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Comparison of laboratory parameters between children with and without febrile convulsion

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The study was approved by the Ethics and Research Committee of Adiyaman University (approval number 2019/1-20).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Febrile convulsion is the most common central nervous system disease of childhood. The etiology of febrile convulsion is not fully brightened. In this study, we aimed to evaluate the relationship between hemogram, biochemical and hormonal parameters and febrile convulsion, and the roles of laboratory parameters in its etiopathogenesis.
Methods: A total of fifty-four patients diagnosed with febrile convulsion in the pediatric neurology outpatient clinic of a tertiary hospital from October 2017 to December 2018 were included in this retrospective cohort study. Age, sex, age of first convulsion, type of convulsion and laboratory parameters of the patients were recorded. ILAE classification system was used for the diagnosis of febrile convulsion. Febrile convulsion patients were included in the study group, while the control group was randomly selected from patients between 6 months and 6 years of age who visited general pediatric outpatient clinic.
Results: A total of 54 patients (30 males, 24 females) in the study group and 82 patients (53 males, 29 females) in the control group were included in the study (P=0.288). The mean ages of the patients in the study and control groups were 30.31 (14.64) months and 32.32 (19.70) months, respectively (P=0.524). Mean platelet volume (MPV), platelet count, 25-OH D3, vitamin B12 and phosphorus values were significantly lower in the study group (P<0.001, P=0.013, P=0.017, P=0.020).
Conclusion: MPV, platelet count, 25 OH D3, vitamin B12 lower levels may be risk factors for febrile convulsion. Studies related to the etiopathogenesis of febrile convulsion are necessary to enlighten the subject and laboratory results will be the guide in this sense.

Keywords: Febrile convulsion, Laboratory parameters, Children, Seizure

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Introduction

Febrile convulsions (FC) are seizures usually accompanied by febrile diseases other than central nervous system (CNS) infections, which do not meet other acute symptomatic convulsion criteria, seen in children between 1 month and 6 years of age without any history of neonatal or afebrile convulsions [1, 2]. The prevalence of FC varies between 2-8% [3]. Although the pathogenesis of FC is not well known, there are studies reporting increased levels of interferon-α and neuron-specific enolase, decreased thyroid-stimulating hormone values, prolactin, growth hormone and cortisol, central thermoregulation disorders, delayed maturation of CNS, increased excitatory amino acids, and iron deficiency anemia [4]. The purpose of this study was to compare the laboratory parameters among children with and without FC.

Materials and methods

A total of fifty-four patients diagnosed with FC in the pediatric neurology outpatient clinic of a tertiary hospital from October 2017 to December 2018 were included in the study. The data were obtained retrospectively by scanning the patient files. Age, sex, age of first convulsion, type of convulsion and laboratory parameters of the patients were recorded. ILAE classification system was used for the diagnosis of FC. Adiyaman University Ethics Committee approved the study with number 2019/1-20.

Febrile convulsion was diagnosed with the following criteria: Patients within the age range of 1 month to 6 years, convulsions accompanied with fever, absence of any infections in the CNS and electrolyte imbalance, metabolic disorder, intoxication, trauma, and pathological neurological findings (mental motor retardation, cerebral palsy) that may cause convulsions. Cases were evaluated as simple and complex FC according to FC classification. Convulsions lasting more than fifteen minutes, with focal features and/or recurrence within 24 hours were interpreted as complex FC and others were considered simple FC. FC patients were included in the study group. Patients diagnosed with febrile convulsion using antiepileptic drugs were not included in the study. The control group was randomly selected from the patients who visited the general pediatric outpatient clinic between 6 months and 6 years of age with a diagnosis code of Z00.1: Encounter for routine child health examination, and who had not previously been diagnosed with FC.

Demographic data (age, sex) and laboratory results [hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), red cell distribution width (RDW), mean platelet volume (MPV), neutrophil/lymphocyte ratio, 25-OH D3, parathormone (PTH), iron, serum iron binding capacity, ferritin, calcium, phosphorus, vitamin B12, folate] were recorded. The ratios of neutrophil and lymphocyte count were calculated from hemogram parameters. Vitamin B12 values below 250 pg/ml were defined as vitamin B12 deficiency.

Statistical analysis

SPSS (Statistical Package for Social Sciences) for Windows 23.0 was used for statistical analysis in the evaluation of data obtained in this study. Independent Sample T test was used for normal distribution parameters and Mann-Whitney U test was used for non-normal distribution parameters. Chi-square test was used to evaluate categorical variables. A *P*-value <0.05 was considered statistically significant.

Results

A total of fifty-four patients (30 males, 24 females) in the study group and eighty-two patients (53 males, 29 females) in the control group were included in the study. The mean age of the patients in study and control groups were 30.31 (14.64) months and 32.32 (19.70) months, respectively. There was no significant difference among the study and control groups in terms of age and gender (*P*=0.524, *P*=0.288) (Table 1).

Of the fifty-four patients in study group, 28 (51.80%) had simple FC and 26 (48.20%) had complex FC. A total of 7 (13%) patients had a single episode of FC while 47 (87%) patients had two or more episodes. Among forty-seven patients had two or more FC episodes, 17 (36.20%) had two episodes of FC, and 30 (63.80%) had three or more episodes of FC.

The Hb, Hct, MCV, MCH, RDW, Neutrophil/Lymphocyte ratio, PTH levels, iron, iron binding capacity, ferritin, calcium and folic acid values of the control and study groups were similar (*P*>0.05) (Tables 1 and 2). MPV, platelet count, 25-OH D3, vitamin B12 and phosphorus levels were significantly lower in the study group (Tables 1 and 2).

Table 1: Distribution and comparison of laboratory parameters between groups

	Study group n (%)	Control group n (%)	
Gender			Total
Male	30 (22.10)	53 (38.90)	83 (61)
Female	24 (17.63)	29 (21.37)	53 (39)
Total	54 (39.73)	82 (60.27)	136 (100)
	Mean (SD)	Mean (SD)	*P*-value
Age (month)	30.31 (14.64)	32.32 (19.70)	0.524
WBC (/mm3)	9.54 (2.08)	10.17 (3.15)	0.196
N/L	0.89 (0.54)	0.82 (0.63)	0.539
Hemoglobin (gr/dl)	11.87 (1.06)	11.84 (1.44)	0.900
Hct %	36.12 (2.82)	35.98 (3.8)	0.816
MCV (fL)	74.47 (5.72)	74.43 (6.71)	0.973
MPV (fL)	6.52 (0.77)	7.52 (1.52)	<0.001*
Platelet (103/µL)	312.5 (93.27)	364.56 (134.55)	0.013*
Lymphocytes	4.64 (1.45)	5.28 (2.33)	0.073
Neutrophil	3.62 (1.54)	3.68 (1.98)	0.876

* Mann-Whitney U test, WBC: White Blood Cell, Hct: Hematocrit, MCV: Mean Corpuscular Volume, MPV: Mean Platelet Volume

Table 2: Comparison of other laboratory parameters in study group and control group

	Study group Mean (SD)	Control group Mean (SD)	*P*-value
Iron (mg/dl)	39 (51)	54 (35)	0.380
Iron binding capacity (ug/dL)	261 (117)	328 (100)	0.100
Ferritin (ml/ng)	22 (18)	17 (12)	0.214
Folate (ng/ml)	12 (8)	10 (9)	0.365
PTH (pg/mL)	26 (18)	15 (10)	0.641
Calcium (mg/dL)	9.57 (0.55)	10 (0.45)	0.660
25 OH D3 (ng/mL)	22 (12)	31 (17)	0.017
Vitamin B12 (pg/ml)	316 (205)	419 (208)	0.039
Phosphorus (mg/dL)	4.86 (0.51)	5.60 (0.83)	0.020

PTH: Parathormone

Discussion

Febrile convulsion is defined as that which occurs during a febrile disease in patients without a history of central nervous system infection, metabolic disorder, or afebrile seizure. The age range varies between 6-60 months and peaks at 18 months [2]. FCs are classified into two groups as simple and complex. Seizures that are generalized from the onset, last for less than 15 minutes and do not recur within 24 hours are defined as simple FC while convulsions with at least one focus at the

onset, last longer than 15 minutes and recur within 24 hours are defined as complex FC [3].

The pathogenesis of FC is not fully known. In the studies conducted, increased levels of interferon-α and neuron-specific enolase, decreased thyroid-stimulating hormone values, prolactin, growth hormone and cortisol, central thermoregulation disorders, delayed maturation of CNS, increased excitatory amino acids, and iron deficiency anemia were detected in children with FC. However, their role in the pathogenesis of FC remains controversial [4]. In the literature, low serum iron levels in iron deficiency have been shown to lower the seizure threshold and lead to febrile convulsions [5]. Sadeghzadeh et al. [6] have shown that anemia is not common in patients diagnosed with FC; however, iron deficiency was observed more frequently in these patients. Contrarily, some studies have reported that iron deficiency is less common in patients diagnosed with FC and that iron deficiency has a protective effect against seizures [7,8]. In the literature, a systemic review and meta-analysis conducted on 2416 FC patients and 2387 healthy individuals in 2017 showed that iron deficiency increases the risk of FD [9]. In their study evaluating 323 patients, Waheed et al. [10] stated that iron deficiency anemia was not common in patients diagnosed with FC and had no role in its pathogenesis. In our study, no statistically significant difference was detected among the study and control groups in term of hemoglobin, serum iron, iron binding capacity and ferritin levels.

Mean platelet volume (MPV) is a laboratory finding that is routinely measured on whole blood count and reflects the average volume of circulating platelets. Inflammatory, infectious and allergic conditions stimulate the bone marrow, leading to increased platelet production and the introduction of larger platelets into the bloodstream. In this case, increase in platelet count and MPV were observed. The increase in MPV occurs before the increase in platelet count [11]. In recent years, the importance of MPV has been investigated in many studies and it has been shown that it reflects platelet functions much better than platelet count [12-14]. MPV is directly associated with platelet function and activation. Increased MPV is an indication that platelets are activated. In the literature, it was shown that MPV was significantly higher among healthy individuals when compared with the FC group [15]. In our study, platelet count and MPV values were also significantly higher in the control group, in line with the literature.

The neutrophil/lymphocyte ratio (N/L) is calculated by neutrophil and lymphocyte counts in whole blood count and considered an indicator of subclinical inflammation. It is the subject of many studies today [16, 17]. Liu et al. [18] reported that N/L ratio was significantly higher in patients with FC compared with the control group. In our study, N/L ratios of the study and control groups were similar. The most common causes of febrile convulsions are viral infections; N/L was thought to be low due to increased lymphocyte ratio in viral infections.

Vitamin B12 is an important vitamin in humans, especially for the central nervous system. In children, vitamin B12 deficiency can develop due to decreased intake, abnormal absorption, dysfunctional transport of vitamin B12 and congenital defects in the metabolism. Low vitamin B12 level plays a role in the occurrence and recurrence of convulsions [19]. Osifo et al. [20] found that serum vitamin B12 levels were lower in patients with FC compared to healthy group and febrile group without seizures. Vitamin B12 levels were significantly lower in our study group compared to the control group, which suggests that low vitamin B12 levels may act a part in the etiopathogenesis of FC.

Vitamin D deficiency is an important public health problem in children [21, 22]. It is thought to be associated with diabetes and oncologic, cardiovascular, autoimmune, and central nervous system diseases [23]. Vitamin D deficiency is common in patients with epilepsy and febrile convulsion [24, 25]. In a case report, a child with recurrent febrile convulsion had rickets due to vitamin D deficiency and another study reported that there were cases of hypocalcemic seizures due to vitamin D deficiency [26, 27]. In our study, vitamin D and phosphorus levels were significantly lower in study group, while PTH and calcium levels were similar. Even though there was a statistically significant difference in phosphorus levels among the groups, the mean phosphorus level of the study group was within normal laboratory range.

Osifo et al. [20] investigated the relationship among serum folic acid values and seizure formation in thirty-two febrile children aged 8 months to 5 years. The authors reported that serum folic acid values in children with FC were significantly higher than those in seizure-free children. Folic acid plays a significant role in cerebral mitochondrial function and nucleic acid synthesis [28]. In addition, a decrease in the oxidative enzyme activity in the brain, seen in folic acid deficiency, has been reported to cause seizure activity [29]. Contrary to the literature data, no statistically significant difference was found among the groups in terms of mean folic acid level. We think that further studies evaluating the relationship between FC and folic acid level are needed.

Limitation

The retrospective design and the inclusion of small number of patients with febrile convulsions constitute the limitations of this study.

Conclusion

MPV, platelet count, 25 OH D3, vitamin B12 lower levels may be a risk factor for the development of febrile convulsion. It is shown that studies related to the etiopathogenesis of febrile convulsion are necessary to enlighten the subject and laboratory results will be the guide in this sense.

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