



NEUTROPHIL LYMPHOCYTE RATIO AS A PREDICTOR IN FEBRILE SEIZURES, A DIAGNOSTIC COMPARATIVE STUDY

Paediatrics

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ABSTRACT

The prevalence of febrile seizures was reported to be 3.28–5.71/1000 in South India and 2.27 per 1000 people from Uttarakhand. Febrile seizure affects 2-14% of all children globally. Febrile seizure is defined as seizure that occurs in children aged six months to five years of age associated with fever (100.4°F or greater) without central nervous system infection. Neutrophil lymphocyte ratio has been proposed as a practical predictor of seizure among febrile children. A comparative cross-sectional study was conducted among children of age group 6 months to 5 years admitted in paediatric department, AVMC. After obtaining informed consent from parents/ guardians, 198 children fulfilling inclusion criteria were enrolled in this study. Among 198 children, 99 children belonged to case group (i.e) febrile seizure and 99 children belong to control group (i.e) fever without seizure. Venous blood sample was collected and sent for complete blood analysis. NLR was calculated by dividing absolute neutrophil count and absolute lymphocyte count and the value was recorded. NLR values in both groups was determined. All the analysis was done using Statistical Package for Social Sciences software (SPSS) version 28. The mean neutrophil lymphocyte ratio for children with febrile seizure was 3.39 ± 1.68 compared to 1.88 ± 1.67 for children with fever without seizure (P value <0.001). Mean NLR in simple febrile seizure is 3.21 ± 1.39 and complex febrile seizure is 3.77 ± 2.15 which is not statistically significant. ROC analysis for case group and control group showed that if the chosen cutoff value for NLR is 2.35, the sensitivity and specificity are 74.7% and 72.7%, respectively ($p = 0.001$, AUC 0.770, CI 0.702-0.838). ROC analysis for SFS and CFS showed that if the chosen cutoff value for NLR is 3.16, the sensitivity and specificity are 68.8% and 49.3%, respectively ($p = 0.17$, AUC 0.58, CI 0.455-0.713). This study shows the mean neutrophil lymphocyte ratio for children with febrile seizure was higher than the mean NLR for children with fever without seizure. The mean NLR in complex febrile seizure is higher than simple febrile seizure but not statistically significant. Hence NLR is proved to be a reliable indicator to predict the occurrence of seizure in febrile children.

KEYWORDS

Neutrophil Lymphocyte Ratio, Simple febrile seizure, Complex febrile seizure

INTRODUCTION

Febrile seizure is defined as seizure that occurs in children aged six months to five years of age associated with fever (100.4°F or greater) without central nervous system infection. Febrile seizure is classified as simple or complex⁽¹⁾. Simple febrile seizures (SFS) is characterized by generalized tonic/tonic-clonic convulsions, that lasts for less than 15 minutes, occurs once in 24 hours (non-recurrent). Seizure that lasts more than 15 minutes and associated with focal neurological findings or recurs within 24 hours of fever is termed as complex febrile seizure⁽⁴⁾. The prevalence of febrile seizures was reported to be 3.28–5.71/1000 in rural South India³, 2.27 per 1000 people from Uttarakhand⁴ and 2-14% of all children globally⁽⁵⁾. NLR has been proposed as a practical predictor of febrile seizure and its types in recent years⁽⁵⁾. The absolute neutrophil count and absolute lymphocyte count in children with febrile seizure was significantly higher than that of children with fever without seizure⁽⁶⁾. There is a 1.95 fold increase in the likelihood of having febrile seizure for every unit rise in NLR⁽⁷⁾. We conducted this study to predict the usefulness of NLR in febrile children who are at risk for developing seizures and the types of febrile seizures.

MATERIAL & METHOD :

A comparative cross-sectional study was conducted among children admitted in paediatric department, AVMC. All the febrile children of age group from 6 months to 5 years without seizures and with seizures of same age group were included in this study. All the children with Family history of genetic and neurological diseases, Subsequent epilepsy after FS, CNS infections, CNS malformation, hydrocephalus, mental retardation and those with chronic systemic diseases were excluded from study. After obtaining informed consent from parents/ guardians, 198 children aged 6 months – 5 years fulfilling inclusion criteria were enrolled in this study. Among 198 children, 99 children belonged to case group (i.e) febrile seizure and 99 children belong to control group (i.e) fever without seizure. Venous blood sample was collected and sent for complete blood analysis. NLR was calculated by dividing absolute neutrophil count and absolute lymphocyte count and the value was recorded. NLR values in both groups was determined. Collected data was analyzed, categorical variables were summarized

represented as frequency and percentages. Continuous variables were summarized as mean $\pm$ standard deviation. Chi-Square test was used to compare the categorical variables between groups. For comparison of continuous variables independent t test or Mann whitney U test was performed. ROC analysis was performed to find optimal cutoff, sensitivity, specificity of NLR. P value <0.05 was considered as statistically significant. All the analysis was done using Statistical Package for Social Sciences software (SPSS) version 28.

RESULT:

There were 198 children aged 6 months to 5 years admitted in paediatrics department, AVMC. Among 198 children, 99 children were taken as case group (children with febrile seizure) and 99 children were taken as control group (febrile children without seizure). NLR was calculated for both groups. Age distribution in case group was 51.5%, 40.4%, 8.1% belonged to age group <1 year, 1-3 years, 3-5 years respectively and in control group age distribution was 21.2%, 20.2%, 58.6% of children who belongs to age group <1 year, 1-3 years, 3-5 years respectively as shown in table 1.

The mean age difference in case group was 1.75 ± 1.04 whereas in control group was 3.48 ± 1.72 which is statistically significant with P value <0.001 as shown in the table 5. Among 198 children 52.5% were male, 47.5% were female in case group and 57.5% of male and 42.4% of female in control group as shown in table 2.

Among 99 children with febrile seizures, 67.7% were diagnosed to have simple febrile seizure and 32.3% children have complex febrile seizure. Among 67.7% of children with simple febrile seizure; 34.3%, 28.3% and 5.1% belongs to age group <1 year, 1-3 years, 3-5 years respectively. In 32.3% of children with complex febrile seizure 17.2%, 12.1% and 3% belongs to age group of <1 year, 1-3 years, 3-5 years respectively as shown in table 3.

The mean interval of fever and seizure was 9.97 ± 3.01 hours and the mean duration of seizures was 30.91 ± 9.15 seconds as shown in table 5. 56.57% had abnormal NLR value in case group whereas 20.20% had abnormal value in control group which was statistically significant

with P value <0.05 as shown in table 4. The mean neutrophil lymphocyte ratio for children with febrile seizure was 3.39 ± 1.68 whereas the mean NLR for children with fever without seizure was 1.88 ± 1.67 and it was statistically significant with P value <0.001 as shown in table 5. Mean NLR in Simple Febrile Seizure is 3.21 ± 1.39 and Complex Febrile Seizure is 3.77 ± 2.15 where there was no significant difference as shown in table 6.

ROC analysis of NLR between cases and control showed that if the chosen cutoff value for NLR is 2.35, the sensitivity and specificity are 74.7% and 72.7%, respectively and was statistically significant ($p = 0.001$, AUC 0.770, CI 0.702-0.838) as shown in figure 1. ROC analysis of NLR between SFS and CFS showed that if the chosen cutoff point for NLR is 3.16, the sensitivity and specificity are 68.8% and 49.3%, respectively and was statistically significant ($p = 0.17$, AUC 0.58, CI 0.455-0.713) as shown in figure 2.

Table 1 : Age Distribution

Age distribution	Study Groups			
	Case	%	Control	%
≤1 Year	51	51.5%	21	21.2%
1-3 Years	40	40.4%	20	20.2%
3-5 Years	8	8.1%	58	58.6%
Total	99	100%	99	100%

Table 2 : Gender Distribution

Gender distribution	Study Group			
	Case		Control	
	N	%	N	%
Male	47	47.5%	57	57.6%
Female	52	52.5%	42	42.4%
Total	99	100%	99	100%

Table 3: Comparison Of Age Distribution With Types Of Seizure

Age distribution	Types of Seizure				Total
	Simple Seizure	%	Complex Seizure	%	
<1 year	34	34.3%	17	17.2%	51 (51.5%)
1 – 3 years	28	28.3%	12	12.1%	40 (40.4%)
3-5 years	5	5.1%	3	3.0%	8 (8.1%)
Total	67	67.7%	32	32.3 %	99 (100%)
	Chi Square test value	0.220	P value	0.896 (p>0.05) NS	

Table 4: Comparison Of NLR In Case And Control Groups

Groups		Cases		Controls		Chi square value	P value
		Frequency	Percentage	Frequency	Percentage		
NLR	Normal	43	43.43	79	79.80	29.71	<0.001*
	Abnormal	56	56.57	20	20.20		
	Total	99	100	99	100		

Table 5 : Comparison Of Variables In Study Groups

Variables	Controls		Cases		Mann-Whitney U	P value
	Mean	Standard deviation	Mean	Standard deviation		
AGE	3.48	1.73	1.76	1.04	6.61	<0.001*
NEUTROPHIL LYMPHOCYTE RATIO	1.88	1.68	3.39	1.69	6.65	<0.001*
FEVER SEIZURE INTERVAL (Hrs)	-	-	9.98	3.01	-	-
DURATION OF SEIZURES (SEC)	-	-	30.91	9.16	-	-

Table 6: Mean Comparison Of NLR, T And P Value Between SFS And CFS

	SEIZURE TYPE	N	Mean	Std. Deviation	Std. Error Mean
NEUTROPHIL LYMPHOCYTE RATIO	Simple	67	3.2127	1.39268	.17014
	Complex	32	3.7759	2.15062	.38018
			t	One-sided p	
NLR	Equal variances assumed		-1.567	.060	

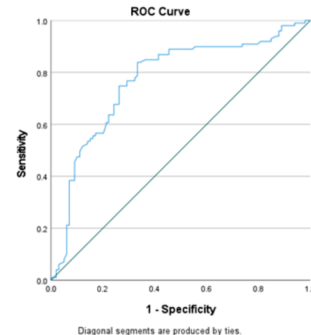


Figure 1 : ROC Curve For NLR (Cases And Controls)

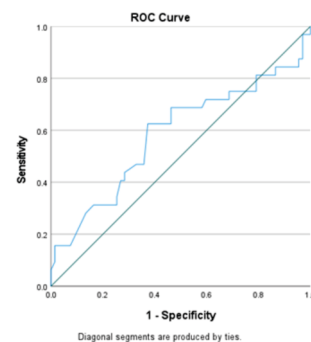


Figure 2 : ROC Curve For NLR (Simple And Complex)

DISCUSSION

Febrile seizure is defined as seizure that occurs in children aged six months to five years of age associated with fever (100.4°F or greater) without central nervous system infection.

Febrile seizure is classified as simple or complex⁽³⁾. Simple febrile seizures (SFS) is characterized by generalized tonic/tonic-clonic convulsions, that lasts for less than 15 minutes, occurs once in 24 hours (non-recurrent). Seizure that lasts more than 15 minutes and associated with focal neurological findings or recurs within 24 hours of fever is termed as complex febrile seizure. NLR has been proposed as a practical predictor of febrile seizure and its types in recent years⁵. The absolute neutrophil count and absolute lymphocyte count in children with febrile seizure was significantly higher than that of children with fever without seizure⁽⁸⁾.

In our study mean age for occurrence of febrile seizure is 21 months in case group and mean age for occurrence of fever without seizure is 41 months in control group which is significant with $p < 0.001$ and it is similar to the study conducted by Khosravi S et al¹² in which the occurrence of febrile seizure is 18 ± 3 months in children with febrile seizure and it is not similar with the study conducted by Sharawat et al⁹ in which the same group of children with fever without seizure and febrile seizures mean age was 26.3 months and 24.9 months. In other studies conducted by albert kurniawan et al¹⁰ and chung et al¹¹ showed febrile seizure occurrence is higher in age group 6–24 months and 18 months respectively which is also not similar to our study.

In our study occurrence of febrile seizure was higher in girls than boys, whereas in studies conducted by singh et al⁹, Yigit et al⁶, Goksugur et al¹³ and Khosravi S et al¹², the occurrence of febrile seizure was higher in boys than girls.

In our study the mean and S.D for control group is 1.88 ± 1.67 whereas

in other studies conducted by Khosravi et al¹², Mhaibes S et al¹⁴, Kurniawan et al¹⁰, showed mean and S.D of 1.990 ± 2.669 , 3.62 ± 2.77 , 3.61 ± 3.92 respectively. On comparison with these studies mean and S.D of control group in our study is less than other studies.

In our study the mean and S.D of febrile seizure children (case group) is 3.39 ± 1.68 and on comparing the mean and S.D of febrile seizure children with other studies conducted by Khosravi et al¹², Kubota J et al¹⁵, Mhaibes S et al¹⁴, Pooja A et al¹⁸, shows the value of 3.066 ± 3.080 , 4.17 ± 2.91 , 3.60 ± 2.72 , 4.5 ± 6.9 respectively. It shows that our study values are similar with studies of Khosravi S et al¹² and Mhaibes S et al¹⁴ whereas it is less when compared with studies of Kubota J et al¹⁵ and Pooja A et al¹⁸.

The present study of ours showed mean and S.D for SFS as 3.21 ± 1.39 and on comparison with other studies conducted by Yigit Y et al⁶, Gaoli C et al, Balikoglu P et al¹⁶ showed mean and S.D for SFS as 2.38 ± 1.60 , 2.16 ± 1.26 , 2.06 ± 1.99 , 4.32 ± 2.97 respectively. The mean and S.D of our study is higher than the results of Yigit Y et al⁶, Balikoglu P et al¹⁶, whereas it is less when compared with study of Kubota J et al¹⁵.

Our study showed the mean and S.D of CFS as 3.77 ± 2.15 and similar study conducted by Goksugur S.B t al¹³, Yigit Y et al⁶, Kubota J et al¹⁵, Liu Z et al¹⁷ showed the mean and S.D of CFS as 3.89 ± 4.28 , 3.42 ± 1.77 , 3.98 ± 3.15 , 3.86 ± 1.36 respectively. It shows all these studies have approximately similar values when compared to our study.

In our study ROC analysis for NLR between case group and control group showed that if the chosen cutoff value for NLR is 2.35, the sensitivity and specificity are 74.7% and 72.7%, respectively which was statistically significant ($p = 0.001$, AUC 0.770, CI 0.702-0.838) which is similar to the study conducted by N. Kabakus et al¹³ that showed in ROC analysis, if the chosen cutoff value for NLR is 1.98, the sensitivity and specificity are 66.7% and 60.3%, respectively which was statistically significant ($p = 0.040$ AUC 0.623, CI 0.503-0.743).

In our study ROC analysis for NLR between SFS and CFS showed that if the chosen cutoff point for NLR is 3.16, the sensitivity and specificity are 68.8% and 49.3%, respectively and was not statistically significant ($p = 0.17$, AUC 0.58, CI 0.455-0.713) and it is not similar when compared with the study conducted by Y. Yigit et al⁶ that showed in ROC curve analysis to differentiate simple and complex seizures, the optimal cut-off value for NRL to be 2.315 (sensitivity 62.7%, specificity 53.8%, AUC: 0.665) and is statistically significant. As mentioned in above table the NLR of SFS and CFS in our present study is approximately similar to most of the studies except the study conducted by Pooja A et al¹⁸ in where the NLR is more in CFS when compared to our current study. The limitation in our study could be overcome by conducting similar studies with large sample size to identify whether NLR could be used as a predictor in differentiating SFS and CFS.

CONCLUSION:

Mean neutrophil lymphocyte ratio for children with febrile seizure was higher than the mean NLR for children with fever without seizure and it was statistically significant. The mean NLR in complex febrile seizure was higher than simple febrile seizure but it was not statistically significant. Hence NLR is proved to be a reliable indicator to predict the occurrence of seizure in febrile children.

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