

**ANEMIA WITH FEBRILE SEIZURE IN CHILDREN
AGED FROM SIX MONTHS OLD TO FIVE YEARS OLD AT GOTONG ROYONG
HOSPITAL SURABAYA**

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ABSTRACT

Introduction: Febrile seizure is one type of seizure that commonly occurs in groups of children less than five years of age, especially at the age of 2 years. The incidence of febrile seizures in children is often very worrying for parents.

Aim: The purpose of the study was to examine the relationship of anemia with the occurrence of febrile seizures in children aged six months - five years old at Gotong Royong Hospital Surabaya.

Methods: This study uses an Observational Study carried out with a case-control design and purposive sampling method. The study was conducted in one bone that took place between July 25 and August 25, 2017. The study was conducted by taking secondary data from medical records of children aged six months - five years who were hospitalized, consisting of 21 children with febrile seizure and 21 children with fever without a seizure, and Hb recorded in hospitalized patients. Analyze with the chi-square test.

Results: Children with anemia, 8.5 times more likely to experience febrile seizures than children who did not experience anemia.

Conclusion: The results showed a significant relationship between anemia and febrile seizure ($p = 0.002$) with an odds ratio of 8.5. Therefore, children with anemia have a higher risk of having a febrile seizure.

Keywords: Anemia, Febrile seizure

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INTRODUCTION

According to the Consensus for the Management of Fever Seizures (Kejang Demam or KD), the Indonesian Pediatrician Association (Ikatan Dokter Anak Indonesia or IDAI), KD is a seizure that occurs at an increase in body temperature (rectal temperature above 38°C) caused by an extracranium process¹. KD is a type of seizure that is common in 2-5% of children aged less than five years old, especially at the age of two years old. The most common age of KD in children is six months to 22 months³. Simple KD is a seizure that lasts less than 15 minutes, does not recur in 24 hours and is the most common form of childhood seizures that occur in 2-5% of children in the United States⁴. In Europe and the United States, 2-5% of children (more common in boys) experience at least one KD before the age of five years. Although preliminary studies in India found up to 10% of children experiencing KD, recent data shows that incidence in India is similar to that in the West⁵. Research in Japan found higher rates, namely: Tsuboi (1986) scored around 7% and Maeda (1993) got 9.7% (in men 10.5% and in women 8.9%)^{6,7}.

Risk factors for KD are age, sex, fever temperature, family history of previous KD members, complications in labor (preterm and Low Birth Weight or

LBW), recurrent infections, and iron status (anemia)².

Incidence of KD in children is often very worrying for parents. According to the study of Wals and Shirasaka (1994), severe anxiety experienced by mothers in children who have KD is caused by mothers worried about brain damage in children, children become injured, unable to breathe, become unconscious, and even die⁸. In the Westerlain and Shirasaka (1994) study it was found that seizure seizures can damage the brain⁹, whereas according to the study of Aicardi and Chevrie (1979), it was reported that of 402 children with KD, 131 found one or more sequels, 114 had epilepsy, 54 had mental retardation, 37 suffered from other neurological disorders including 24 with hemiplegia. Children who suffer from this sequel, before KD are normal and also found that the occurrence of sequels is greater if KD lasts longer than 30 minutes or is unilateral compared to short and bilateral ones¹⁰.

The results of Van Stuijven Berg's research (1999) shows that 17% of parents of children with KD have no knowledge of seizures and 47-77% consider their children to be seriously ill and will end in death. The Parmar study (2001) in India found 77.9% of parents of KD patients had no knowledge of KD and 90% thought their child would die, while 52% of

parents said that they checked their child's temperature every ≤ 1 hour when their child had a fever, 25% give antipyretics for temperatures $< 37.8^\circ\text{C}$ ($< 100^\circ\text{F}$), and 85% will wake their children to give antipyretics. Unfortunately, most parents give the wrong antipyretic dose, 15% of parents give an excessive dose of acetaminophen or ibuprofen. Parents' excessive worry is the main cause of the incident^{11,12}.

According to the study of Pellock (2013), it was found that anemia is one of the risk factors for KD². Anemia is a condition where a person experiences a shortage of red blood cell volume and low concentration of hemoglobin (Hb) in the blood¹³. Anemia can also be interpreted as a state of red blood cells that can not carry enough oxygen (O₂) into the body's tissues¹⁴, so that anemia causes reduced ability to transport O₂ into the tissue. Lack of O₂ in tissues can cause hypoxia where O₂ is needed in the active transport process of Na⁺-K⁺ ions which is useful to stabilize the condition of nerve cell membranes, disruption of nerve cell membrane stability can result in intracellular Na⁺ ion concentrations increasing, triggering depolarization, if this condition is at a level which can still lead to KD during fever¹⁵.

According to the World Health Organization (WHO) in the Worldwide

Prevalence of Anemia, the total world population suffering from anemia is 1.62 billion people with a prevalence in pre-school children 47.4% (767 million), while in primary school children 25.4% (411 million) and 305 million school children worldwide suffer from anemia¹³. Nearly 50% of children in developing countries experience anemia. In Indonesia, the incidence of anemia in children is still often found. Globally, the prevalence of anemia in school-age children shows a high rate, which is 37%, while in Thailand it is 13.4% and in India 85.5%. The prevalence of anemia among children in Asia reaches 58.4%. This figure is higher than the average in Africa, where the prevalence of anemia in Africa is only 49.8%¹⁶.

There is some debate about the role of anemia in KD. Research that supports that there is a significant relationship between anemia and KD, namely Malla research (2015), Dasmayanti (2015), Sharawat (2016), Srinivasa (2014), Khanis (2010), and Hartfield (2009) report that anemia is one of risk factors that can reduce the threshold of seizures during fever which facilitates KD¹⁷⁻²², whereas according to the study of Bidabadi (2009), Amirsalari (2010), Omran (2009), and Sherjil (2010) it was reported that anemia did not have a significant relationship as a risk factor for KD²³⁻²⁵. The research results

above, will be explained further in the discussion chapter.

Pisacane research (1996) reports that anemia is a risk factor for KD generation in children under 2 years old²⁶. Mittal's research (2002) reported that iron deficiency in experimental animals showed a significant decrease in the levels of aminobutyric acid gamma (GABA) in the brain. Agarwal's (2002) study reported that iron deficiency showed a significant increase in glutamic acid levels in the brain. An imbalance between the neurotransmitter glutamic acid facilitator and GABA inhibitors plays a role in the onset of seizures²⁷.

Because anemia can be a risk factor for KD in children, researchers are interested in examining the relationship of anemia to the occurrence of KD in children aged 6 months old - 5 years old. Thus, it is hoped that the incidence of KD can be prevented by improving the condition of anemia in children.

Based on the data that has been obtained and the results of several related studies, we investigate the relationship of anemia with the occurrence of KD in children aged 6 months old - 5 years old.

METHODS

This study uses a retrospective observational analytic research method with a case control research design. The

calculation of sample size takes into account the longest group or not, and whether there exist a control group.

The number of samples in this study were 42 samples, consisting of 21 groups of KD and 21 groups of fever without seizures from 1 January 2016 to 31 July 2017. The inclusion criteria for this study were KD pediatric patients and fever without seizures for men and women aged 6 months old - 5 years old with a temperature of $\geq 38^{\circ}\text{C}$ measured when first arrived, and have a good nutritional status of the hospitalized, as well as Hb inpatient data at the first examination recorded in the medical record.

The exclusion criteria for this study were patients who had previous neurological abnormalities, seizures caused by intracranial infections, seizures due to other causes, patients who had a history of previous epilepsy, KD pediatric patients and fever without seizures with temperatures $<38^{\circ}\text{C}$, examination of hemoglobin levels from the clinic or home other illnesses, and KD child patients who have a history of KD before. We also used the purposive sampling technique in this study.

The research was begun by determining the study population; namely, all children aged 6 months - 5 years with fever who were treated at the Gotong Royong Hospital Surabaya in the period

January 2016 to July 2017. From this population, samples were taken using a purposive sampling technique, where all members populations that meet the inclusion and exclusion criteria. Data collection is taken from medical record data. Data taken from medical records are gender, age, cause of fever, temperature, and hemoglobin level at the first examination at Gotong Royong Hospital, Surabaya. The examination of blood samples is done by taking three ccs of blood (vein mediana cubiti). Blood samples are inserted into the EDTA tube then homogenised. Then, the EDTA tube is opened when the blood is homogenous. The blood sample is calculated using a tool automatic hematology analyzer, the Sysmex KX-21 brand, which has the same standard values with WHO. Data compilation and tabulation is done after all data has been collected to facilitate data analysis. Data regarding anemia and KD were analyzed using the help of the SPSS program version 23.0. The results of data analysis are presented in tabular and narrative form. All results of data collection and analysis are discussed, and conclusions are drawn from the study, and suggestions are given for further research.

RESULT

The results of the distribution of the research sample on the medical record

data of children aged 6 months old - 5 years old who were hospitalized in Surabaya Gotong Royong Hospital in July-August 2017, we found children with KD (add up to 100%) and also children with fever without seizures (add up to 100%).

Table 1 Sample Distribution Based on Gender

Sex	Children w/ KD	Children w/ fever without seizures
Male	9 (42,86%)	11 (52,38%)
Female	12 (57,14%)	10 (47,62%)

Based on **Table 1**, boys with KD were nine samples (42.86%), and girls with KD were 12 samples (57.14%). We also gathered data on boys with fever without seizures for 11 samples (52.38%) and girls with fever without seizures for ten samples (47.62%).

Table 2 Sample Distribution Based on Age

Age	Children w/ KD	Children w/ fever without seizures	Total
6-12 m/o	9 (42,86%)	3 (14,29%)	12
1-2 y/o	9 (42,86%)	3 (14,29%)	12
2-3 y/o	-	4 (19,05%)	8
3-4 y/o	-	4 (19,05%)	4
4-5 y/o	1 (4,76%)	4 (19,05%)	5

Based on **Table 2**, most children experience KD in the age range between 6 months old to 12 months old, as many as nine patients (42.86%) and the age range of 1 year old to 2 years old, as many as nine patients (42.86%).

Table 3 Sample Distribution Based on Temperature

Body Temperature (°C)	Children w/ KD	Children w/ fever without seizures
38,1-38,5	7 (33,33%)	9 (42,86%)

38,5-39,0	6 (28,57%)	7 (33,33%)
39,1-39,5	7 (33,33%)	5 (23,81%)
39,6-40,0	1 (4,78%)	-
Total	21 (100%)	21 (100%)

Based on **Table 3**, as many as seven patients experienced the most KD, namely at temperatures of 38°C to 38.5°C, with a percentage of 33.33% and with the same number of patients at temperatures of 39.1°C to 39.5°C, with a percentage of 33.33 %.

Table 4 Percentage of Fever Causes in KD Children Aged 6 Months Old - 5 Years Old at Gotong Royong Hospital Surabaya

	Fever Causes in KD
Acute Pharyngitis	19 (90,48%)
Bronchiolitis	1 (4,76%)
Bronchitis	1 (4,76%)

Based on **Table 4**, the percentage of causes of fever in KD children aged 6 months old - 5 years old at Gotong Royong Hospital Surabaya, we get 90.48% in acute pharyngitis, 4.76% in bronchiolitis, and 4.76% in bronchitis.

Table 5 Percentage of Causes of Fever Without Seizures Children 6 Months Old - 5 Years Old at Gotong Royong Hospital Surabaya

	Fever Causes (without seizures)
Acute Pharyngitis	4 (19,04%)
Dengue Fever	4 (19,04%)
Dengue Hemorrhagic Fever	4 (19,04%)
Acute Diarrhea with Moderate Dehydration	4 (19,04%)
Typhoid Fever	3 (14,28%)

Salmonella Typosa	1 (4,76%)
Bronchitis	1 (4,76%)

Based on **Table 5**, the percentage of causes of fever in febrile seizures in children was 19.04% in Acute Pharyngitis, 19.04 in dengue fever, 19.04% in dengue hemorrhagic fever, 19.04% in acute diarrhea, moderate dehydration, 14, 28% in Typhoid Fever, 4.76% in bronchitis and 4.76% in Salmonella Typosa.

Table 6 Distribusi Sampel Berdasarkan Kadar Hb

	Children w/ KD	Children w/ fever without seizures
Mean	10,85 g/dL	11,70 g/dL
Minimum	9,2 g/dL	9,3 g/dL
Maximum	12,9 g/dL	13,6 g/dL

Based on **Table 6**, the children with KD group of Hb levels during the first laboratory examination at Gotong Royong Hospital had the lowest value of 9.2 g / dL, the highest of 12.9 g / dL, and an average of 10.85 g / dL. In the fever without seizure group, the Hb number at the first laboratory examination at the Gotong Royong Hospital had the lowest value of 9.3 g / dL, the highest of 13.6 g / dL, and an average of 11.70 g / dL.

Table 7 Cross tabulation between anemia and KD

Hb Value	KD	Fever without seizures	Odds Ratio	Significance
Hb <11	14 (77,8%)	4 (22,2%)	8,5	p= 0,002
Hb ≥11	7 (29,2%)	17 (70,8%)		
Total	21 (50%)	21 (50%)		

Cross tabulation data, as shown in Table 7, then analyzed using the chi-

square test to find the relationship between variables. From the analysis, it was obtained a significance value of 0.002 ($p = 0.002$) which means $p < \alpha$ ($\alpha = 0.05$) which means that H_0 was rejected and H_1 was accepted, so it can be concluded that in this study there was a significant relationship between Anemia and the occurrence of KD with an odds ratio of 8.5.

DISCUSSION

This chapter explains the discussion of research results covering the demographic characteristics of KD patients and the results of the analysis of the relationship between anemia and the occurrence of KD in pediatric patients aged 6 months old - 5 years old at Gotong Royong Hospital, Surabaya. The study was conducted on 21 groups of children with KD and 21 groups children with fever without seizures" who were hospitalized from January 1, 2016, to July 31, 2017, at the Gotong Royong Hospital in Surabaya, which met the criteria for inclusion and exclusion of researchers. Samples were taken using a purposive sampling technique on July 25, 2017-August 25, 2017, with diagnostic data and hemoglobin levels from medical records.

In this study, most KD patients by gender were female, as many as 12

patients (57.14%). In the age group, the incidence of KD in many children occurs at the age of 6 months old to 12 months old. That is because age is related to the brain development phase, namely the developmental windows, which are the brain development phase of the organization.

Based on the temperature, the highest temperature obtained by KD patients ranged from 38.1-38.5°C and 39.1-39.5°C as many as 14 KD patients out of 21 KD patients. Based on the cause of fever, the most common cause of KD patients and fever without seizures, namely in the form of acute pharyngitis by 90.48% and 19.04%. Based on Hb levels, the KD group had an average Hb level of 10.85 g/dL, while the group of fever without seizures had an average Hb level of 11.70 g / dL.

Based on the results of the chi-square test, we obtained the p-value of 0.002 ($p\text{-value} < 0.05$). This means that there is a significant relationship of anemia with KD in children aged 6 months old to age 5 years old at Gotong Hospital Royong Surabaya. This finding is in line with Malla's study (2015), which reported that of 162 children aged 6 months old - 5 years old consisting of 92 KD children and 70 children with fever without seizures, it was found that KD children had anemia of 61.95%, while children with fever without

Anemic seizures were 21.42% (17) and Dasmayanti (2015) also reported that 22 out of 25 KD samples were anemic (Hb <11 g / dL). In contrast, only 2 out of 25 fever samples without seizures had anemia. (18). The calculation of the odds ratio in this study was 8.5, so it can be interpreted that children (aged 6 months old - 5 years old) with anemia have an 8.5 times risk of developing KD compared with children who do not have anemia. This finding is in line with research conducted by Khanis (2010) who reported that children with anemia had a risk of developing KD 10.8 times greater than children without anemia (21), Hartfield's study (2009) also reported that children with anemia had two times greater risk for developing KD seizures (22), and Putri's research (2017) reported that 45.2% of the 42 KD groups had more anemia than the fever without seizure group, that only had 19%. Children with anemia had a risk of 3.5 times more likely to experience KD compared to children who do not have anemia²⁸.

CONCLUSION

Based on the results of research conducted on the relationship of anemia with the occurrence of KD in children aged 6 months old - 5 years old at Gotong Royong Hospital Surabaya against 42 samples, consisting of 21 groups of KD

and 21 groups of fever without seizures from 1 January 2016 to 31 July 2017, it was concluded that there was a significant relationship between anemia and the occurrence of KD in children aged 6 months old - 5 years old. From the data obtained in this study, it can be concluded that anemia in children (Hb level <11 g / dL) is one of the significant indicators and needs more attention as a risk factor for KD.

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