

The ratio of neutrophils I and the mean platelet volume to platelet count ratio as risk factors for febrile convulsions in Zakho

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Abstract

Background and objective: The most prevalent cause of convulsions in young children is febrile convulsions. The ratio of neutrophils to lymphocytes (NLR), the mean platelet volume (MPV), and the platelet count are indicators of inflammation. Children with febrile seizures usually have higher NLR and MPV and less platelet count. The aim of the study is to evaluate the importance of NLR, MPV, Platelet count, MPV/Platelet, and RDW in feverish children with febrile convulsions.

Methods: A case-control study included 163 children with febrile seizures and 163 controls with fever but no seizures. All participants were sent for a red blood cell count (RBC), a white blood cell count (WBC), a hematocrit (Hct), hemoglobin (Hb), a red blood cell distribution width (RDW), a mean corpuscular volume (MCV), a platelet count (PLT), a mean platelet volume (MPV), a monocyte, a lymphocyte, and a neutrophil count, and their percentages were calculated. The absolute neutrophil count divided by the absolute lymphocyte count yields the neutrophil/lymphocyte ratio (NLR). The Mean Platelet volume to platelet count ratio (MPR) was the result of dividing the MPV by platelet count.

Results: The mean ages of cases and controls 22.98 ± 12.43 and 23.05 ± 12.60 respectively were not significantly different 55.8% of cases and 45.4% of controls were male. Between cases and controls, WBC count, MPV, neutrophil count, and NLR were significantly higher in cases ($P = 0.001, 0.001, 0.033$, and 0.001 respectively) while lymphocyte and platelet count were significantly lower in cases.

Conclusion: children with febrile seizures had significantly greater NLR ratios, MPVs, and lower platelet counts.

Keywords: Febrile; Neutrophil; Platelet; Ration; Seizure.

Introduction

The febrile convulsions are recognized as the commonest cause of seizures in young children.¹ In children between 6 months and 5 years old, febrile seizures strike 2-5% of them. They are linked to a temperature that rises quickly and is higher than 38°C without any signs of metabolic disease, an infection of the central nervous system, or a history of a febrile convulsions.⁽¹⁻³⁾ Most commonly, they are brief and self-limiting without recurrence and no permanent sequel.⁽¹⁾

Tumor necrosis factor (TNF), interleukin-6, and interleukin-1 are pro-inflammatory cytokines that cause fever during infections. Previous studies found that the inflammatory process, which causes fever, is responsible for producing febrile convulsions. These studies concluded that inflammatory cytokines may have a significant role in causing febrile convulsions.⁽⁴⁻¹⁰⁾

Red blood cell distribution width (RDW), neutrophil/lymphocyte ratio (NLR), and mean platelet volume (MPV) are all

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regarded as indicators of the inflammatory process.⁽¹¹⁻¹⁵⁾ Children with febrile seizures have significantly higher neutrophil levels by comparison with the children who have a fever but no convulsions while lymphocyte number is lower in children who have febrile convulsions.⁽¹⁶⁾ By dividing the neutrophil count by the lymphocyte count, the NLR is computed. It is an inflammation index calculated from a complete blood picture. Recent research has revealed a link between aberrant NLR and cardiovascular disease,^(17,18) vascular diseases of the brain, hepatic disorders,⁽¹⁹⁾ and autoimmune disorders.^(20,21) The association of NLR with febrile seizures may be related to the IL-1 β induction of fever and neutrophilia and the neutrophils' migration into tissues.⁽²²⁾

MPV is the average size of platelets which is machine-calculated. It displays the size of platelets as well as the pace of their marrow formation. It is thought to be an indication of the activation of the platelets and inflammation severity.⁽²³⁾ Platelets, when activated, produce crucial mediators of inflammation.⁽²⁴⁾ According to studies, MPV is inversely related to platelet counts in patients who are considerably ill.^(25,26) It is suggested that there is more clinical significance in combining MPV and platelet count than using either one alone.⁽²⁵⁻²⁹⁾ Moreover, when there is an inflammation in the blood, there is an interaction between neutrophils and activated platelets.⁽³⁰⁾

Numerous research attempted to link the levels of Neutrophil to Lymphocyte Ratio, Mean Platelet Volume, platelet count, and red cell distribution width to febrile seizures but found conflicting findings.

Being a common and relatively frightening event for the parents, knowing the relevance of predicting factors like the aforementioned ones can help determine those febrile children at risk of developing febrile seizures and do their best to prevent their occurrence.

Aim

To investigate the relevance of platelet count, mean platelet volume, neutrophil to

lymphocyte ratio, red cell distribution width, and mean platelet volume /platelet in feverish children who have and who do not have febrile convulsions.

Methods

A case-control research was carried out in Zakho General Hospital in the north of Iraq in the period from April 1 2021 till April 1, 2022. It included 163 children of six months to six years of age who presented with febrile convulsions and 163 controls who were age- and sex-matched and presented with fever but no seizures. We excluded children with diseases that are expected to cause convulsions in the absence of a fever.

The criteria of exclusion included a history of epilepsy or febrile convulsions, prematurity, family history of neurological and genetic conditions; anomalies in organic acid analysis, amino acid levels, and brain magnetic resonance imaging; subsequent epilepsy after FS; hydrocephalus; electrolyte disorders; static encephalopathy; meningitis; history of CNS infection; stroke; demyelinating disease; mental retardation and acute or chronic disease like hematologic diseases, cancer and or rheumatologic diseases. The International Classification of Diseases, Ninth Revision (ICD-9) codes (ICD-9 780.31, 780.32) were used to make the diagnosis of febrile convulsions.

After obtaining verbal consent from the parents and ethical approval from the general directorate of health in Zakho, in EDTA tubes, blood samples were drawn from peripheral veins, after two hours of admission to the hospital from the cases and controls. Blood cell counts for red blood cells, white blood cells, hemoglobin, mean corpuscular volume, hematocrit, red blood cell distribution width, platelets, neutrophils, monocytes, and lymphocytes were calculated as counts and percentages. By dividing the neutrophil count by the lymphocyte count, the neutrophil/lymphocyte ratio (NLR) was calculated. By dividing the mean platelet

volume by the platelet count, the mean platelet volume/platelet count ratio (MPR) was discovered.

Using the Windows version of the SPSS Statistics 23.0 application from SPSS Inc., Chicago, Illinois, USA, we performed the statistical analysis. Numbers, percentages, mean and standard deviation were used to represent data and student t-test and Chi-square were applied. A *P*-value of <0.05 was considered statistically significant.

Results

The study included 326 patients classified as 163 cases and 163 controls. The mean ages of cases and controls were not

significantly different. Among cases, the male was predominant while in control female was more common however, as can be shown in Table 1, the change was not substantial.

The laboratory parameters showed significantly higher values of each of WBC count, MPV, neutrophil count and percentage, and neutrophil/lymphocyte ratio in cases than controls due to significantly lower count of platelet and lymphocyte.

According to Table 2, no discernible differences between patients and controls were found when each RBC, Hb, PCV, MCV, RDW, and MPR were taken into account.

Table 1 Age and gender of patients with and without febrile convulsion

Variable	Cases group (Mean ± SD)	Control group (Mean ± SD)	<i>P</i> values
Age (months)	22.98 ± 12.43	23.05 ± 12.60	0.293
Gender	Number (%)	Number (%)	<i>P</i> values
Male	91 (55.8%)	74 (45.4%)	0.060
Female	72 (44.2%)	89 (54.6%)	
Total	163 (100%)	163 (100%)	

Table 2 Laboratory parameters in cases and controls febrile convulsion

Lab parameter	case	control	<i>P</i> value
WBC	13.75 ± 7.27	11.04 ± 5.61	0.001
RBC	4.46 ± 0.40	4.486 ± 0.467	0.238
Hb	11.23 ± 0.82	11.197 ± 1.13	0.906
PCV	33.09 ± 3.40	33.21 ± 4.027	0.081
MCV	74.23 ± 6.58	75.51 ± 6.69	0.259
MPV	8.65 ± 1.22	7.33 ± 0.83	0.001
Platelets	218.01 ± 74.53	351.71 ± 136.06	0.033
MPR	0.04538 ± 0.01827	0.02431 ± 0.0100	0.202
Neutrophils %	70.20 ± 14.66	50.09 ± 18.39	0.002
Neutrophils count	9.90 ± 6.36	5.94 ± 4.69	0.001
Lymphocytes %	22.72 ± 13.07	41.32 ± 16.86	0.001
Lymphocytes count	2.84 ± 1.84	3.98 ± 2.06	0.001
NLR	4.79 ± 3.63	1.99 ± 2.36	0.001
RDW%	12.66 ± 1.32	12.98 ± 1.54	0.695

Discussion

In our study, individuals who experienced febrile seizures had NLR ratios that were considerably greater than those of febrile children who did not have seizures. This can be explained by that in febrile seizure, there is an increase in inflammation that depends on neutrophils and a decrease in anti-inflammatory response mediated by the lymphocyte. The first cells of the host defense system to produce inflammatory cytokines are neutrophils. Additionally, they multiply quickly during the strong skeletal muscular activity that occurs during seizures.^(31,32) Also, similar results were found in other studies.^(31,33,34) Reactive oxygen species (ROS) are generated by neutrophils^(33,36) and there is a cause-and-effect relationship between epileptic seizures and ROS production.^(37,38) Additionally, they cause the release of IL-1 and TNF- α , which significantly contribute to the causation of febrile convulsions.⁽³⁹⁾ Moreover, neutrophils express NaV1.3 sodium channels that may be opened up by gradual ramp depolarizations and result in a steady sodium current.⁽⁴⁰⁾

In the current study, platelet count is significantly less and MPV is significantly more in cases than in controls. Similar results were found by other studies^(33,41-43) while contrary to other studies, there were no significant differences in MPR between controls and cases.⁽³³⁾

MPV and platelet count can help to evaluate platelet activation.⁽³³⁾ High MPV indicates the presence of more reactive and larger platelets due to increased turnover of platelets and reflects the severity of inflammation.⁽²³⁾ Platelet activation can result from increased circulating levels of bacterial lipopolysaccharide (LPS). Platelets can store several pro-inflammatory and regulating mediators that are generated in inflammatory regions while platelets are activated and bind to neutrophils to activate inflammatory cytokines.⁽⁴⁴⁾ Therefore, it is postulated that the interaction between neutrophils and platelets contributes to the

likelihood of febrile convulsions.

Conclusion

Children with febrile convulsion had significantly higher NLR ratio and MPV and significantly lower platelet counts as compared to those without seizures. To determine if these variables may be considered separate risk factors for febrile seizures, bigger studies must be conducted.

Competing interests

The authors declare that they have no competing interests.

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