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Original Research Article

Evaluation of hematological profiles in pediatrics: a focus on blood cell indices and electrolyte changes in febrile seizures

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ABSTRACT

Background: Febrile seizures (FS) are the most common neurological disorder in children, often associated with systemic and hematological changes. Laboratory investigations play a crucial role in identifying potential biomarkers that may aid in risk evaluation and management. This study aims to evaluate various laboratory parameters, including platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), Hemoglobin (Hgb), serum sodium, platelet count (PLT), and white blood cell count (WBC), to assess their role as predictive markers in febrile seizures.
Methods: A prospective observational study was conducted on pediatric patients diagnosed with febrile seizures. Blood samples were analyzed for hematological and biochemical markers. The collected data were statistically analyzed to determine significant associations between these parameters and febrile seizures.
Results: The study findings highlight variations in hematological and biochemical markers among febrile seizure patients. Altered PLR and NLR levels were observed, indicating a possible inflammatory response. MCV, MCH, and Hgb levels were assessed for potential anemia-related influences, while serum sodium levels were evaluated for their role in seizure pathophysiology.
Conclusion: The study provides insights into the laboratory profile of febrile seizure patients, which may help in early identification, risk assessment, and management. Further large-scale studies are required to validate these findings and establish potential predictive markers.

Keywords: Febrile seizure, simple febrile seizure, complex febrile seizure, anemia, Inflammation, sodium.

INTRODUCTION

Febrile seizures (FS) are convulsions commonly seen in children aged six months to six years, not attributable to any infection or inflammation of the central nervous system. They are classified into simple and complex types based on clinical features. Simple febrile seizures (SFS) are generalized seizures that last less than 15 minutes, do not recur within 24 hours, and are not associated with any long-term cognitive or neurological deficits. Conversely, complex febrile seizures (CFS) may occur multiple times within a 24-hour span, exceed 15 minutes in duration, and often present with focal neurological symptoms.[1] Research commonly evaluates the complete blood count (CBC) parameters in relation to conditions such as acute and chronic inflammation, infectious diseases, and cancers, as these parameters are useful in differential diagnoses. Systemic inflammation is closely linked to febrile seizures, with several accessible and cost-effective laboratory markers available to estimate the level of inflammation. The platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) are among the most prominent markers. Changes in white blood cell counts, indicative of the

immune system's response to inflammation, injury, or stress, are exemplified by increased neutrophils (neutrophilia) and a decrease in lymphocytes (lymphopenia), which are also reflected in NLR and PLR measures. Additionally, iron is an essential nutrient for hemoglobin synthesis and plays a critical role in numerous enzymatic processes.

Neurological symptoms linked to iron deficiency anemia, including diminished attention, memory loss, delayed motor skills, and behavioral issues, are extensively documented. Studies indicate that fever may exacerbate the adverse effects of iron deficiency on cognitive function, potentially heightening the risk of febrile seizures in children with iron deficiency. Furthermore, iron deficiency could affect the type, duration, and frequency of seizures.

Consequently, it is plausible that iron deficiency anemia not only plays a role in the occurrence of febrile seizures but may also make individuals more susceptible to other neurological problems, such as irritability and cognitive deficits. Iron is a crucial nutrient necessary for the production of hemoglobin and is integral to various enzymatic processes that facilitate neurochemical reactions, including myelin synthesis, brain energy metabolism, and neurotransmitter activity.

It is also essential for enzymes like monoamine oxidase and aldehyde oxidase. A deficiency in iron diminishes the expression of cytochrome C oxidase, a significant indicator of neuronal metabolic function, which may subsequently modify the seizure threshold in infants and children.[2]

This study seeks to evaluate whether hematological markers can act as predictive indicators for febrile seizures in children. It will examine the correlation between inflammatory markers (PLR and NLR) and febrile seizures, as well as assess variations in hematological indices (MCV, MCH, Hgb, PLT, and WBC) in patients experiencing febrile seizures. Additionally, the study will explore the impact of electrolyte imbalances, particularly serum sodium levels, on seizure occurrences.

METHODS

Study type

This was a prospective study.

Study place

The study was conducted at the Department of Pediatrics, Government Medical College Hospital, Nagapattinam.

Study duration

The study was from April 2024 to September 2024.

All cases of febrile seizure in children aged 6 months to 12 years were included. After obtaining informed consent from the patient's attendant, a detailed history was recorded

Assessment of anemia and hematological parameters

To diagnose the anemia occurrence in febrile seizure and evaluation of hemoglobin (HGB), mean cell volume (MCV) means cell hemoglobin concentration (MCHC). Anemia is characterized by a hemoglobin concentration of less than 11g/dl. Microcytosis is defined as a mean corpuscular volume (MCV) below the normal age-specific reference values for red blood cell size with an MCV of less than 70 fl in children.

Data collection and processing

Patient data were collected using a standardized data collection form and recorded via written form. The collected data were then transferred to Microsoft Excel, where it was compiled into a structured spreadsheet for analysis. Before data entry, manual verification was conducted to ensure data accuracy and consistency. After entry, the dataset was reviewed for errors, and necessary verifications and corrections were made by cross referencing the original questionnaires before proceeding with statistical analysis.

Inclusion criteria

All the patients of age group between 6 months to 12 year and diagnosed as febrile seizures were included in the study.

Exclusion criteria

Any chronic systemic illness (cardiac, renal, metabolic), Neurodevelopmental delay, acute CNS infection, children on iron therapy.

Statistical analysis

Z-score standardization

The Z-score was calculated for platelet-lymphocyte ratio, neutrophil-lymphocyte ratio (NLR), mean cell volume (MCV), mean hemoglobin concentration (MCH), hemoglobin (HGB), platelet counts (PLT), white blood cell counts (WBC), and sodium level to standardize and compare variations in febrile seizure patients. The Z-score represents the number of standard deviations a value is from the mean and was used to improve the precision of parameter comparisons.

Significance testing

The two-tailed Z-test was used to determine the statistical significance of findings. The Z-score formula used was

$$Z=(X-\mu) / \sigma$$

where X is the sample mean, μ is the population mean, and σ is the standard deviation. The p-value was obtained using the standard normal distribution table, and for two-tailed tests, the probability was doubled to account for both tails. A p value<0.05 was considered statistically significant.

RESULTS

Among the 105 pediatric patients in our study, 42.86% had normal WBC counts, while 57.14% exhibited varying degrees of leukocytosis. Mild leukocytosis was observed in 20.00% of cases, followed by moderate leukocytosis (17.14%), severe leukocytosis (8.57%), and moderate to severe leukocytosis (3.81%). A small proportion of patients (0.95%) exhibited very severe leukocytosis, whereas mild leukopenia was recorded in 2.86% of cases (Table 1).

Table 1: Distribution of WBC in febrile seizure.

WBC count	Number of cases (n=105)	%
Leukopenia (3000-6000 cells μ/l)	3	2. 9
Normal (6000-12000 cells μ/l)	45	42.9
Mild leukocytosis (12000–15000 cells μ/l)	21	20. 0
Moderate leukocytosis (15000-21000 cells μ/l)	22	21. 0
Severe leukocytosis (21000- 30000 cells μ/l)	14	13. 3

A majority of cases 70.48% exhibited some degree of anemia, with 39.05% having mild anemia (Hb 10–10.9 g/dL), 30.48% having moderate anemia (Hb 7–9.9 g/dl), and 0.95% presenting with severe anemia (Hb <7.0 g/dl). Normal hemoglobin levels (>11.0 g/dl) were observed in 29.52% of patients (Figure 1).

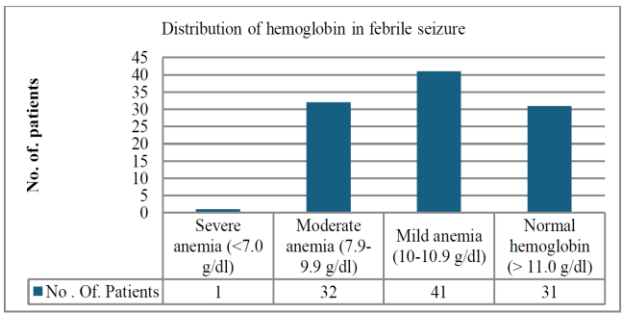

Figure 1: Distribution of haemoglobin in febrile seizure.

The findings indicate that 94.29% of the patients showed microcytosis. This was categorized as follows: 46.67% had moderate microcytosis (mean corpuscular volume (MCV) of 61–70 fl), 36.19% experienced mild microcytosis (MCV of 71-80 fl), and 11.43% were classified with severe microcytosis (MCV of 50–60 fl). Only 5.71% of patients had normal MCV values, which range from 81 to 90 fl (Figure 2). In study of 105 children with febrile seizures, 69 (66%) were male, and 36 (34%) were female.

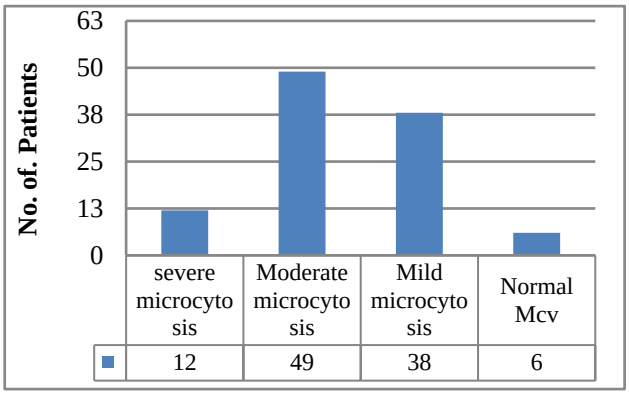

Figure 2: Distribution of MCV in febrile seizure.

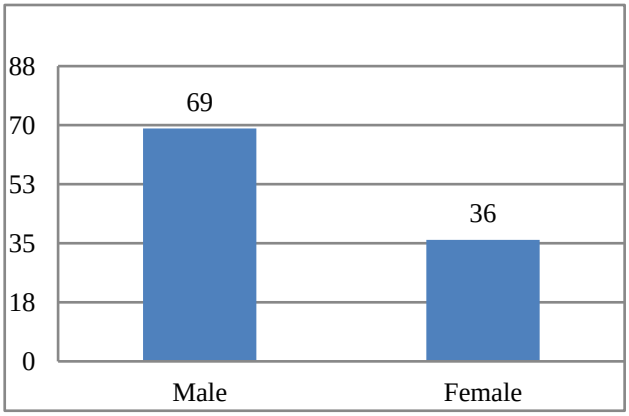

Figure 3: Distribution of gender-wise in febrile seizure.

This indicates a higher prevalence of febrile seizures in males compared to females (Figure 3). In this study 80.95% of patients exhibited hypochromia. Among these, 60.95% were classified as having mild to borderline hypochromia (mean corpuscular hemoglobin, MCH, levels of 21–25 pg), 17.14% as having mild to moderate hypochromia (MCH levels of 16–20 pg), and 2.86% as having severe hypochromia (MCH levels of 11–15 pg). Normal MCH values (26–30 pg) were observed in 16.19% of patients, while 2.86% were identified with microcytic anemia (MCH levels of 31–35 pg) (Figure 4).

The majority of significant proportion of patients (65.71%) demonstrated a low platelet-to-lymphocyte ratio (PLR). In contrast, 14.29% displayed normal PLR levels, while 20.00% exhibited elevated PLR values. These findings indicate a potential association between platelet activation and the inflammatory response in instances of febrile seizures (Figure 5). The majority of patients 65.71% had normal NLR values, with 20.00%

exhibiting low NLR and 13.33% showing high NLR levels.

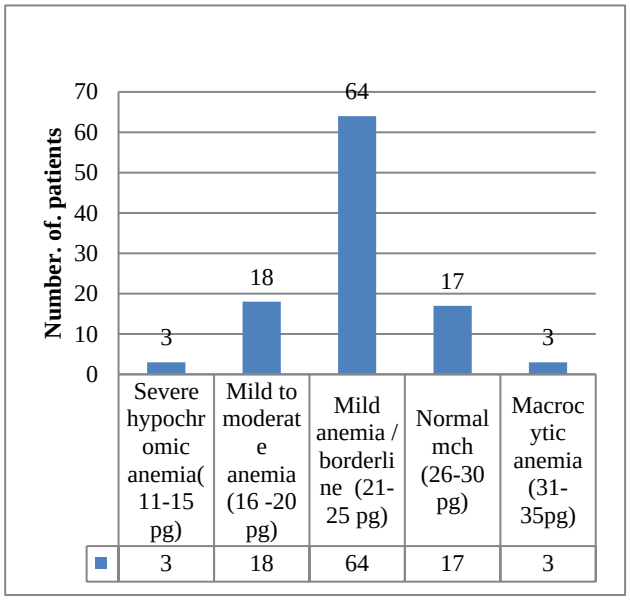

Figure 4: Distribution of MCH in febrile seizure.

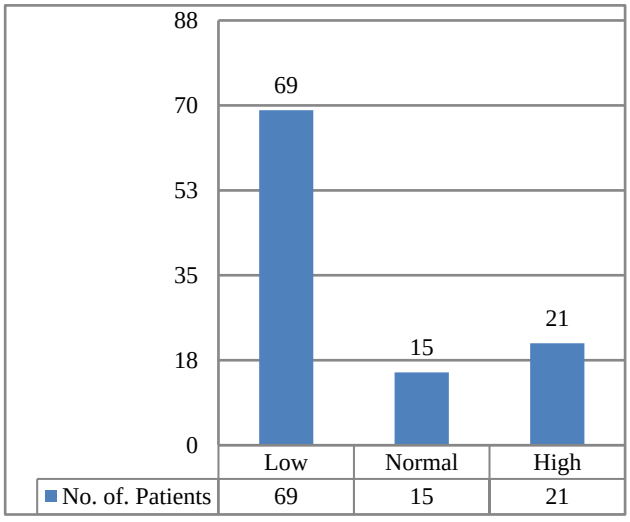

Figure 5: Distribution of PLR in febrile seizure.

Figure 6 illustrates the data. A normal platelet count was recorded in 56. 19% of patients, while 43.81% exhibited platelet abnormalities. Mild thrombocytopenia was observed in 6.67% of cases, whereas thrombocytosis was noted in 37.14% of patients, with 21.90% classified as mild thrombocytosis, 10.48% as moderate thrombocytosis, and 4.76% as severe thrombocytosis. These findings highlight platelet count variations in febrile seizure patients, suggesting a possible link between thrombocytic activity and inflammatory response. Data representation is shown in Figure 7.

Among 105 pediatric patients with febrile seizures, the majority (66%) had normal sodium levels (136-140 mEq/l), observed in 69 patients. Mild hyponatremia (131-135 mEq/l) was present in 31 patients (29%), while moderate hyponatremia (126-130 mEq/l) was seen in 1 patient (1%). Severe hyponatremia (121-125 mEq/l) and higher sodium levels (141-145 mEq/l) were each observed in 2 patients (2%). The findings are depicted in Figure 7.

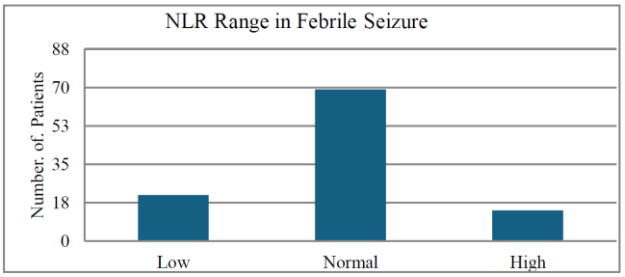

Figure 6: Distribution of NLR in febrile seizure.

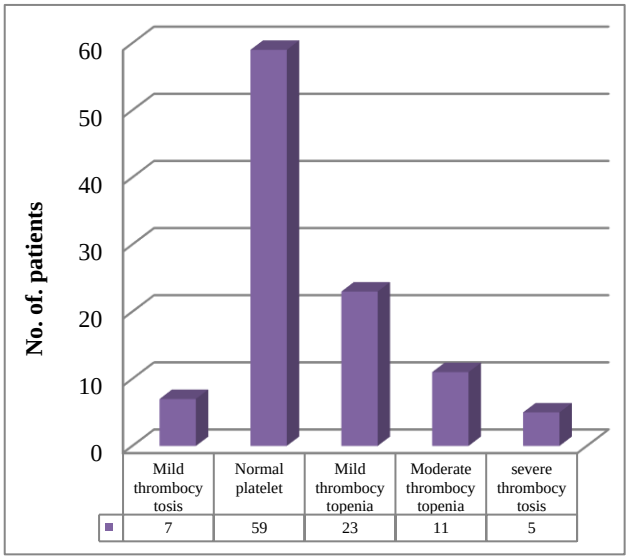

Figure 7: Distribution of platelet in febrile seizure.

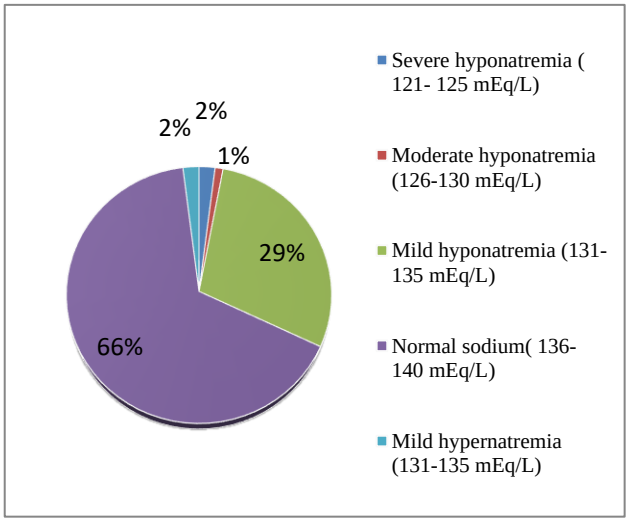

Figure 8: Distribution of serum sodium level in febrile seizure.

DISCUSSION

Our analysis revealed that hemoglobin (HGB) levels between 8.6 and 10.5 g/dl, indicative of moderate anemia, were found in 46% of the cases, highlighting a notable prevalence of anemia. This finding supports the research by Rukmani et al, which links low hemoglobin levels to impaired oxygen delivery to the brain. Anemia may also disrupt neurotransmitter balance, increasing the likelihood of seizures.[2] Furthermore, we found that 47% of cases had a mean corpuscular volume (MCV) ranging from 61 to 70 fl, which consistent with the findings of Rukmani et al research on microcytosis and iron deficiency. A decreased MCV may impair oxygen transport, thereby lowering the seizure threshold, as iron deficiency has been linked to an increased risk of febrile seizures.[2]

Additionally, mean corpuscular hemoglobin (MCH) levels between 21 and 25 pg, indicative of mild hypochromic anemia, were noted in 61% of cases Rukmani et al suggested that disruptions in iron metabolism could lead to heightened neuronal excitability, and low MCH levels may negatively impact brain function, thus contributing to seizure risk. Our results also align with those of Romanowska et al., who identified significant differences in platelet counts between patients experiencing febrile seizures and febrile controls.[2] Febrile seizure represents a common cause of convulsions in young children. Male children (66%) were more commonly affected than females (36%). This aligns with the findings of Tarhani et al, suggesting a possible genetic or hormonal influence in seizure susceptibility among males.[3]

Our research corroborates the findings of Romanowska et al., who reported significant differences in platelet counts between patients experiencing febrile seizures and febrile controls. In our analysis, we discovered that 56.19% of the patients maintained normal platelet counts, while 43.81% presented with either thrombocytopenia or thrombocytosis, thereby underscoring the possible involvement of platelet activation in febrile seizures. Elevated platelet counts may indicate systemic inflammation, which could contribute to the onset of seizures. Pro-inflammatory mediators may play a role in enhancing neuronal excitability.[4]

In our study, leukocytosis (WBC>11×10^9/l) was observed in 64% of the cases, indicating an inflammatory response to infection. This observation is consistent with the findings of Priyanshiben et al, who associated leukocytosis with febrile seizures, suggesting that immune activation may intensify fever and elevate seizure risk.[5] Additionally, consistent with the observations of Özdemir et al, we noted a significant variation in PLR values among febrile seizure patients, with 65.71% exhibiting low PLR and 20% showing elevated levels, implying a potential link between platelet activation and systemic inflammation.[6] Our research indicated that 13% of patients exhibited elevated NLR levels. This is consistent with the observations made by Balıkoğlu et al and colleagues, who recognized NLR as a valuable indicator in the classification of febrile seizures. This correlation implies that higher NLR levels could be linked to a heightened inflammatory response.[7]

Lastly, we observed hyponatremia in 32% of cases, with lower sodium levels being more common among febrile seizure patients. These results are consistent with the study by Shil et al, which established a significant relationship between hyponatremia and complex febrile seizures, emphasizing the importance of serum sodium evaluation in assessing seizure risk and enhancing clinical management.[8]

This study was done in a single hospital, so the results may not apply to all settings. The number of patients was limited. There was no control group for comparison. Some factors like nutrition and other hidden illnesses were not checked. Also, only sodium levels were studied; other electrolytes were not included. Lastly, the study assessed only serum sodium levels, without analyzing other relevant electrolytes like calcium or potassium. The study did not include a follow-up of patients to evaluate long-term neurological outcomes or the recurrence of febrile seizures in relation to initial hematological abnormalities.

CONCLUSION

The results of the study suggest that hyponatremia, mid hypochromic anemia, and platelet abnormalities may play a role in febrile seizures. Elevated inflammatory markers like NLR and PLR indicate a potential link between systemic inflammation and seizure risk. Routine evaluation of these parameters may aid in risk assessment and clinical management of febrile seizures. Further research is needed to strengthen these findings.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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