Original Article

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Relationship between Neutrophil-Lymphocyte Ratio and Type of Febrile Seizures Event

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Abstract

Background: Febrile seizure is a common neurological condition affecting children. Complete blood count (CBC) is often used as the initial test to help determine the etiology of fever based on hematology parameters in the emergency ward.

Objective: To analyze the relationship between neutrophil-lymphocyte ratio (NLR) and the type of febrile seizure among pediatric patients admitted to Wangaya General Hospital Denpasar, Indonesia.

Methods: A cross-sectional design was implemented on a study using medical records of 44 children aged 6 month-5 years old admitted to the Wangaya Hospital between January 1, 2023, and September 8, 2024. Participants were grouped into simple and complex febrile seizures.

Results: Among patients who experienced the first febrile seizure, the complex type accounted for most hospitalizations (n=33, 75.0%). The majority of cases occurred in children aged ≤24 months (n=32, 72.7%) with a temperature of >38°C (n=27, 61.4%). Seizure duration was ≤15 minutes in most cases (n=41, 93.9%), with upper Respiratory Infection being the most common etiology (n=20, 45.5%). NLR did not differ significantly between the simple and complex febrile seizures (P value =0.894), with a prevalence ratio (PR) of 1.1. Additionally, leukopenia, lymphocytopenia, and neutrophilia were observed in 28 (63.6%), 23 (52.3%), and 24 (54.5%) patients, respectively.

Conclusion: There is no significant relationship between NLR and the type of first febrile seizures. Seizures are more frequently observed in males, particularly those aged 6-24 months with body temperature exceeding 38°C. The mean NLR of 2.78 ± 2.38 and upper respiratory infection are the most frequently associated conditions.

Keywords: Febrile seizures, leukocyte, neutrophil, neutrophil-lymphocyte ratio

Introduction

Febrile seizure, the most common neurological disorder, is a convulsive episode occurring in children aged 6 months to 5 years. The condition is associated with fever exceeding 38°C, without central or intracranial process.[1] The exact mechanism underlying fever-induced seizures remains unclear, but inflammation, particularly the release of cytokines, is considered a key factor. Cytokines act as a mediator that interacts with the host immune response, triggering fever during the acute phase.[2] The diagnostic approach for febrile seizures is primarily based on clinical manifestation. A previous study by Goksugur *et al.* stated that neutrophil-lymphocyte ratio (NLR) helped in distinguishing between types of febrile seizures during the acute phase, particularly at the first episode.[3]

Peripheral blood NLR serves as an indicator of infection severity and systemic inflammation. It is an inexpensive and practical

diagnostic maker that may help characterize febrile seizure subtypes. Patients admitted to the hospital were subjected to basic hematological examination in the emergency ward to assess their hematological status. The clinical significance of identifying between the neutrophil-to-lymphocyte ratio (NLR) and different types of seizures is scientifically important because seizure type reflects distinct clinical severity, risk of recurrence, and potential for longterm complications. This suggests that NLR may serve not just as a general marker of seizure presence, but also a marker of seizure severity and risk stratification.[4,5,6]

Previous studies had presented inconsistent results regarding the relationship between NLR and the type of first febrile seizures. Since NLR reflects the proportion of systemic neutrophils and lymphocytes, it offers a cost-effective method for evaluating inflammatory responses.[7] This study aims to analyze the relationship between NLR and the type of febrile seizure among patients experiencing first seizure episodes at Wangaya General Hospital from 2023 to 2024.

Methods

This observational analytic study was conducted at Wangaya General Hospital using secondary data from medical records. The population included children aged 6 months to 5 years diagnosed with first febrile seizure and hospitalized between 1 January 2023 and 8 September 2024. Ethical approval was granted by Wangaya General Hospital Health and Research Ethics Committee, with the number of ethics: 000.9.2/7268/RSUDW.

The inclusion criteria covered hospitalized patients in the specified age range of 6 months to 5 years, diagnosed with febrile seizures and fever above 38°C. Participants were excluded based on incomplete records, confirmed intracranial pathology, previous history of a febrile seizures, prolonged corticosteroid use, type 1 or 2 diabetes mellitus, epilepsy, cerebral palsy, global developmental delay, and hematologic disorders. Data collected were sex, seizure type, age, temperature at onset, duration of seizures, and hematological parameters from the emergency ward, including white blood cell (WBC), neutrophil, lymphocyte, as well as NLR analyzed as categorical variables.

A consecutive sampling method was used, with a minimum sample size of 44. The size was determined using the independent group interval method based on the NLR cut-off value reported by Pooja *et al*. in India.[8] The consecutive sampling was conducted by including all patients who met the inclusion criteria during the study period. So, this sample can reflected the actual clinical population without preferential selection.

Diagnosis of febrile seizures was based solely on clinical manifestation criteria established by the Indonesia Pediatrics Society (IDAI) consensus.[9] Data on NLR concentration at the time of emergency ward admission were obtained from medical reports. The information system in the hospital for diagnosis was classified according to ICD-10 criteria. Data were presented as categorical variables and percentages, with febrile seizures categorized under simple or complex. NLR classification followed a previous study cut-off value of ≤1.13 and >1.13. Data extraction and processing were performed using Microsoft Excel and SPSS 25 statistical software package.

Univariate analysis was conducted for baseline characteristics. Kolmogorov Smirnov test assessed the normality of NLR distribution. Bivariate analysis, with a 95% confidence interval (CI), evaluated the relationship between type of febrile seizure and NLR. The chi-square test was used to analyze neutrophil, lymphocyte, and leukocyte levels, duration of seizure, temperature, and associated illnesses. Mann-Whitney test assessed the relationship between NLR and type of febrile seizure, with a p-value of < 0.05 considered statistically significant.

Results

A total of 44 children met the inclusion criteria and were diagnosed with febrile seizures based on medical records from January 1, 2023, to September 8, 2024. This condition occurred predominantly in children aged 6–24 months, with males comprising 71.0% of cases. Most seizures were triggered by a fever exceeding 38°C, while the mean WBC count was 11.3×10^3/UL with the majority presenting lower levels. The result of neutrophil counts was elevated compared to the normal limit with a mean of 52.30%. It was important to acknowledge that the majority had lower levels of lymphocyte with a mean of 30.66%. Based on observation , NLR exceeded the 1.3 cut-off in 70.5% of cases. Complex febrile seizures were the most frequently observed, often associated with upper respiratory infections. The characteristics of patients are

Table 1 Study Population Characteristics

Variable (n=44)	Total (n=44)
Age (month)	
6-24	32 (72.7%)
>24	12 (27.3%)
Sex	
Male	31 (71.0%)
Female	13 (29.0%)
Temperature (Celsius)	
<38°	17 (38.6%)
>38°	27 (61.4%)
WBC (White Blood Cell)	
Mean ± SD	11.13 ± 4.16
Decrease	28 (63.6%)
Increase	16 (36.4%)
Neutrophil	
Mean ± SD	52.30 ± 15.92
Decrease	4 (9.1%)
Normal	16 (36.4%)
Increase	24 (54.5%)
Lymphocyte	
Mean ± SD	30.66 ± 13.03
Decrease	23 (52.3%)
Normal	21 (47.4%)
Duration of seizure	
Mean ± SD	4.45 ± 2.51
≤15 minutes	41 (93.9%)
>15 minutes	3 (6.8%)
Ratio neutrophil-lymphocyte	
Mean ± SD	2.78 ± 2.38
≤1.13	13 (29.5%)
>1.13	31 (70.5%)
History of Disease	
Diarrhea	18 (40.9%)
Upper respiratory tract infection	20 (45.5%)
Acute otitis media	3 (6.8%)
Pneumonia	3 (6.8%)
Type of febrile seizures	
Simple	11 (25.0%)
Complex	33 (75.0%)

summarized in Table 1.

Based on bivariate analysis using chi-square test showed no significant relationship between type of febrile seizure and NLR (p-value: 0.894). Complex febrile seizures were most frequently associated with NLR values above the cut-off point. Additionally, the prevalence ratio (PR) was 1.159, with a confidence interval of 0.253-5.340, crossing 1. The results showed that NLR as an independent variable, was not a protective factor for type of febrile seizure, as presented in Table 2.

Discussion

Febrile seizures were more common in males, which may be related to anatomical differences, particularly a narrower parietal region in the cranium.[10] Based on observation, children aged 6 – 24 months comprised 72.7% of cases. This is in line with the results from Shen *et al* in China, where younger children were more susceptible due to incomplete myelination and less effective excitatory as well as inhibitory brain function.[11] The duration of first febrile seizures was a crucial risk factor, with 93.9% of cases lasting less than 15 minutes. This result is in line with Shen *et al*., who reported a mean duration of 6.1 minutes, emphasizing an increased risk of recurrence due to immature brain development.[11]

Most patients in this study presented with a body temperature exceeding 38°C during febrile seizures in the emergency ward. The role of fever in triggering seizures remains a subject of debate. A recent prospective study by Tang *et al* reported higher peak temperatures during hospital admission in first-time febrile seizure cases. This is attributed to infection and inflammation-induced neuronal excitability.[12]

A significant proportion (45.5%) of children in this study experienced upper respiratory tract infections, including flu-like symptoms and rhinopharyngitis, before their first febrile seizure. This is in line with the results from Erdede *et al*., who identified respiratory tract infections as a common cause of febrile

Table 2 Association between Type of Febrile Seizures and NLR

Variable	Type of Febrile Seizures		Ratio Prevalence (95% CI)	p-value
	Complex	Simple		
NLR cut off				
≤1.13	10 (30.3%)	3 (27.3%)	1.159 (0.253 – 5.304)	0.894
>1.13	23 (69.7%)	8 (72.7%)		

The p-value is obtained from the *Kolmogorov-Smirnov* test between the 2 groups

seizures. Furthermore, respiratory syncytial virus (RSV) and influenza were considered the primary etiologies, with laboratory confirmation being uncommon.[13]

The viral infection triggered the release of pro-inflammatory cytokine, including interleukin (IL)-6, tumor necrosis factors (TNF)-alfa, IL-10, and IL-Beta, which were highly thermosensitive and induced neuronal excitability.[14] Study in China finding the case of febrile seizure not related with season but peak of viral epidemic compared to the non-epidemic period.[14,20]

A higher leukocyte count signifies infection, which can trigger seizures. This study did not observe a higher count, commonly associated with bacterial infection.[15] However, approximately 63.6% had lower leukocyte, suggesting a viral etiology, often manifesting as upper respiratory tract infections. Due to resource limitations, this study did not identify specific viral pathogens, as laboratory confirmation is uncommon. In the acute phase of seizure, neutrophil levels commonly exhibit a marked increase in response to pro-inflammatory cytokines. This response is associated with elevated levels of IL-4, IL-10, and serum cortisol, typically peaking within 4–5 hours following the onset of fever and subsequently declining as the infection is brought under control.[16]

The study showed no significant relationship between type of febrile seizure and NLR (p-value: 0.05). This is in line with the results from Goksugur *et al*, where NLR values above the 1.13 cut-off were observed.[3] Conversely, Liu *et al* reported that NLR above 1.13 increased the risk of recurrent febrile seizures 10 folds. There was no significant correlation between this independent variable and type of febrile seizures.[17] The study conducted by Putri and Windiyanto in Bali also reported no significant association between NLR and seizure type with a P value of 0.97.[18] The variation in NLR, as reported by Moosmann *et al*. showed higher values mostly during the first 2 years of life, followed by a gradual decline before peaking again at puberty. This fluctuation suggests that ongoing infections at the time of febrile seizure may have introduced bias.[19,20] Additionally, Shen *et al*. reported lower values in the first-time seizures due to infectious agents.[11] Based on this study result shows that no significance association between NLR values and seizure type may be explained by wide confidence intervals and a high p-value suggest low statistical power and precision. This result also can be caused by small sample size, low NLR cutt-off, and minimal inflamatory differences (e.c underlying infection) between groups of seizure.

This study had limitations based on sample size, which was restricted to cases of febrile seizure admitted to the emergency ward. Data were obtained retrospectively from medical records, and temperature measurements were taken only upon hospital admission, making it difficult to determine the exact temperature at seizure onset. This cross-sectional study used the NLR cut-off from previous investigations.

Future studies with larger, multicenter samples and consideration of sociodemographic factors and racial differences were needed to establish more precise NLR cut-off values as a predictive marker for febrile seizures or to detect its potential associations.

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