (especially < 12 –18 months) is a risk factor for recurrence; it also highlights the role of family history and fever temperature (Sawires, Buttery, & Fahey, 2022).

Gender also showed a significant association with the occurrence of febrile seizures. Girls were

recorded more frequently. experienced recurrent seizures (82.8%) compared to boys (17.2%), with an odds ratio of 20.509 (95% CI: 1.208-9.863; $p < 0.001$). This means that girls have a much higher risk of experiencing recurrent febrile seizures than boys. This indicates biological and immunological differences between the sexes that may affect seizure thresholds and responses to fever. Scientifically, differences in hormones, brain development, and genetic factors such as the X chromosome can affect immune response and susceptibility to seizures. Estrogen in girls, for example, may act as an immune activator (involved in CD4+ T cells), which may cause different inflammatory patterns compared to boys (Sari, Hasan, & Rahman, 2022). Previous research conducted by Kumar (2018) showed that from a cohort study of 528 children, the difference in the percentage of girls vs. boys was not statistically significant ($p = 0.116$) (Kumar, 2018). Gender was not significant in the occurrence of recurrent febrile seizures (Shen et al., 2024).

The results of the study show that birth weight is also significantly associated with recurrent febrile seizures. Children with birth weight < 2500 grams have a 2.5 times higher risk of experiencing recurrent febrile seizures compared to children with a normal birth weight (> 2500 grams) (OR 2.496; 95% CI: 1.181-5.275; $p = 0.016$). This indicates that nutritional status from birth affects a child's susceptibility to recurrent seizures. This is supported by the statement that low birth weight (< 2500 g) is significantly associated with the occurrence of febrile seizures (Al-Obeidi, 2022). Iron levels, height, and age are significant predictors of febrile seizure recurrence. Low birth weight is not discussed directly, but early physiological status remains a concern. This condition may be due to incomplete maturation of the nervous system, making the brain more susceptible to electrical disturbances during fever. Nutritional status and low iron reserves have been identified as risk factors for febrile seizures and their recurrence (Papež et al., 2023).

Biologically and epidemiologically, this relationship is reasonable and supported by several plausible mechanisms. Low birth weight infants often reflect prematurity or intrauterine disorders that result in incomplete brain maturation, susceptibility to homeostasis disorders such as temperature

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regulation, metabolism, iron/zinc status, and recurrent infections, all factors that can lower the seizure threshold in children. Additionally, low birth weight correlates with the risk of long-term neurological development (e.g., developmental delays, epilepsy), which can also increase susceptibility to seizures. The statement regarding an increased risk of seizures associated with decreased birth weight and gestational age is supported by large cohort studies (Christensen, Dreier, Skotte, Feenstra, Grove, Børghlum, & Christensen, 2021).

Previous research has shown that a Korean population cohort study (n = 830,000) reported that full-term infants with low birth weight <2500 g had a higher risk of developmental disorders and were also more frequently recorded as having epilepsy and febrile seizures at 5-7 years of age, strengthening the long-term association between low birth weight and neurological vulnerability (Kim, Cho, Ahn, Hong, Oh, & Kim, 2024).

The results of the study show that a family history of febrile seizures is a very strong risk factor for recurrent febrile seizures. This is supported by Shen et al., who found that family history is one of the significant independent risk factors for recurrence of febrile seizures; children with such a history have an OR >2 ($p < 0.01$) for recurrent seizures (Shen et al., 2024). The underlying biological mechanism may be related to genetic factors, such as ion channel abnormalities (e.g., SCN1A mutations) or hereditary epilepsy syndromes (such as Genetic Epilepsy with Febrile Seizures Plus/GEFS-Plus). Febrile seizures have a multifactorial hereditary pattern, and children who have close relatives (parents or siblings) with a history of febrile seizures are clearly more susceptible to a lower seizure threshold when experiencing fever.

Positive family history (FS/epilepsy) increases the risk of FS and the possibility of recurrence; that genetic and environmental effects interact with each other. This review also confirms that although family factors are important, the strength of the association varies between studies and definitions (Sawires et al., 2021).

The results of the study show that body temperature during seizures also has a significant effect. Children who experience seizures at temperatures > 39°C have a 4.5 times greater risk of experiencing recurrent seizures compared to children

with seizure temperatures < 39°C. This shows that the higher the body temperature during seizures, the greater the likelihood of children experiencing recurrent febrile seizures. High fever reflects a stronger inflammatory response and physiological changes (e.g., cytokine release, changes in neuronal ion balance) that can lower the seizure threshold and facilitate the recurrence of seizures during the same period of illness. A rapid and high increase in body temperature is likely to lower the seizure threshold and trigger temporary neuronal dysfunction, thereby facilitating recurrence. This is in line with a recent international study that also showed an association between high temperature and an increased risk of febrile seizure recurrence. This is supported by another study, where a 10-year medical record-based analysis found that a peak temperature $\geq 39^\circ\text{C}$ increased the risk of seizure recurrence within 24 hours (11% vs. 4%; OR = 2.9; $p < 0.001$) (Castellazzi, La Vecchia, Scali, Agostoni, Di Pietro, & Milani, 2024). Research conducted by Kim et al. (2024) showed that a body temperature below 39°C upon arrival at the hospital (OR = 2.377) was significantly associated with early seizure recurrence. This requires close monitoring for 6 to 8 hours when there is a history of early recurrence or if seizures occur at low body temperatures (Kwon, Kim, Jang, Son, Kim, Kim, & Kim, 2024).

CONCLUSION

Based on the results of the study, it can be concluded that most children who experience recurrent febrile seizures aged 2.5 times more likely to experience recurrent febrile seizures than children aged > 2 years. Female gender increases the risk of recurrent febrile seizures by 6.2 times in children. Birth weight < 2500 grams increases the risk of recurrent febrile seizures by 2.5 times in children. A positive family history of febrile seizures increases the risk of recurrent febrile seizures by 7.2 times in children. All factors studied (age, gender, birth weight, family history, and body temperature during seizures) had a statistically significant relationship with the incidence of recurrent febrile seizures in children.

SUGGESTION

Healthcare workers, especially doctors and nurses in primary healthcare services, are expected

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to conduct initial screening and educate parents about risk factors for recurrent febrile seizures, such as the child's age, body temperature during fever, and family history. Parents are advised to be more aware of the family history of febrile seizures and to immediately take their child to a health facility when they have a high fever to prevent recurrent seizures. Hospitals and health centers can develop clinical guidelines or standard operating procedures (SOPs) for the management of recurrent febrile seizures based on the risk factors identified in this study.

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