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Original Research Article

Assessment of neutrophil-to-lymphocyte ratio and mean platelet volume as inflammatory biomarkers in children with febrile seizures

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ABSTRACT

Background: Febrile seizures are common neurological events in children aged 6 months to 5 years and are usually associated with acute febrile illnesses. Inflammatory mechanisms may contribute to seizure occurrence during fever. Neutrophil-to-lymphocyte ratio (NLR) and mean platelet volume (MPV) are simple complete blood count-derived markers that may reflect systemic inflammatory activity.
Methods: This descriptive cross-sectional study was conducted in the Department of Pediatrics at a tertiary care centre in Cuddalore district over a period of 12 months. The study included 40 children aged 6 months to 60 months who presented with febrile seizures. Demographic details, clinical profile, etiology of febrile illness and hematological parameters were recorded. NLR and MPV were calculated from complete blood count analysis. Data were summarized using descriptive statistics.
Results: During a study 40 children with febrile seizures includes in the study who fulfilled inclusion and exclusion criteria, in the study toddlers constituted the majority, accounting for 57.5%. Acute gastroenteritis was the most common etiology of febrile illness. The mean hemoglobin level was low 10.10±1.35 g/dl, mean MPV was (8.65±0.88 fl) normal, mean NLR was (4.00±1.52) elevated among the children with Febrile seizure
Conclusions: Children with febrile seizures had a low mean hemoglobin level, elevated mean NLR, and normal MPV. NLR may serve as a simple, inexpensive, and readily available inflammatory marker in children with febrile seizures. Further well-designed case-control studies are needed to determine whether NLR can be used as a reliable predictor of febrile seizures.

Keywords: Febrile seizure, Children, Neutrophil-to-lymphocyte ratio, Mean platelet volume, Inflammatory biomarker

INTRODUCTION

Febrile seizures are among the most common seizure disorders encountered in early childhood and represent an important cause of emergency pediatric consultation.[1] They typically occur in children between 6 months and 5 years of age in association with fever, without evidence of central nervous system infection, acute metabolic imbalance, or previous afebrile seizures.[2] Although febrile seizures are generally benign and self-limiting, they often create considerable anxiety among parents and caregivers. Clinical evaluation of children with febrile seizures requires careful assessment of age, fever profile, seizure characteristics, family history, and associated systemic illness.[3]

The occurrence of febrile seizures is influenced by the interaction between fever, inflammatory response, and the developing nervous system.[4] Young children have an immature brain with increased susceptibility to seizure activity, and fever may lower the seizure threshold through multiple physiological mechanisms.[5] The rapid rise in body temperature, underlying infectious trigger, cytokine release, and immune activation may contribute

to neuronal excitability.[6] Hence, febrile seizures are not merely temperature-related events but may also reflect an underlying systemic inflammatory response.[7]

Common infectious triggers for febrile seizures include upper respiratory tract infections, acute gastroenteritis, lower respiratory tract infections, viral fever, and urinary tract infections.[8] The duration of fever before seizure onset and the fever-seizure interval are clinically relevant because many febrile seizures occur early in the course of illness.[9] Seizure duration and seizure type are also important in clinical classification and management. Most febrile seizures are generalized and short-lasting, but prolonged, recurrent, or focal episodes require closer evaluation to exclude complex febrile seizures or other neurological conditions.[10]

In recent years, hematological inflammatory biomarker derived from routine complete blood count have gained attention in pediatric clinical research.[11] These markers are inexpensive, widely available, and can be obtained rapidly in emergency and inpatient settings. Among them, NLR has emerged as a practical indicator of systemic inflammation.[12] It reflects relationship between neutrophil mediated innate immune activation and lymphocyte related immune regulation. In children with febrile seizures, changes in neutrophil and lymphocyte counts may occur due to infection, inflammation, physiological stress and seizure-related immune activation.[13]

MPV is another complete blood count-derived parameter that reflects platelet size and platelet activation. Larger platelets considered more active and may be associated with inflammatory and thrombotic processes.[14] Platelets play an important role in immune response, endothelial interaction and inflammatory signaling. Although role of MPV in febrile seizures is less consistent than that of NLR, its assessment may provide additional information regarding platelet related inflammatory activity in children presenting with febrile seizures.[15]

Despite the generally favorable prognosis of febrile seizures, identifying simple biomarker that reflect inflammatory activity may help improve clinical understanding and risk assessment. NLR and MPV are attractive markers because they can be calculated or obtained from routine blood investigations without additional cost.[17-19] However, their clinical relevance in febrile seizures requires further evaluation in different pediatric populations. The present study was therefore conducted to assess NLR and MPV as inflammatory biomarker among children aged 6 months to 5 years presenting with febrile seizures.

Aim

Aim was to assess NLR and MPV as inflammatory biomarker among children aged 6 months to 5 years presenting with febrile seizures.

Objectives

Objectives were to describe the demographic and clinical profile of children with febrile seizures, to estimate the NLR and MPV among children with febrile seizures.

METHODS

Study design and setting

This study was conducted as a descriptive cross-sectional study in the Department of Pediatrics at a tertiary care centre in Cuddalore. The study was designed to assess complete blood count-derived inflammatory biomarkers, particularly NLR and MPV, among children presenting with febrile seizures.

Study population

The study population included children aged 6 months to 60 months.

Study duration

The study was conducted over a period of 12 months.

Sample size

The febrile seizure group consisting of 40 children was included for analysis. Eligible children who fulfilled the inclusion criteria were selected using a purposive sampling technique.

Inclusion and exclusion criteria

Children aged between 6 months and 60 months who presented with febrile seizures were included in the study. Children with afebrile seizures, fever without seizures, central nervous system infections, central nervous system malformations, hydrocephalus, mental retardation, known chronic systemic diseases, history of vaccination in the preceding 72 hours, and family history of genetic or neurological disorders were excluded from the present analysis.

Study procedure

After obtaining approval from the institutional ethics committee and written informed consent from the parents or legal guardians, eligible children fulfilling the inclusion criteria were enrolled in the study. Demographic details such as age and gender were recorded using a structured case record form. Clinical details including duration of fever, fever-seizure interval, seizure duration, type of seizure, and etiology of febrile illness were documented.

A detailed general and systemic examination was performed for each child. Body temperature was recorded, and seizure-related characteristics were

assessed based on history obtained from parents or caregivers and clinical evaluation at presentation. Peripheral venous blood samples were collected under aseptic precautions at the time of presentation. Complete blood count analysis was performed using an automated hematology analyser. Hemoglobin, neutrophil count, lymphocyte count, platelet parameters, and MPV were recorded. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. All clinical and laboratory data were entered into a digital database for analysis.

RESULTS

Age and gender

A total of 40 children as per inclusion criteria were included, their baseline demographic characteristics, including age and gender distribution, are presented in Table 1.

Toddlers constituted the largest age group, with 58 children, followed by preschool children and infants. Female predominance was observed in the febrile seizure group.

Fever duration

The fever duration of the study participants, including fever duration and fever-to-seizure interval, is presented in Table 2.

Most febrile seizures occurred within the first 24 hours of fever, with the highest proportion occurring between 12 and 24 hours after fever onset (Table 2).

Seizure characteristics

The distribution of seizure duration and seizure type among children with febrile seizures is presented in Table 3.

Febrile seizures in the present study were predominantly generalized in nature, with most episodes lasting between 5 and 15 minutes (Table 3).

Fever etiology

The distribution of etiological causes of febrile illness among children with febrile seizures is presented in Table 4.

Acute gastroenteritis was the most common etiology in the febrile seizure group, followed by upper respiratory tract infection (Table 4).

Hematological parameters

Hematological parameters of study presented in Table 5.

The mean hemoglobin level was significantly lower than the normal reference range of 10.5-14.0 g/dl, while the mean NLR was significantly higher than the normal reference range of 0.3 to 1.88. In contrast, the MPV remained within the normal reference range of 7.5-11.5 fL. The observed NLR suggests the presence of systemic inflammatory response among children presenting with febrile seizures (Table 5).

Table 1: Baseline demographic characteristics of children with febrile seizures, (n=40).

Variables	Category	N	Percentage (%)
Age group	Infant	12	30.0
	Toddler	23	57.5
	Preschool	5	12.5
Gender	Male	16	40.0
	Female	24	60.0

Table 2: Fever duration and fever–seizure interval among children with febrile seizures, (n=40).

Variables	Category	N	Percentage (%)
Fever duration (in hours)	<24	34	85.0
	24-72	6	15.0
	>72	0	0.0
Fever-seizure interval (in hours)	<3	5	12.5
	3-6	13	32.5
	6-12	7	17.5
	12-24	15	37.5

Table 3: Seizure characteristics among children with febrile seizures, (n=40).

Variables	Category	N	Percentage (%)
Seizure duration	<5 minutes	11	27.5
	5-15 minutes	29	72.5
Type of seizure	Generalized	40	100

Table 4: Etiology of febrile illness among children with febrile seizures, (n=40).

Etiology of febrile illness	N	Percentage (%)
Upper respiratory tract infection	13	32.5
Acute gastroenteritis	15	37.5
Lower respiratory tract infection	3	7.5
Viral fever	5	12.5
Urinary tract infection	4	10.0

Table 5: Hematological parameters, NLR, and MPV among children with febrile seizures, (n=40).

Parameters	Mean±SD
Haemoglobin, (g/dl)	10.10±1.35
NLR	4.00±1.52
MPV, (fl)	8.65±0.88

DISCUSSION

In the present study, the majority of children with febrile seizures belonged to the toddler age group, accounting for 57.5% (n=23), followed by infants at 30% (n=12) and preschool children at 12.5% (n=5). This indicates that febrile seizures were more commonly observed among children in the younger age groups, particularly toddlers. This finding is consistent with the established clinical understanding that febrile seizures commonly occur between 6 months and 5 years of age, with peak occurrence in the second year of life.[2,10,12] Yazar et al also studied febrile seizures in young children and emphasized that this condition is largely confined to early childhood.[1] Similarly, Aroor and Soans reported febrile seizures among children within the typical vulnerable pediatric age group.[3] In the present study, female children constituted 60% (n=24), while males constituted 40.0% (n=16). Although several studies have reported slight male predominance in febrile seizures, gender distribution varies across study populations and is not considered a consistent independent determinant of febrile seizure occurrence.[1,3,8]

In the current study, 85% (n=34) of children developed febrile seizures within the first 24 hours of fever, while 15% (n=6) had fever duration of 24-72 hours before seizure onset. None of the children had fever for more than 72 hours. The most common fever-seizure interval was 12-24 hours, observed in 37.5% (n=15), followed by 3-6 hours in 32.5% (n=13), 6-12 hours in 17.5% (n=7), and less than 3 hours in 12.5% (n=5). These findings indicate that febrile seizures commonly occurred early in the febrile illness, mostly within the first day of fever. This observation is consistent with standard descriptions of febrile seizures.[2,10,14]

Most children had seizure duration between 5 and 15 minutes, accounting for 72.5% (n=29), while 27.5% (n=11) had seizures lasting less than 5 minutes. All children had generalized seizures, and no focal seizures were observed. These findings indicate that generalized seizure activity was the predominant presentation among children with febrile seizures in the present study. This is consistent with the usual clinical pattern of simple febrile seizures, which are typically generalized and short-lasting.[1-3,10,12,14] Dilber et al further emphasized that seizure duration, recurrence, and focality are important clinical features for distinguishing simple from complex febrile seizures and for assessing recurrence risk.[5] Therefore, the predominance of generalized seizures in the present study is broadly comparable with previous literature, although the relatively higher proportion of seizures lasting 5-15 minutes highlights the need for careful clinical monitoring.

Acute gastroenteritis was the most common etiology of febrile illness, observed in 37.5% (n=15), followed by upper respiratory tract infection in 32.5% (n=13), viral fever in 12.5% (n=5), urinary tract infection in 10% (n=4), and lower respiratory tract infection in 7.5% (n=3). These findings indicate that most febrile seizures in the present study occurred in the setting of common childhood infections. Similar observations have been described in febrile seizure literature, where upper respiratory infections, viral illnesses, gastroenteritis, and other acute infections are common precipitating illnesses.[10,11,14] Sawires et al emphasized the role of viral triggers and infection-related inflammatory responses in the pathophysiology of febrile seizures.[11] Kaushik et al also highlighted the importance of identifying the source of fever while avoiding unnecessary investigations in otherwise uncomplicated febrile seizures.[12] Thus, the present findings are consistent with existing literature reinforce that febrile seizures commonly occur in association with acute, self-limiting childhood infections.

The mean hemoglobin level among children with febrile seizures was (10.10±1.35 g/dl) low. The mean NLR was (4.00±1.52) high, while the MPV was (8.65±0.88 fl) was normal. These findings describe the hematological inflammatory biomarker profile of children with febrile seizures. The elevated NLR observed in the present study supports the role of systemic inflammation in febrile seizures. Yazar et al reported that NLR and MPV were significantly elevated in febrile seizure and acute febrile illness groups compared with healthy controls, suggesting their potential role as inflammatory markers.[1] Aroor and Soans found that elevated NLR was significantly more frequent among children with febrile seizures compared with febrile children without seizures.[3] Söğütlü and Altaş also reported significantly higher NLR and other inflammatory indices in children with febrile seizures, supporting the inflammatory basis of seizure occurrence during febrile illness.[4] Dilber et al observed that NLR, RDW, and MPV were associated with febrile seizure risk and recurrence.[5] Similarly, Hosseini et al in a systematic review and meta-analysis, concluded that NLR has clinical relevance in febrile seizures.[16] In present study, MPV was 8.65±0.88 fL, which is comparable with previous reports showing variable findings regarding MPV in febrile seizures. The present study, children with febrile seizures had significantly higher NLR values that indicating a greater inflammatory response, whereas MPV did not differ significantly. These findings are in agreement with the age-specific pediatric reference studies by Moosmann et a and Zhang et al which demonstrated that NLR is an age dependent inflammatory marker and may be useful in evaluation of inflammatory conditions in children.[17,18] In contrast, Beyan and Beyan emphasized that MPV should be interpreted cautiously because it is influenced by pre-analytical factors and analyzer-specific variations.[19] Some studies have suggested that MPV may be increased in febrile seizure cohorts, while others have reported less consistent associations with seizure severity/ recurrence.[1,5,7,9] Therefore, the present findings suggest that NLR may be a more useful inflammatory marker than MPV in children with febrile seizures, although controlled studies are required to establish its diagnostic and prognostic utility.

CONCLUSION

The present study assessed neutrophil-to-lymphocyte ratio and mean platelet volume as inflammatory bio markers among children with febrile seizures. Febrile seizures were more commonly observed among toddlers, with a female predominance in the study population. Most children developed seizures within the first 24 hours of fever, and generalized seizures were observed in all cases. Acute gastroenteritis and upper respiratory tract infection were the commonest etiologies of febrile illness. The mean neutrophil-to-lymphocyte ratio was 4.00±1.52, suggesting the presence of systemic inflammatory response among children with febrile seizures, while the mean platelet volume was (8.65±0.88 fl) normal.

Based on the findings, neutrophil-to-lymphocyte ratio may be considered as simple, inexpensive, and readily available hematological markers in the evaluation of children with febrile seizures. A higher neutrophil lymphocyte ratio may serve as potential marker for identifying febrile children at increased risk of developing febrile seizure. Although hemoglobin was not included as one of the study parameters, low hemoglobin levels were observed among children with febrile seizure. Mean platelet volume remained within normal range. However, these markers should be interpreted along with clinical findings and should not replace standard clinical assessment. Further studies with larger sample sizes, control groups, and follow-up assessment are recommended to determine the diagnostic, prognostic, and recurrence-predictive value of NLR and MPV in children with febrile seizures.

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Ethical approval: The study was approved by the Institutional Ethics Committee Government medical College and hospital Cuddalore district Ref no. EC/1415/2025, the Registration number of IHEC is EC/NEW/INST/2024/4798.

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