

Leukocyte count and C reactive protein as diagnostic factors in febrile convulsion



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ABSTRACT

Background: Febrile convulsion (FC) is the most common seizure disorder in childhood. White blood cell (WBC) and C reactive protein (CRP) are commonly measured in FC. **Aims and Objectives:** To compare WBC and CRP in febrile children, aged 6 months to five years, with and without FC, in order to determine whether leukocytosis and elevated CRP can be used as diagnostic tool for febrile seizure. **Materials and Methods:** In this cross sectional study 214 children (112 with FC), aged 6 months to 5 years, admitted to in the first 48 hours of their febrile disease, either with or without seizure, were evaluated over a 12 months period. Age, sex, temperature; WBC, CRP and hemoglobin were recorded in all children. There was a significant increase of WBC ($P < 0.001$) in children with FC so we can deduct that leukocytosis encountered in children with FC can be due to convulsion in itself. **Results:** When comparing FC and non-FC children, we encountered a significant increase of WBC ($P = 0.0005$) in children with FC, measured at the time of admission to pediatric medicine ward. There was no significant difference regarding CRP between the two groups. In fact, elevated CRP is a result of underlying pathology. **Conclusion:** In stable patients, if there's no reason to suspect a bacterial infection or who don't have any indication of lumbar puncture, there's no need to assess WBC as an indicator of underlying infection. Any child with febrile seizure with a high CRP value should be evaluated for infection

Key words: Seizures, Febrile, C reactive protein, Leukocytosis

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INTRODUCTION

Febrile convulsion (FC) is the most common seizure disorder occurring in childhood, especially in those aged 6-24 months.¹ In large population-based studies, the prevalence of FC has been estimated to be 2-5%.^{2,3} Simple febrile convulsion is a primary generalized, usually tonic-clonic seizure, usually lasting less than 15 minutes, which occurs only once during 24 hour period. It is not associated with infection of central nervous system (CNS) or a metabolic disorder. The great majority of FCs are medically benign. When FC attack proceeds for more than 15 minutes, recur within 24 hours or show focal signs, a more serious condition might be present which is called complex FC.^{3,4}

A febrile convulsion could be a response to invasion of the blood stream or central nervous system by a micro-

organism which is usually a virus. Invasion may be of such brief duration that successful isolation of the virus from the blood, CSF, or urine is not commonly achieved.⁵ Viral infections play a role in the etiology of FC by more than one possible mechanism: Fever per se; a degree of fever that exceeds the individual threshold convulsive temperature and an elevated level of cytokines.⁶ Human Herpes Virus 6, Herpes Simplex Virus and Influenza Virus A, B are mentioned by many text books as being the leading cause of FC. Bacterial infections are much less indicated as the underlying etiology of FC.^{2,7}

In most cases, the source of infection is easily found by a meticulous history taking and physical examination. American Academy of Pediatrics considers blood test as a way of finding the infectious source of fever, not a routine procedure for evaluating FC.^{8,9} Several diagnostic

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guidelines have been designated to approach FC in children. The main issue in all of them is to find the possible source of infection and to rule out metabolic or CNS disorders.

White blood cell (WBC) and C reactive protein (CRP) are measured in all complicated febrile children. Situations such as fever, trauma, vomiting, dehydration, bleeding and metabolic disorders can lead to changes in leukocyte count. The two indices are elevated as a result of epinephrine release and demargination of neutrophils; so, the above blood tests must carefully be interpreted by the clinician.

As these two tests are done routinely for all cases of FC in our Hospital, this cross sectional study aims to compare WBC and CRP in febrile children, aged 6 months to five years, with and without FC, in order to determine whether leukocytosis and elevated CRP can be used as diagnostic tests in children with FC.

MATERIALS AND METHODS

This is a cross sectional study of children admitted to Pediatric Medicine Departments of Institute of Child Health, Kolkata and ICARE Institute of Medical Sciences, Haldia, Purba Medinipur, because of their febrile disease, either with or without seizure, over a 12 months period from September 2015 to September 2016. Institutional Ethics Committees permission were taken. All children included in the study were 6 months to 5 years old. They all attended emergency ward in the first 48 hours of their febrile disease. None of them had taken antibiotics before admission. Fever was defined as having an axillary temperature more than 37.3°C at the time of admission.

On arrival, temperature was measured. A detailed history was obtained from the parents including description of the seizure, symptoms pertaining all the systems, presence or absence of focal features, duration of the febrile seizure and whether repeated episodes within the same febrile illness occurred and the duration of fever prior to the seizure. Total leukocyte count, differential count, haemoglobin and CRP were done in each child. Other investigations were done when necessary as decided by the treating physician like chest X-ray, blood culture, urine analysis and culture, stool exam and culture and lumbar puncture. Total count >11000 per cu mm was regarded as leukocytosis and CRP > 5mg/dl was considered abnormal. Those diagnosed as having a FC attack, fulfilled the criteria for either simple or complex FC.

The patients who were not in the age group mentioned above, those who were febrile for more than 48 hours, who had taken antibiotics during or before admission to hospital, who had any abnormality in their urine, stool, cerebrospinal fluid and blood culture and had any clinical

suspicion of bacterial infection were excluded from the study. Those with an attack of seizure who had any finding indicating CNS infection were also excluded from the study. To analyze the data, we used t-test for comparing quantitative data and chi square test for qualitative data.

RESULTS

A total of 214 children (86 girls and 128 boys), aged 6 months to 5 years (mean age 22.5 months) were included in the study; 112 of which were diagnosed as having an attack of FC. The youngest study participant was 6 months and the eldest was 58 months old. None of the children had a history of trauma or bleeding. The mean temperature was 38.3°C, the lowest degree of fever was 37.5 and the highest 40°C. The different clinical as well as hematological findings are summarized in Table 1. Out of 112 cases of FC, Boys were 68 (60.7%), girls 44 (39.35); 72 cases (64.3%) were simple FC and 40 cases (35.7%) were complex FC. Mean, median, and range of WBC count (per cu mm) were 13400, 14,800, 4,500-22,500 respectively and mean, median, and range of CRP (mg/dl) were 11.67, 9.1, 0.7-56; those of Hb (gm/dl) were 10.67, 10.3, 4.4-12.9 respectively (Table 2). When comparing FC and non-FC children, we encountered a significant increase of WBC ($P=0.0005$) in children with FC, measured at the time of admission to pediatric medicine ward.

There was no significant difference regarding CRP ($P=0.66$) and hemoglobin ($P=0.345$) between the two groups. None of the children, either with or without FC, had a history of trauma or bleeding. On the other hand, the majority of non-FC patients had a history of vomiting. This led to a

Table 1: Characteristics of febrile children

	With FC (112)	Without FC (102)
Boys	68 (60.7%)	60 (58.8%)
Girls	44 (39.3%)	42 (41.2%)
Mean age (months)	21.1	24.7
Positive history of vomiting	64 (57.1%)	82 (80.4%)
Positive history of bleeding	-	-
Positive history of trauma	-	-
WBC (per cu mm) (Mean)	13400	10243
CRP (mg/dl) (Mean)	11.67	13.89
Hb (mg/dl) (Mean)	10.67	11.43

Table 2: Levels of WBC, CRP and Hb in children with FC

Total cases- 112			
	Boys	Girls	
Simple FC	68 (60.7%)	44 (39.3%)	
Complex FC	72 (64.3%)	40 (35.7%)	
	Mean	Median	Range
WBC (per cu mm)	13400	14,800	4,500-22,500
CRP (mg/dl)	11.67	9.1	0.7-56
Hb (mg/dl)	10.67	10.3	4.4-12.9

statistically significant difference between the two groups regarding history of vomiting ($\chi^2=13.310$, $P=0.0003$).

DISCUSSION

In this cross sectional study, we compared leukocyte count and CRP level in febrile children with and without FC attending emergency department of Institute of Child Health, Kolkata and ICARE Institute of Medical Sciences, Haldia, Purba Medinipur during 12 months period. No significant difference was observed among the two groups regarding CRP level but a statistically significant difference was observed in leukocyte count.

In two observational studies performed in Iran¹⁰ and the Netherlands,¹¹ the researchers agreed that elevated WBC in FC cases is due to the underlying infection, not a result of convulsion as a stressor. Warden et al have recommended routine WBC assessment for children with FC in their systematic review about febrile seizure.¹² On the other hand, Effects of electrically induced convulsion (EIC) in rabbits on peripheral leukocyte-count levels were studied in Japan. Leukocyte-counts increased immediately after the EIC (phase-1) and 4 hours later (phase-2).¹³ American Academy of Pediatrics does not recommend the routine tests of complete blood count, serum electrolytes and plasma glucose for children with FC.⁹

In our cross sectional study, the FC patients were encountered with an additional stressor: Seizure. Since WBC level was significantly higher in children with FC, we can deduct that leukocytosis can be due to the stress of convulsion, not just an indicator of underlying infection. Several factors such as trauma, bleeding, vomiting and dehydration can confound our results. Some of these factors are taken into account: None of the children had a previous history of trauma and bleeding. Vomiting was more encountered in non-FC patients whose leukocyte count was significantly lower than the FC group. However we didn't directly assess dehydration and metabolic disorders as the possible causes of leukocytosis. Authors suggest that these two and other possible confounding factors be compared in FC and non-FC children in future studies. There was no significant difference in CRP level among the two groups ($P>0.05$). In fact, elevated CRP is a result of underlying infection. According to McCarthy, the evaluation of an ambulatory, febrile child with acute-phase reactants should include at least determination of CRP since high CRP demonstrated the best balance of specificity and sensitivity for bacteremia.¹⁴

CONCLUSION

Most of FC cases are of simple FC type and viral infections are the leading underlying cause. Authors recommend for stable children with febrile seizure who are not suspected as the case of bacterial infection or don't have any indication of lumbar puncture, there's no need to assess WBC as an indicator of underlying infection. Any child with febrile seizure with a high CRP value should be evaluated for infection and it is an initial good tool in evaluating the cause of fever in all these children.

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GB, SKR, MM, KS - Concept, design, manuscript preparation, editing and review; GB and SKR - Data analysis; KC, SS, PKM - Manuscript preparation, editing and review.

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