

# The Correlation between Hematological Profiles with Types of Febrile Seizures in Children at RSUD dr. Adhyatma, MPH Semarang

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**Abstract:** Seizures known as febrile seizures occur in children between the ages of six months and five years when they have an increase in body temperature (any temperature above 38 degrees Celsius), which is not brought on by an intracranial process. The research aims to determine the correlation between hematological profile, temperature, and nutritional status with the type of children's febrile seizure at RSUD dr. Adhyatma, MPH Semarang. This study used an analytical observational method with a cross-sectional approach and total sampling technique. Accordingly, medical records at RSUD dr. Adhyatma MPH Semarang became the source of data in this study. Moreover, analysis of the study's data utilized the Chi-square test. Based on bivariate analysis, it was found that a p-value of 0.511 between temperature and type of febrile seizure, a p-value of 0.624 between nutritional status and type of febrile seizure, a p-value of 0.100 between hemoglobin levels and type of febrile seizure, and p-value of 0.026 number of leukocytes was related to the type of febrile seizure. There is a relationship between the number of leukocytes and the type of febrile seizure.

**Keywords:** Type of Febrile Seizure, Temperature, Nutritional Status, Hemoglobin Level, Number of Leukocytes.

## INTRODUCTION

Febrile seizures are seizures which are experienced by children aged six months to five years, where the body temperature increases (above 38°C using various methods for measuring temperature), which is not brought on by an intracranial process.<sup>1</sup> Simple febrile seizures and complex febrile seizures are the two categories of febrile seizures. Simple febrile seizures have a short half-life of under fifteen minutes with a generalized seizure form (tonic or clonic) without focal movements. Meanwhile, complex febrile seizures have a longer duration, namely above 15 minutes. Generalized seizures are preceded by partial seizures, focal seizures on one side or partial, and recur more than once in 24 hours.<sup>2,3</sup>

The incidence of febrile seizures globally, according to WHO, is estimated at over 21.65 million children, and those who died aged between 1 month and 1 year with a history of febrile seizures reached 216,000 children (77%).<sup>4</sup> These figures vary widely in many countries. It is noted that the annual incidence of febrile seizures in America and the West Side of Europe is 2-14%, in Japan 8.8%, and in India it reaches 5-10%.<sup>5</sup>

The exact cause of febrile seizures has not been determined with certainty, so it can only be reviewed based on risk factors, such as zinc and iron deficiency, a history of febrile seizures in the family, and developmental delays.<sup>6</sup> Furthermore, fever and elevated body temperature are major contributors to the development of febrile seizures.<sup>7</sup> High body temperature can increase body metabolism, which can cause changes in membrane potential in the brain, resulting in the release of electrical charges and spreading throughout the body.<sup>8</sup> The process of febrile seizures due to infection is also related to the immune process in the body. The immune system in the body is formed due to the good nutritional status of children.<sup>9</sup> A

decrease in the amount of hemoglobin results in a decrease in the blood's ability to bind oxygen, which can cause hypoxia.<sup>10</sup> In another study, it was found that patients with febrile seizures were more often found with normal hemoglobin levels. When hemoglobin decreases significantly, it is more likely to cause children to experience complex febrile seizures.<sup>2</sup> Leukocytes will increase when the body experiences an infection.<sup>5</sup> In addition, other studies state that temperature, nutritional status, hemoglobin levels, and the number of leukocytes have an effect on febrile seizures in children aged 0-60 months. However, no distinction are present between the risk factor of simple and complex febrile seizures.<sup>9</sup>

Previous studies analyzed risk factors associated with the type of febrile seizures, but some of the studies stated different results. Therefore, researchers are interested in conducting research related to the relationship between hematological profiles and types of febrile seizures in children at RSUD dr. Adhyatma, MPH Semarang.

## **MATERIALS AND METHOD**

An analytical observational method using a cross-sectional design was applied in this research. Moreover, the research's data were medical record data of pediatric patients diagnosed with febrile seizures at RSUD dr. Adhyatma, MPH Semarang for the period January 2022-October 2023. The sampling technique was total sampling. The study variables included the number of leukocytes, hemoglobin levels, temperature, and nutritional status. Assessment of the number of leukocytes included leukocytosis (age 6-23 months:  $>14 \times 10^3 / \mu\text{L}$  and age 2-5 years:  $>12 \times 10^3 / \mu\text{L}$ ), leukopenia (age 6-23 months:  $<6 \times 10^3 / \mu\text{L}$  and age 2-5 years:  $<4 \times 10^3 / \mu\text{L}$ ) and normal leukocyte count (age 6-23 months:  $6 \times 10^3 - 14 \times 10^3 / \mu\text{L}$  and age 2-5 years:  $4 \times 10^3 - 12 \times 10^3 / \mu\text{L}$ ).<sup>11</sup>

The inclusion criteria included patients with febrile seizures aged 6 months to 5 years with complete medical records. Meanwhile, the exclusion criteria included pediatric patients with a history of epilepsy, pediatric patients with impaired brain development, central nervous system infections, and long-term use of anticonvulsant drugs and incomplete data on the variables studied in the medical records.

The Chi-Square statistical test was the bivariate analysis employed in this research. In addition, this study was conducted after the researcher obtained ethical permission from the KEPK RSUD dr. Adhyatma, MPH, Semarang (Number: 016/KEPK.EC/III/2024).

## **RESULT**

The frequency distribution of sample characteristics is presented in Table I. Based on Table I, the characteristics of the research subjects were that most of the research subjects were male, while in the nutritional status variable, most of them had normal nutrition, as many as 77 children. In the hemoglobin level category, most children had normal hemoglobin levels of 67 children, while in the leukocyte count variable, most children had an increased leukocyte count of 49 children. In the type of febrile seizures, more children were found with simple febrile seizures of 53 children compared to complex febrile seizures of 39 children.

**Table 1.** Frequency Distribution of Sample Characteristics

Sample characteristics and research variables	Frequency (%)
<b>Gender</b>	
Male	61 (66,3)
Female	31 (33,7)
<b>Children age (months)</b>	
6-24	45 (48,9)
25-60	47 (51,1)
<b>Temperature</b>	
≥38°C	52 (56,5)
<38°C	40 (43,5)
<b>Nutritional status</b>	
Poor nutrition (<-3 SD)	2 (2,2)
Malnutrition (-3 s/d <-2 SD)	6 (6,5)
Overnutrition (>+2 SD)	7 (7,6)
Normal nutrition (-2 s/d +2 SD)	77 (83,7)
<b>Hemoglobin levels (g/dL)</b>	
Abnormal hemoglobin levels (<11)	25 (27,2)
Normal hemoglobin levels (≥11)	67 (72,8)
<b>Leukocyte counts</b>	
Leukocytosis	47 (51,1)
Leukopenia	2 (2,2)
Normal leukocyte count	43 (46,7)
<b>Type of febrile seizure</b>	
Simple febrile seizure	53 (57,6)
Complex febrile seizure	39 (42,4)

The results of the statistical analysis of the relationship between hemoglobin levels, leukocyte counts, temperature, and nutritional status with the type of febrile seizures are presented in Table 2. Table 2 provides information that there is a significant correlation between the number of leukocytes and the type of febrile seizures.

**Table 2.** Analysis of the Relationship between Temperature, Nutritional Status, Hemoglobin Levels, and Leukocyte Counts with Types of Febrile Seizures

Variable	Simple febrile seizure n(%)	Complex febrile seizure n(%)	<i>P</i>
<b>Hemoglobin levels</b>			
Abnormal hemoglobin levels	14 (56)	11 (44)	0,100
Normal hemoglobin levels	39 (58,2)	28 (41,8)	
<b>Leukocyte Counts</b>			
Abnormal	34 (69,4)	15 (30,6)	0,026*
Normal	19 (44,2)	24 (55,8)	
<b>Temperature</b>			
≥38°C	32 (61,5)	20 (38,5)	0,511
<38°C	21 (52,5)	19 (47,5)	
<b>Nutrition Status</b>			
Malnutrition	10 (66,7)	5 (33,3)	0,624
Normal nutrition	43 (55,8)	34 (44,2)	

Simple febrile seizures and complex febrile seizures are the two categories of febrile seizures. Simple febrile seizures have a short half-life of under fifteen minutes with a generalized seizure form (tonic or clonic) without focal movements. Meanwhile, complex febrile seizures have a longer duration, namely above 15 minutes. Generalized seizures are preceded by partial seizures, focal seizures on one side or partial, and recur more than once in 24 hours.<sup>2,3</sup>

## DISCUSSION

This study shows that hemoglobin levels are not related to the type of febrile seizures. This explanation is in accordance with the research that was conducted at Ulin Banjarmasin Hospital, which found that there is no difference in decreased hemoglobin levels in simple febrile seizures as well as complex febrile seizures in kids 6 months to 5 years of age.<sup>2</sup> This is in accordance with research at RSIA Fatimah Lamongan, which obtained the results of a significant relationship between Hb levels of febrile seizures and febrile seizures in children aged 6-60 months.<sup>12</sup> In addition, another study shows that anemia is a factor of risk for complex febrile seizures since it is found that hemoglobin levels, hematocrit, Mean Corpuscular Volume (MCV) are lower, and Red Cell Distribution Width (RDW) is higher in patients with complex febrile seizures than simple febrile seizures.<sup>13</sup>

This research demonstrates that patients with low hemoglobin are found to be more likely in patients with simple febrile seizures. This explanation is in accordance with a study conducted at Al-Azhar University Hospital, which shows that children with iron deficiency anemia experience simple febrile seizures more frequently than complex ones.<sup>14</sup> In addition, It is consistent with other research that discovered iron deficiency anemia to be a major risk factor for kids with simple febrile seizures, albeit it might not have an effect on the occurrence of simple febrile seizures.<sup>15</sup>

Hemoglobin has an influence on the frequency of children's febrile seizures. Since the function of hemoglobin is to transport oxygen to the tissues from the lungs. It can result in a reduction in the amount of oxygen supply when hemoglobin levels are low. Therefore, there is a disruption in the ATP production process, which benefits the active transport activity of K<sup>+</sup> and Na<sup>+</sup> ions. The role of both is to maintain the balance of ions outside and inside the cell.<sup>2</sup>

The results of this study are that the number of leukocytes is related to the type of febrile seizure. This study shows that abnormal leukocytes occur more in patients with simple febrile seizures than in complex febrile seizures. However, the research findings are in contrast to the study that was conducted at Abdul Wahab Sjahranie Hospital Samarinda. There is no discernible difference in the number of leukocytes between simple and complex febrile seizures in children between the ages of 6 months and 5 years.<sup>9</sup>

These results are in accordance with the explanation that the number of leukocytes related to the type of febrile seizures in toddlers is related since an increase in leukocytes indicates that the body is fighting an infection. In conditions of infection, leukocytes will automatically destroy the organisms that trigger the infection or perform phagocytosis.<sup>5</sup> During an infection, macrophages and lymphocytes stimulate the production of pro-inflammatory cytokines such as IL-1 $\beta$ , TNF- $\alpha$ , as well as IL-6.<sup>9</sup> In addition, alongside anti-inflammatory cytokines, pro-inflammatory cytokines are also released, which are IL-1 $\alpha$ . IL-1 $\beta$  and IL-1 $\alpha$  during febrile seizures will be released simultaneously, making IL-1 $\alpha$  and IL-1 $\beta$  unbalanced. Seizure trigger excitation and inhibition are mainly caused by IL-1 $\beta$ .<sup>16</sup>

The study's findings demonstrate that temperature is not related to the type of febrile seizure. It is in accordance with a study that was conducted at Abdul Wahab Sjahranie Hospital, Samarinda, that no major differences are present in temperature between simple febrile seizures and complex febrile seizures in children 6 months to 5 years of age.<sup>9</sup> The research's findings show that, in contrast to individuals experiencing complex febrile seizures, those with simple febrile seizures experienced temperatures of  $\geq 38$  degrees Celsius. Moreover, other studies state that the risk factor for febrile seizures is the highest temperature achieved during a fever, not the speed of the temperature increase. In addition, other risk factors that affect febrile seizures are seizure thresholds that vary between individuals and change with age and development.<sup>17</sup> The difference in the results of this study could occur since the body temperature data used were body temperature examinations conducted in the hospital, so body temperature was not obtained during the seizure episode.

Changes in body temperature increases can affect neural excitability values and seizure thresholds.<sup>18</sup> Rising temperatures can affect ATP production, ion channels, and cellular metabolism. A body temperature that rises by 1 degree Celsius can increase carbohydrate metabolism by around 10-15%, which results in increased oxygen and glucose needs in the body so that in the body, there will be changes in neuron balance and changes in ion diffusion, which can cause seizures.<sup>5</sup>

The result of this study is that nutritional status is not related to the type of febrile seizures. This is in accordance with a study conducted at Abdul Wahab Sjahranie Hospital Samarinda, namely, the nutritional status between complex febrile seizures and simple febrile seizures in children aged 6 months to 5 years is not significantly different.<sup>9</sup> This study shows that most of the samples have normal nutrition 83.7%, and only

16.3% have malnutrition nutritional status, so in the sample, malnutrition nutritional status is underrepresented.

It is believed that a child's condition of febrile seizures is related to their nutritional status, but the status of nutrition is not a major risk factor influencing febrile seizures.<sup>19,20</sup> A sufficient diet that includes vitamins (such as C, D, and E), minerals (like zinc and selenium), and other bioactive substances are all crucial for preserving the immune system's functionality and is what determines a person's nutritional condition.<sup>21</sup> Furthermore, micronutrients, including zinc, are essential for the growth of cellular immunity, especially T lymphocytes, and maintaining the normal function of macrophages and natural killer cells.<sup>9</sup> In addition, protein has a crucial role in supporting immunity. Protein deficiencies can impair immune function by causing disruptions in the generation of antibodies necessary for adaptive immunity, which weakens the body's defense against pathogens. Protein influences the production of cytokines that control the immune response and is necessary for the proper functioning of immune cells, such as T and B cells.<sup>22</sup> Under normal conditions, cytokines contribute to a significant part of the central nervous system, namely regulating and developing nerves. However, in conditions of infection, elevated cytokine levels have been demonstrated to be a significant factor in the beginning of febrile seizures.<sup>16</sup> Cytokines associated with febrile seizures are IL-1 $\beta$  and TNF- $\alpha$ , which can directly or indirectly affect neurons, and they are neurotoxic when inflammation occurs.<sup>9</sup>

This study has limitations in measuring the child's temperature, which is the temperature at the time of admission to the hospital, so the temperature during the seizure is not known. This study also did not examine other factors related to febrile seizures, including age, gender, LBW (Low Birth Weight), and family history of febrile seizures.

## CONCLUSION

According to the study's findings, children at RSUD dr. Adhyatma, MPH Semarang experience different types of febrile seizures depending on the quantity of leukocytes in their blood.

## CONFLICT OF INTEREST

The researchers state that no conflict of interest is present in this study.

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