

Original Research Article

The usefulness of neutrophil to lymphocyte ratio in febrile seizure

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ABSTRACT

Background: Febrile seizure is an event in infancy or childhood, usually occurring between 3 months and 5 years of age associated with fever but without evidence of intracranial infection. The aim of the study was to estimate the usefulness of neutrophil-to-lymphocyte ratio (NLR) in patients with simple and complex febrile seizures.

Methods: Retrospective case control study was done in a paediatric in patients admitted to tertiary care hospital. Study period was from January 2017 to December 2019. 200 children were analysed in the study. 100 out of 200 were under control group (febrile children without seizure). Remaining 100 were under case group (children with febrile seizure), 54 out of 100 children had complex febrile seizure, 46 out of 100 had simple febrile seizure. NLR ratio was done in all children.

Results: Total 200 children were analysed in this study. High NLR ratio was noted among the cases (87 out of 100) compared to control (30 out of 100) p value = <0.001. Among the cases CFS had high NLR ratio compared to SFS, however p value was not significant (0.072).

Conclusions: Children with febrile seizure had high NLR ratio compared to those without seizures. However no significant difference was noted between those with simple febrile seizure and complex febrile seizure. However, larger trials are required to assess whether higher NLR can be taken as an independent risk factor for febrile seizure.

Keywords: Complex Febrile Seizures, Intracranial infection, Neutrophil-to-Lymphocyte Ratio, Simple Febrile Seizures, Tertiary care hospital

INTRODUCTION

A febrile seizure is an event in infancy or childhood, usually occurring between 3 months and 5 years of age associated with fever but without evidence of intracranial infection or defined cause. American Academy of Paediatrics (AAP) published a clinical practice guideline defining a febrile seizure as “a seizure accompanied by fever (temperature $\geq 100.4^{\circ}\text{F}$ or 38°C by any method), without central nervous system infection, that occurs in infants and children 6 to 60 months of age.¹ International league against epilepsy (ILAE) defines febrile seizure as “a seizure occurring in childhood after one month of age associated with a febrile illness not caused by an infection of the central nervous system, without previous

neonatal seizures or a previous unprovoked seizure, and not meeting the criteria for other acute symptomatic seizures.² Most of the febrile seizures are generalized seizures of a single episode that last for a duration of less than 15 minutes, but in approximately 10 to 30 percent of these type of seizures are complicated.³

Febrile seizures are typically divided into two types simple febrile seizures (SFS) and complex febrile seizures (CFS). Studies have suggested that inflammation, which is intrinsic to the fever response, is involved in the generation of febrile seizure.⁴ These studies suggested that inflammatory cytokines, especially IL-1 β , IL-6 and TNF- α can play important role in the generation of FS. Although inflammatory cytokines are

useful biomarkers, their increased cost and limited availability are its major drawbacks.

Peripheral blood neutrophil-to-lymphocyte ratio (NLR), is a novel indicator of inflammation. NLR is a measure of the proportion of systemic neutrophils and lymphocytes, and may serve as an emerging parameter that reflects systemic inflammation of various diseases. In recent years, NLR has been suggested as one of practical predictor for differentiating FS types. Children with FS had statistically significant higher neutrophils level compared to those with fever without seizures and the number of lymphocytes was lower in children with FS than in children with fever without seizures.⁵

Neutrophils are the first cells to migrate into the area of injury as part of the host defense system, and can induce the secretion of several inflammatory cytokines associated with the risk of FS, especially IL-1 β and TNF- α play an important role in the pathogenesis of FS.⁶ Neutrophil-to-lymphocyte ratio are increased in various inflammation-related diseases. NLR which is calculated as the absolute count of neutrophils divided by the absolute count of lymphocytes, is an inflammation index that can be easily detected from a complete blood count.

Hence our study aimed at to know whether NLR ratio can be an easy, cost-effective, tool in predicting CFS and SFS. Aim of the study was to estimate the usefulness of neutrophil-to-lymphocyte ratio (NLR) in patients with simple and complex febrile seizures.

METHODS

Retrospective case control study was done in a paediatric in patients admitted to tertiary care hospital. Study period was from January 2017 to December 2019. Total number of patients included in this study was 200, 100 out of 200 were under control group which included febrile children without seizure. Remaining 100 were under case group which included children with febrile seizure. Among those with febrile seizure 54 out of 100 children had complex febrile seizure, 46 out of 100 had simple febrile seizure. Blood routine investigations were done in all cases and controls. Peripheral venous blood samples were collected in EDTA tubes during admission. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count and analysed. Neutrophil-to-lymphocyte ratio (NLR) above 1.13 is considered as high NLR ratio 7.

Inclusion criteria

All children in the age group from 6 month to 5 years who presented with febrile seizure were included in this study. Febrile children of the same age group without seizure were taken as control.

Exclusion criteria

- Family history of genetic and neurological diseases
- Subsequent epilepsy after FS
- CNS infection
- CNS malformation, hydrocephalus, Mental retardation.
- Children with chronic systemic diseases

Haematological parameter were taken and compared. Data was entered into excel sheet and cases and control were compared statistically using IBM SPSS version 25. The p value less than 0.05 was considered statistically significant.

RESULTS

Retrospective analysis was done in the study and control group. Demographic characteristic are shown in table 1.

Table 1: Frequency of age and gender distribution in the study.

	Control	SFS	CFS
Male	52	27	30
Female	48	19	24
Age (in months)	28 \pm 6	32 \pm 8	36 \pm 4
Mean \pm SD	months	months	months

In table 2 - NLR analysed in the 3 groups revealed that high NLR ratio was noted among the cases (87 out of 100) compared to control (30 out of 100) p value = <0.001 very highly significant. Among the cases higher number in CFS had high NLR ratio compared to SFS, however p value was not significant (0.072).

Table 2: Frequency distribution of NLR among the study group.

Frequency distribution of NLR	High NLR	Normal NLR	Total
Control	30 30%	70 70 %	100
SFS	37 80.4%	9 19.6 %	46
CFS	50 92.6 %	4 7.4 %	54

Table 3: Correlation of NLR ratio between study group.

Study group	Mean	SD	P value
Complex febrile seizure (CFS) (n = 54)	5.5	8.5	>0.05
Simple febrile seizure (SFS) (n= 46)	3.3	4.0	>0.05
Total (n= 100)	4.5	6.9	<0.05
Control group (n = 100)	1.2	1.8	<0.05

In table 3 -Mean NLR values was higher in CFS group compared to SFS group, however this difference was not statistically significant. However mean level of NLR was significantly higher in cases compared to control group).

DISCUSSION

In this study NLR ratio is significantly higher in those with febrile seizure compared to febrile children without seizure, which may be due to increased neutrophil dependent inflammation and reduced lymphocyte mediated anti-inflammatory response seen in febrile seizure. Neutrophils are specialised cells of the innate immune system that play a role in host defense through phagocytosis and generation of reactive oxygen species. Neutrophil are the first cells to migrate into the area of injury as part of the host defense system, and can induce several inflammatory cytokines. The number of neutrophils can rapidly increase during intense skeletal muscle activity like seizure which explains high NLR ratio in febrile seizure. Inflammatory cytokines also have role in development of febrile seizure.⁸

In our study significantly higher number of the patients in febrile seizure group had high NLR ratio compared to control group. This is similar to study done by Romanowska et al in 306 children who were grouped into febrile seizure and febrile children without seizure and statistically significant difference existed between the number of lymphocyte and neutrophil ($p = <0.001$) among the 2 groups. Another study conducted by Liu Z et al included 250 children who were divided into case and control group in which 83.9% of febrile seizure group had high NLR when compared to 36.5% of control group (febrile children).

Mean NLR ratio was higher in febrile seizure group. This is similar to study done by Romanowska et al on 306 children who were divided into case and control group and mean NLR ratio in case group was 3 and that of control was 1.3 which was statistically significant. Liu Z et al in his study included 250 children as case and 250 as control in which NLR ratio in case group was 3.2 and that of control 1.6.

In this study though NLR ratio was high in CFS when compared to SFS the difference was not statistically significant. Study conducted by Liu Z et al noticed high NLR ratio exist between SFS and CFS. However significant difference have been shown in previous study by Goksugar et al on 58 children with SFS and 38 with CFS showed significantly high NLR ratio in CFS.⁹ Similar results was noted in the study conducted by Yigit Y et al in which NLR ratio was high in CFS group. We have also noted higher values in CFS group though statistically not significant.¹⁰ However study on a larger group may yield a clearer picture.

CONCLUSION

Children with febrile seizure had high NLR ratio compared to those without seizures. However no significant difference was noted between those with simple febrile seizure and complex febrile seizure. However larger trials are required to assess whether higher NLR can be taken as an independent risk factor for febrile seizure.

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