



The role of mean platelet volume/platelet count in differentiation of simple and complex febrile seizures

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Abstract

Aim: Our study aimed to find the relationship between MPV (Mean Platelet Volume) levels, a marker of inflammation, and platelet counts between simple and complex febrile seizures.

Materials and Methods: In this retrospective comparative study, we analyzed the records of 283 children between the ages of 6 months and 6 years who were diagnosed with simple and complex febrile seizures (BFN/CFN) in the Pediatric Neurology Clinic of Inonu University, Faculty of Medicine between January 2021 and December 2022.

Results: The mean age and gender characteristics of the patients were similar in both groups. The MPV of the CFN group (69 patients) (6.53 ± 0.39 fl) was lower than that of the BFN group (214 patients) (7.81 ± 0.43 fl) and this difference was statistically significant ($p < 0.01$). The platelet count of the CFN group ($257.42 \times 103 \pm 126.01 \times 103$) was higher than that of the BFN group ($191.23 \times 103 \pm 68.29 \times 103$) and the difference was statistically significant ($p < 0.01$).

Conclusion: There was a significant difference between BFN and CFN groups in terms of both MPV values and platelet counts. This study suggests that detailed and comprehensive studies on MPV and platelet counts may guide cases where clinical findings are suspicious and the distinction between BFN and CFN cannot be clearly differentiated.



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Introduction

The International League against Epilepsy (ILAE) provides a definition of febrile seizure as "a seizure linked with a febrile illness without CNS (central nervous system) infections, acute electrolyte imbalance, and metabolic imbalance in children who have not experienced afebrile seizure before" [1]. The occurrence of febrile seizures is most frequent in children aged between "6 months" and "5 years", with their onset above the age of seven being extremely rare [2,3]. Febrile convulsions can be categorized into two types: Simple and Complex. Simple febrile convulsions (BFS) last for a brief period of time (<15 minutes), affect the whole body and happen once in a day. Although majority of febrile convulsions are harmless, one in three cases are complicated. Its complexity can result in a greater probability of developing epilepsy, which is often a source of distress for families. Complicated febrile seizures (CFS) are seizures that are either focal or focal to generalized, last longer than 15 minutes, have postictal neurological

findings and may occur more than once within a 24-hour period [4-6].

The inheritance model of febrile seizure remains unclear, though some genetic alterations, compounded by inadequate CNS maturation and environmental factors, are believed to contribute to the development of this age-specific epilepsy syndrome [7]. Numerous studies have explored the link between iron deficiency anemia and febrile seizures. Recently, it is known that iron deficiency findings are due to enzyme system dysfunction involving iron. Platelets, which contain iron enzyme systems, may also be affected by iron deficiency [8,9]. There's some supporting evidence for the existence of this relationship [10-12]. Two critical conditions of platelet count and mean platelet volume (MPV) are shown: platelet size and bone marrow platelet production rate. Thus, it can serve as an indicator of the severity of platelet activation and inflammation. However, there is a dearth of studies that investigate the correlation between platelet count, MPV levels and febrile seizure types [11-14].

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In this study, the authors present a novel hypothesis re-

garding the association between FS and MPV levels. They posit that epilepsy constitutes a form of brain inflammation disorder, and that inflammatory changes are more pronounced in patients with FS - a significant risk factor for subsequent epilepsy - compared to BFS. Consequently, the authors suggest that MPV levels are lower in the FS cohort versus the SFS group [12]. In the present study, we assessed the levels of mean platelet volume (MPV) and platelet counts in paediatric patients diagnosed with Simple (BFS) and Complex (CFS) febrile seizures at a tertiary care hospital located in the eastern region of the country.

Materials and Methods

In this retrospective comparative study, the digital file records of 289 children aged between 6 months and 6 years, who were diagnosed with simple and complex febrile seizures (BFS/CFS) in the Pediatric Neurology Clinic of Inonu University/Faculty of Medicine between January 2021 and December 2022, were analyzed. Approval was obtained from Inonu University Ethics Committee with decision number 2023/4421. Patients who were consulted or directly admitted to our pediatric neurology clinic and were diagnosed with febrile convulsions as a result of the evaluation of a pediatric neurologist were included in the study group. Six patients were excluded due to CNS infection and electrolyte imbalance, leaving 283 patients included in this study. The patients were divided into two groups: BFS and CFS, based on febrile seizure definitions established by ILAE [1]. Age, gender, mean platelet volume, and platelet counts were extracted from the patients' records.

Statistical analysis

Data analysis was conducted using SPSS 20.0 for Windows (Chicago, IL, USA). Mean and standard deviation were used to express the results. Continuous variables were compared using a T test, while categorical variables were compared using a Chi-square test. Mann-Whitney-U test was used to evaluate the relationship between laboratory values and seizure types. Statistical significance was determined by a p value of less than 0.05.

Results

Upon examining the records of 283 children (158 boys/125 girls) with diagnosed simple and complex febrile seizures (BFS/CFS) who visited the Pediatric Neurology Clinic between the ages of 6 months and 6 years, it was found that 214 patients (75.6%) were part of the BFS group, while 69 patients (24.3%) belonged to the CFS group. The average age of children in the BFS group was 28.32 ± 27.65

months, while the average age for those in the CFS group was 33.02 ± 20.31 months. The average age of children in the BFS group was 28.32 ± 27.65 months, while the average age for those in the CFS group was 33.02 ± 20.31 months. The mean platelet volume (MPV) of the CFS group (6.53 ± 0.39 fl) was lower than that of the BFS group (7.81 ± 0.43 fl) and these results were statistically significant at $p < 0.01$. Additionally, the platelet count of the CFS group ($257.42 \times 103 \pm 126.01 \times 103$) was higher than that of the BFS group ($191.23 \times 103 \pm 68.29 \times 103$) and this also meets statistical significance at $p < 0.01$ (Table 1).

Discussion

The occurrence of febrile seizures (FS) in only a subset of children with febrile illness has sparked interest in several factors. The conditions that have been most extensively studied highlight the significance of patient clinical factors related to infection and genetic susceptibility. Furthermore, inflammation is implicated in the development of both FS and post-FS epilepsy. In addition to the inflammatory process, inflammation in the central nervous system increases neuronal excitability, leading to a reduction in the seizure threshold. There is robust evidence supporting the notion that the cascade processes trigger the molecular, synaptic, and structural alterations observed in epileptogenesis. Inflammatory cytokines like TNF- α , IL-1 β , and IL-6 instigate fever, culminating in the evolution of FS. Endogenous pyrogenic cytokine, IL-1 β specifically contributes to the fever-induced reaction of FS. It is believed that cytokine gene polymorphisms affecting cytokine production levels are linked to FS pathogenesis. Platelets possess a diverse array of receptors that enable them to engage with white blood cells, pathogens, tumor necrosis factor (TNF), interleukins (IL-1, IL-6), and endothelium exposed to inflammation. This multifunctionality underscores the inflammatory function of platelets [11-15]. Thus; we aimed in this study to investigate how to play the role of platelets in simple and complex febrile seizure. Recently, Nikkiah et al. discovered that there were no statistically significant differences in mean platelet volume (MPV) and platelet count between BFS and CFS groups [13]. Liu and colleagues discovered a significant decrease in MPV values, and an increase in neutrophil/lymphocyte ratios in the CFS group in comparison to the BFS group [14]. Furthermore, MPV levels were found to be low in our study.

Platelet volume is established during platelet formation from megakaryocytes in the bone marrow. Circulating platelets do not undergo maturation. Thus, factors that activate the bone marrow, such as inflammation and infection, may trigger modifications in platelet volume and quantity. MPV alterations occur prior to the changes in platelet count. It is believed that alterations in MPV during the initial stages may detect inflammation effectively [15]. Although pathophysiological mechanisms are still not to be clearly, numerous hypotheses could be proposed. Elevated MPV is an indicator of larger, more reactive platelets resulting from an increased platelet turnover, and it may be used as an indicator of platelet activation and severity of inflammation [16]. Multiple recent studies have indicated that platelet indices play a critical role in the inflammatory response and that platelet dimensions are

Table 1. Standart deviations and mean values of age groups and laboratory findings.

	BFS (n: 214)	CSF (n: 69)	p value
Age (months)	28.32 \pm 27.65	33.02 \pm 20.31	0.26
MPV	7.81 \pm 0.43fl	6.53 \pm 0.39fl	0.003
Platelet count	191.23 \times 103 \pm 68.29 \times 103	257.42 \times 103 \pm 126.01 \times 103	0.002

MPV: mean platelet volume; SFS: simple febrile seizure; CFS: complex febrile seizure.

linked to the magnitude of inflammation. The significance of MPV as a crucial and effortless indicator of platelet function has been examined by numerous authors in connection to diverse inflammatory ailments including infections, ulcerative colitis, cystic fibrosis, familial Mediterranean fever, rheumatoid arthritis. MPV values exhibited an inverse relationship to inflammation, signifying that platelets were reduced in size, whilst the platelet count was increased. High-grade inflammatory conditions such as ischemic stroke, major surgeries and cancer are conditions in which small and increased numbers of platelets with predominantly low MPV levels circulate [10-15,17]. Recent studies have shown that the platelet count was significantly lower 28,30,33 and MPV was significantly higher 30 in children with FS compared to febrile children without FS [16]. A study by Tang et al. found notable differences in platelet counts between BFS and CFS groups [18]. Additionally, a study conducted in our country by Polat et al. established a significant correlation between low MPV levels, high platelet counts, and CFS [19]. In Chinese manuscript, they found that the MPV value was higher in the FS group; however, the value of platelet count was lower. They thought increased MPV level could be serve as a reliable predictive marker for FS risk [16]. In our research we researched MPV levels affects in simple and complex febrile seizure and also found lower levels of MPV could indicate CFS. Thus, this is one of the first research that identify MPV roles in differences between CFS and BFS.

Chronic epilepsy syndromes, such as temporal lobe epilepsy with hippocampal sclerosis, are recognized to have an association with CFS. Nevertheless, the precise mechanisms accountable for this have not been entirely clarified. Certain studies imply that inflammation may contribute to the onset of temporal lobe epilepsy following febrile seizures [20]. Even though the number of patients in our study was small, the elevation of inflammatory processes in the CFS group is consistent with evidence indicating a correlation between CFS, temporal lobe epilepsy and hippocampal sclerosis in younger patients. Our research outcome demonstrates a relationship between elevated platelet levels and CFS. Considering the increased association of CFS with epilepsy, MPV and platelet count may be important biomarkers.

It can be said that the most important limitation of this study was its single centered nature and retrospective design.

Conclusion

This study demonstrated that MPV and platelet counts obtained as a result of an inexpensive and easily accessible hemogram study are important indicators for the differentiation of CFS and BFS. It is very important to conduct multicenter and large participatory studies on this subject in the future.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

The study was approved by the Inonu University Institutional Ethics Committee (project number: 2023/4421).

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