



# Febrile children with and without seizure: A comparison between CBC, ESR and CRP

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### ABSTRACT

**Introduction:** The aim of this study is the evaluation and comparison of the white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) in febrile children with and without convulsion.

**Methods:** We studied 368 febrile children aged 6 to 60 months with and without convulsion. Demographic data, WBC, ESR, and CRP were compared and analyzed.

**Results:** In this study, 368 children, 184 patients with febrile convulsion as the case group and 184 febrile patients without convulsion as the control group, were enrolled with an average age of  $26.6 \pm 14.4$  months and  $17.71 \pm 15.4$  months respectively ( $P = 0.001$ ). In the case group, 59.78%, and in the control group, 43.48% were male ( $P = 0.002$ ). There was no statistically significant difference between the groups regarding the WBC, ESR, and CRP. There was however a significant relationship between the leukocytosis and convulsion in patients with longer than 15 minutes convulsion ( $P = 0.03$ ). There was no significant difference between different febrile convulsion subgroups in ESR and CRP levels, according to the type, duration, and frequency of convulsion.

**Conclusion:** Leukocytosis and elevated ESR and CRP levels in patients with febrile convulsion may represent the underlying etiology of the fever, and they may not be due to convulsion itself. But longer than 15 minutes convulsions may lead to leukocytosis.

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### Introduction

Febrile convulsion (FC) is one of the common disorders in children (1). The prevalence of FC has been estimated to be 2-5% (2-4). FC is classified into simple and complex types (5). In children with complicated convulsion, white blood cells (WBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are evaluated. Because of some conditions such as fever, trauma, vomiting, dehydration, bleeding, and metabolic disorders which affect the WBC, ESR, and CRP levels, the American Academy of Pediatrics suggests blood test as the

method of identifying the infectious source of fever (6, 7). Therefore, the blood test results should carefully be interpreted by the clinicians.

There are not many articles that evaluated the WBC count, ESR, and CRP in children with febrile convulsion (8, 9), as well, there is no unique interpretation of the values. Since WBC and ESR are commonly measured in children with FC, the present study was carried out to compare the WBC count, ESR, and CRP in febrile children aged 6 to 60 months with and without convulsion to

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determine whether leukocytosis and elevated ESR and CRP levels are due to the underlying disease or the convulsion itself.

### Patients and methods

This descriptive-analytical study was performed retrospectively from 2012 to 2014 in the Ghaem Hospital, affiliated to the Mashhad University of Medical Sciences (Mashhad, Iran). We studied 368 febrile children, aged 6-60 months, admitted to the emergency room. They included 184 cases with febrile convulsion (case group) and 184 febrile patients without convulsion (control group). All patients in the FC group presented with the classic criteria of FC. Patients in the control group were febrile but without convulsion. The auxiliary body temperature was measured according to the standard protocol, and a temperature of 38 °C or greater was considered as fever. The diagnosis of FC was confirmed by a pediatrician based on the clinical symptoms. Patients with meningitis, encephalitis, brain hemorrhage, a history of trauma, or a history of antibiotic use within the 48 hours before admission were excluded. The WBC, ESR, CRP, hemoglobin, and platelet levels were measured and compared between the groups.

### Analysis

Statistical analysis was conducted using SPSS software version 16.0. Normality was checked via the Kolmogorov-Smirnov test. All experimental values are presented as mean  $\pm$  standard deviation (SD) for quantitative variables and frequency percent for categorical ones. The Chi-square test was used to screen the association of symptoms. An independent t-test or an equivalent nonparametric was used for comparison between groups. A P-value of less than 0.05 was considered statistically significant.

## Results

### Baseline characteristics

Out of 368 children with an average age of  $22.20 \pm 1.56$  months, 184 patients were in each group. In the case group, 40.22% (n = 74) were female and 59.78% (n = 110) were male, while in the control group, 56.52% (n = 104) were female and 43.48% (n = 80) were male. The sex distribution difference between the groups was significant (P = 0.002). The average age of patients in the case and control groups was respectively  $26.6 \pm 14.4$  and  $17.71 \pm 15.4$  months, and the difference was significant too (P = 0.001). Upper respiratory tract infection (URTI) in the FC group and gastroenteritis (GE) in the non-FC (control) group were the most common cause of fever (54.3% and

35.9% respectively). Other results are presented in Table 1.

**Table 1.** Underlying disease in febrile children with and without convulsion.

| Underlying disease | FC group (n=184) | Non FC group (n=184) |
|--------------------|------------------|----------------------|
| URTI               | 100 (54.35)      | (%16.3) 30           |
| Pneumonia          | 6 (3.3%)         | 50 (27.2%)           |
| Gastroenteritis    | 56 (30.4%)       | (35.9%) 66           |
| UTI                | %2.2) 4)         | 10 (5.4%)            |
| Otitis media       | 2 (1.1%)         | 0                    |
| Hidden bacteremia  | 6 (3.3%)         | 16 (8.7%)            |
| Others             | 10 (5.4%)        | 12 (6.5%)            |
| Total              | 184 (100%)       | 184 (100%)           |

FC: febrile convulsion, URTI: upper respiratory tract infection, UTI: urinary tract infection

### Blood test results

#### WBC count

Severe bacterial infections cause leukocytosis with a leukocyte count of more than 15000/mm<sup>3</sup>. In the FC group, 24% (n = 44) of patients and in the non-FC group, 18.5% of patients (n = 34) had a WBC count more than 15000/mm<sup>3</sup>. The difference between the two groups was not significant (P > 0.05).

#### Platelets

The mean platelet count was  $266.61 \pm 92.13$  and  $322.41 \pm 99.94$  cells/mm<sup>3</sup> in the case and control groups respectively, and the difference was significant (P = 0.001).

#### Hemoglobin

Anemia is defined when the hemoglobin level is below 10.5 gr/dl. The hemoglobin level was less than 10.5 gr/dl in 38% of patients (n = 70) and 52% (n = 96) in the FC and non-FC groups respectively. The difference between the groups was significant (P=0.006).

#### ESR level

The mean ESR level in the FC group was  $28.80 \pm 16.34$  mm/hour, and in the non-FC group was  $26.56 \pm 30.19$  mm/hour. The difference was not significant.

#### CRP level

In the FC group, 64.14% (n = 118) of patients had a positive CRP test, while in the non-FC group, 52.17% (n = 96) had a positive CRP assessment. The difference between the groups was not significant (P > 0.05).

The comparison of complete blood count (CBC), ESR, and CRP results between the groups is

presented in Table 2.

**Table 2.** Comparison of CBC, ESR and CRP in febrile children with and without convulsion

| Variables                   | FC group (n=184) | Non FC group (n=184) | P value |
|-----------------------------|------------------|----------------------|---------|
| WBC (cell/mm <sup>3</sup> ) |                  |                      |         |
| >15000                      | 44 (24%)         | 34 (18.5%)           | 0.403*  |
| 10000-15000                 | 52 (28.2%)       | (28.2%) 52           |         |
| <10000                      | %47.8) 88)       | 98 (53.3%)           |         |
| Hemoglobin (gram/Liter)     |                  |                      |         |
| <10.5                       | 70 (38%)         | 96 (52%)             | *0.006  |
| >=10.5                      | 114 (62%)        | 88 (48%)             |         |
| Platelet (cell/ml)          | 266.61±92.13     | 322.41±99.94         | 0.001#  |
| ESR (mm/hour)               | 28.80±16.34      | 26.56±30.19          | 0.091#  |
| CRP                         |                  |                      |         |
| -                           | 66 (35.86%)      | 88 (47.83%)          | 0.403*  |
| +                           | 52 (28.27%)      | 52 (28.27%)          |         |
| ++                          | 42 (22.83%)      | 14 (7.6%)            |         |
| +++                         | 24 (13.04%)      | 30 (16.3%)           |         |

**FC:** febrile convulsion, **CBC:** complete blood count, **WBC:** white blood cell, **ESR:** erythrocyte sedimentation rate, **CRP:** C reactive protein, \* chi square test, # independent t test.

### **Clinical and laboratory data in the simple and complex FC subgroups**

In the FC group, 124 patients (67.4%) had simple convulsion and 60 patients (32.6%) had complex convulsion. In the simple FC subgroup, 30 patients (24.2%) had a WBC count of more than 15000/mm<sup>3</sup>. In the complex FC subgroup, 14 patients (23.33%) had this condition, and the difference between the two subgroups was not significant. Moreover, 42 patients (33.87%) in the simple FC subgroup and 28 patients (46.67%) in the complex FC subgroup had a hemoglobin level below 10.5 gr/Ldl. The difference was not significant either ( $P = 0.09$ ). The mean platelet count in the simple and complex FC subgroups was  $265.18 \pm 101.08$  and  $269.57 \pm 95.74$  cell/mL mm<sup>3</sup> respectively, and the difference was not statistically significant either ( $P = 0.77$ ).

### **Clinical and laboratory data in the FC group according to the duration of convulsion**

In the FC group, the duration of convulsion was shorter than 15 minutes in 178 patients (96.7%) and longer than 15 minutes in 6 patients (3.3%). Among these 6 patients, 4 cases had a WBC count of more than 15000/mm<sup>3</sup>. In the subgroup with shorter than 15 minutes convulsions, 40 patients out of 178 (22.27%) had this condition. The difference between the subgroups was significant ( $P = 0.03$ ).

### **Clinical and laboratory data in the FC group according to the frequency of convulsion**

In the FC group, 148 patients (80.4%) had one convulsion and 36 patients (19.6%) had more than one convulsion. Among the patients with one convulsion, 38 cases (25.68%) had a WBC count of more than 15000/mm<sup>3</sup>. In 36 patients with more than one convulsion, 6 patients (16.67%) had this WBC condition. The difference between the two subgroups was not significant ( $P = 0.2$ ).

## **Discussion**

We studied 368 febrile children with and without convulsion comparing the WBC, hemoglobin, ESR, CRP, and platelets level. There was a statistically significant difference between the FC and non-FC groups regarding the hemoglobin and platelet levels, but not in the WBC, ESR, and CRP. Further, there was a significant difference between the FC patients with shorter than 15 minutes convulsion and patients with longer than 15 minutes convulsion in the WBC count ( $P = 0.03$ ), but not in the ESR, hemoglobin, and CRP levels.

According to our findings, there was no significant difference between the FC and non-FC groups in WBC count. The WBC count thus represents the underlying etiology of the fever and may not be due to the convulsion itself. There are inconsistent reports about the WBC count, CRP, and ESR in FC patients (8, 9). In some studies, convulsion has been considered the cause of leukocytosis (10, 11), while in other studies, fever was recognized as the responsible factor (8, 12). It has been reported that convulsion can cause a transient leukocytosis that takes up to 24 hours after the attack(s); afterward, it will return to normal.

Leukocytosis can occur as an acute phase reactant (APR) due to infection, so it is persistent until the infection clears up. So in the case of febrile convulsion, the leukocytosis may be due to an infection. However, according to our results in cases with a long duration of convulsion (more than 15 minutes), leukocytosis can be due to the convulsion attack itself.

In a study on 214 febrile children aged 6-60 months with and without convulsion, it has been reported that the WBC count increased significantly in the FC patients, but there was no significant difference in the CRP and hemoglobin levels between the FC and non-FC patients (9). In another study on 410 children (160 patients with FC) aged 6-60 months, it was similarly reported that the WBC count was higher in children with FC, but ESR and hemoglobin did not differ (8).

In other studies, it has been suggested that the increased WBC count in patients with FC is not a

result of convulsion itself, and it may be because of an underlying infection. In spite of no difference between our studied groups regarding the WBC count, according to a systematic review by Warden et al., a WBC assessment for FC patients is suggested (13). But, the American Academy of Pediatrics does not recommend the routine tests of blood cell count in FC patients (7). In the present study, no significant association between the hemoglobin, ESR, and CRP level and the convulsion characteristics including type, duration, and frequency was observed. However, there was a significant relationship between the occurrence of leukocytosis and the duration of convulsion. Nonetheless, in another study on 203 children with FC, they reported that there was no significant association between the duration of convulsion and leukocytosis (12).

Heydarian et al., in a study on 240 febrile children with and without convulsion, reported that 37.5% in the FC group and 36.7% in the non-FC group suffered from anemia with no significant difference (14). However, in our results, the hemoglobin level was significantly different between the FC and non-FC patients.

In our patients, the type of convulsion was simple in 67.4% of patients. Some other studies confirmed similarly that simple FC is more prevalent (15).

## Conclusion

Leukocytosis and an elevated ESR and CRP level in patients with febrile convulsion can represent the underlying etiology of the fever, and they may not be due to the convulsion itself. But longer than 15 minutes convulsions may lead to leukocytosis.

## Limitations

Multicenter prospective studies with more samples are suggested.

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## Conflict of Interest

The authors declare no conflict of interest.

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