ISSN 1220-8841 (Print)
ISSN 2344-4959 (Online)

ROMANIAN
NEUROSURGERY

Vol. XXXV | No. 4 December 2021

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DOI: 10.33962/roneuro-2021-086

Romanian Neurosurgery (2021) XXXV (4): pp. 503-507
DOI: 10.33962/roneuro-2021-086
www.journals.lapub.co.uk/index.php/roneurosurgery

Correlation of neutrophil lymphocyte ratio to clinical outcomes based on 6 months surveillance on traumatic brain injury patients at Haji Adam Malik General Hospital (2018-2020)

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Keywords
traumatic brain injury, neutrophils, lymphocytes, NLR, Glasgow Outcome Scale

ABSTRACT

Introduction: Traumatic brain injury is a major cause of disability, death, and economic loss in many countries around the world. The annual incidence in the United States is reported to reach 1.7 million sufferers, in Europe it is reported as 262 per 100,000 people per year, and in Indonesia, the incidence is increasing by 1% every year. Direct and indirect damage resulting from a traumatic brain injury can cause inflammation by activating glial cells and leukocytes, inducing the release of proinflammatory cytokines, and accelerating neurodegeneration and neuroinflammation. Recently, the neutrophil-to-lymphocyte ratio (NLR) has been proposed to be a predictor of clinical outcomes for various neurological diseases such as stroke and traumatic brain injury. To put it simply, elevated NLR levels in patients with intracerebral haemorrhage were independently associated with worse clinical outcomes. Researchers want to research the relationship between NLR and outcome based on 6 months GOS in traumatic brain injury patients at Haji Adam Malik General Hospital Medan.

Methods: An observational analytic study with a retrospective cohort design. Samples were selected based on inclusion and exclusion criteria from a traumatic brain injury at H. Adam Malik General Hospital Medan in 2018-2020.

Results: The research data were normally distributed and analyzed by the Pearson trial; the sig value was obtained. (2-tailed) of 0.798 ($P > 0.05$), which means there is no between NLR and 6 months GOS outcome in traumatic brain injury patients.

Conclusion: There was no relationship between *NLR* and outcome based on GOS 6 months of traumatic brain injury patients.

INTRODUCTION

Traumatic brain injury is a major cause of disability, death, and economic loss in many countries around the world.[1] The annual incidence in the United States is reported to reach 1.7 million sufferers, in Europe it is reported as 262 per 100,000 people per year, and in

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ISSN online 2344-4959
© Romanian Society of Neurosurgery

First published
December 2021 by
London Academic Publishing
www.lapub.co.uk

Indonesia, the incidence is increasing by 1% every year.2. based on RISKESDAS data in 2018 that the incidence of traumatic brain injury increases every year from 8.2% in 2013 to 9.2% in 2018. The highest prevalence is experienced by male patients (11%) with an average age of 15 – 24 years (12.2%) with the most locations in urban areas (9.4%). Road traffic accidents still account for the highest proportion (31.4%) with motorcycle riders being the most common cause of traumatic brain injury (72.7%).3 The incidence of traumatic brain injury is also a problem faced by many neurosurgeons, especially in the city of Medan. Based on data from patients served by SMF Neurosurgery, H. Adam Malik Hospital Medan in 2013 – 2017, traumatic brain injury sufferers were still listed as the most patients with the highest number reported reaching 32.64% in 2014 and the lowest figure found to be 15.83% in 2014. 2017.4 Direct and indirect damage resulting from a traumatic brain injury can cause inflammation by activating glial cells and leukocytes, inducing the release of proinflammatory cytokines, and accelerating neurodegeneration and neuroinflammation.5 Recently, the neutrophil-to-lymphocyte ratio (NLR) has been proposed to be a predictor of clinical outcome for various neurological diseases such as stroke and traumatic brain injury.[6]

Neutrophil Lymphocyte Ratio (NLR) is calculated as the ratio of neutrophil cell count to lymphocyte cell count in peripheral blood. NLR is an objective, readily available, inexpensive, and reproducible indicator of inflammation. NLR is also a sign of extensive secondary damage by neutrophils and their products to cerebral tissues and attenuation of cell-mediated immunity associated with systemic inflammation. Its prognostic role has been investigated in various neurological disorders such as stroke, multiple sclerosis, and traumatic brain injury. [7]

Evidence has suggested that patients with higher neutrophil cell counts, and lower lymphocyte cell counts have worse clinical outcomes. In addition, a higher NLR ratio was also associated with a worse clinical outcome at 1 year after traumatic brain injury.[8]

It has been found that NLR values in patients with severe traumatic brain injury on the first day of hospital admission are independent predictors of mortality and functional clinical outcome. The power of the NLR test to predict functional clinical outcome in these patients appears to be like the power of the Glasgow Coma Scale (GCS). There is a reported good correlation between NLR and GCS, where higher NLR is associated with lower GCS. However, the association between NLR and mortality was thought to be weaker than that of GCS, indicating the superiority of the GCS in predicting mortality in patients with traumatic brain injury.[9]

NLR examination has several benefits for predicting patient prognosis compared to GCS. First, the NLR is more objective than the GCS, and individual judgment is not involved in the NLR. Second, the slightest change in the patient's general condition related to the disease may not be directly reflected by the GCS, but the NLR is able to describe these changes. Third, GCS assessment is impaired if the patient is sedated or on mechanical ventilation. However, in emergency situations, NLR retrieval takes a long time, which is around 30-40 minutes to get results.[8]

To put it simply, elevated NLR levels in patients with intracerebral hemorrhage were independently associated with worse clinical outcomes. Researchers want to research the relationship between NLR, and outcome based on 6 months GOS in traumatic brain injury patients at Haji Adam Malik General Hospital Medan.

Methods

This study was an observational analytic study with a retrospective cohort study design to assess the relationship between neutrophil lymphocyte ratio and clinical outcome based on 6-month GOS in traumatic brain injury patients. Neutrophil Lymphocyte Ratio data from non-operative traumatic brain injury patients who came to Haji Adam Malik Hospital in Medan from 2018-2020 were compared to the clinical outcomes of patients based on the Glasgow Outcome Scale (GOS) at 6 months post-injury.

The independent variable in this study was the Neutrophil Lymphocyte Ratio of patients with non-operative traumatic brain injury on the first day of coming to Haji Adam Malik General Hospital, Medan, while the dependent variable included clinical outcomes of patients based on GOS 6 months after injury.

Inclusion criteria to be used as research samples are non-operative brain injury patients, head CT-

Scan criteria have features of Epidural Hematoma, subdural hematoma, Intraparenchymal hemorrhage, brain contusion, and subarachnoid hematoma, aged more than 10 years and less than 70 years, and have data neutrophils and lymphocytes on the first day of hospital admission. While the exclusion criteria in this sample were patients with penetrating brain injury, post-traumatic patients who had multiple injuries other than in the head region as evidenced by clinical and radiological findings, patients with a history of previous head injuries, patients with a history of comorbid diseases such as stroke, brain tumors, lung disorders. and heart disease, chronic kidney disease, and previous systemic infectious disease.

Sample is total sampling of the traumatic brain injury patients who were treated at Haji Adam Hospital Medan from 2018 to July 2020 who had met the inclusion and exclusion criteria. The study was conducted at H. Adam Malik Hospital using medical record data of non-operative traumatic brain injury patients from 2018-2020. Data collection was carried out after obtaining approval from the USU Medical Faculty ethics committee. Before starting the research, the researcher asked for ethical clearance from the Permanent Committee for Assessing Research Ethics, Faculty of Medicine, University of North Sumatra.

The data obtained were then collected for data processing using SPSS software version 25.0. To determine the characteristics of patients with traumatic brain injury and to determine the clinical outcome of patients 6 months after traumatic brain injury based on the Glasgow Outcome Scale, categorical data is presented in the form of a frequency distribution of n (%), tables and graphs, and numerical data is presented in the form of mean ± standard deviation. or median. The mortality rate is presented in the form of a rate.

To determine the relationship between Neutrophil Lymphocyte Ratio (NLR) on clinical outcomes of patients based on 6-month GOS in traumatic brain injury patients, Pearson correlation test analysis was performed if the data were normally distributed, or Spearman's Rank test was performed if the data were not normally distributed. Normality test using the Kolmogorov-Smirnov test (n>50), the data is said to be normally distributed if p>0.05.

Results

In this study, 77 samples from the total sampling met the inclusion and exclusion criteria. The sample data are patients who experienced traumatic brain injury at Haji Adam Malik Hospital Medan from 2018 - 2020. The description of the characteristics of the research sample is described as follows:

Table 1. Distribution of samples by gender

Genders	Total	Percentage
Male	63	81,82%
Female	14	18,18%
Total	77	100%

Based on table 1, it was found that the male research sample amounted to 63 people with a presentation of 81.82% and the female research sample amounted to 4 people with a presentation of 18.18%. From these data, it was found that the male research sample was more than the female patient.

Table 2. Sample distribution based on GCS

GCS	Total	Percentage
13-15	29	37,66%
9-12	28	36,36%
< 9	20	25,98%
Total	77	100%

Based on table 2 get the research sample with GCS 13-15 totaling 29 people with a percentage of 37.66%, research samples with GCS 9-12 totaling 28 people with a percentage of 36.36% and research samples with GCS < 9 totaling 20 people with a presentation of 25 ,98%. From these data, it was found that the study sample with GCS 13-15 was more than the GCS 9-12 and <9.

Table 3. Sample distribution by trauma onset

Onset of Trauma	Total	Percentage
< 24 h	66	85,71%
> 24 h	11	14,29%
Total	77	100%

Based on table 3, the research sample with trauma onset less than 24 hours was 66 people with a percentage of 85.71% and the study sample with trauma onset more than 24 hours amounted to 11 patients with a percentage of 14.29%.

The data normality test was performed using the Kolmogorov-Smirnov test. Normality test was conducted to determine the difference test to be used next.

Table 4. Sample normality data using the One-Sample Kolmogorov-Smirnov Test

N		77
Normal Parameters[a,b]	Mean	,0000000
	Std. Deviation	1,94132437
Most Extreme Differences	Absolute	,318
	Positive	,274
	Negative	-,318
Test Statistic		,318
Asymp. Sig. (2-tailed)		,000[c]

From table 4, the results of the normality test of the research sample data with a significance value (P < 0.05) suggest that the data are normally distributed. Data with normal distribution will be tested for Pearson Correlation.

To determine the correlation between GCS and 6-month GOS outcomes in patients with traumatic brain injury at H. Adam Malik Hospital Medan, the Pearson correlation test was performed.

Table 5. GCS correlation test results data with 6-month GOS outcomes

GCS			GOS
GCS	Pearson Correlation	1	,783**
	Sig. (2-tailed)		,000
	N	77	77
GOS	Pearson Correlation	,783**	1
	Sig. (2-tailed)	,000	
	N	77	77

** Correlation is significant at the 0.01 level (2-tailed).

From table 5. obtained a sig. (2-tailed) value of 0.00 and a positive value on the Pearson Correlation, which means that there is a positive correlation between GCS and 6-month GOS outcomes, with a P value of < 0.05.

To determine the correlation between NLR and 6-month GOS outcomes in patients with traumatic brain injury at H. Adam Malik General Hospital Medan, the Pearson correlation test was performed.

Table 6. NLR Correlation Test Results Data with 6 months GOS clinical outcome

NLR			GOS
NLR	Pearson Correlation	1	-,030
	Sig. (2-tailed)		,798
	N	77	77
GOS	Pearson Correlation	-,030	1
	Sig. (2-tailed)	,798	
	N	77	77

From table 6. sig value is obtained. (2-tailed) of 0.798 (P > 0.05) which means that there is no correlation between NLR and 6-month GOS outcomes in traumatic brain injury patients.

Conclusion

The NLR correlation test has been carried out on the clinical outcome of traumatic brain injury patients based on 6 months GOS which obtained a sig value. (2- tailed) of 0.798 (P > 0.05) which means that there is no correlation between NLR and 6-month GOS outcomes in traumatic brain injury patients.

The results in this study are different another which stated that there is evidence of a correlation between high NLR and the worst functional clinical outcome and vice versa, lower NLR has a clinical outcome good functionality.9 An NLR value >15.63 at first hospital admission was a predictor of poorer clinical outcome and mortality at 28 days. Chen et al also reported that NLR levels with a cut-off value of 18.16 were correlated with clinical outcomes with a sensitivity of 74.3% and a specificity of 72.9%.8

In this study, different results were obtained from previous studies, where there was no relationship between NLR and clinical outcomes of traumatic brain injury patients. It is suspected that many factors can influence the results of this study. One of the types of intracranial lesions that occur due to impact on the head is thought to affect the NLR value itself. NLR values were seen to be significantly higher in brain injury patients with diffuse axonal injury than in patients with cerebral edema, intracerebral hemorrhage, subdural or epideral hematoma, and subarachnoid hemorrhage. In this study sample, there were heterogeneous types of intracranial lesions which were thought to have an impact on the results of the study. Thus, the same study can be carried out again with more homogeneous intracranial lesions from each study sample so that it can have maximum results.[10]

In addition to the type of intracranial lesion due to a blow to the head, the onset of trauma upon admission to the hospital and the time the patient's blood sample was taken were thought to also play a role in NLR levels. NLR levels peak in the first 24 hours of onset of traumatic brain injury. In the sample of this study, 14.29% of the sample with onset more than 24 hours after the incident of traumatic brain injury before routine blood tests were performed. This is thought to affect the results of this study.[6]

The research sample size is also suspected to affect the results of this study. Small differences in clinical outcomes can be statistically significant if the number of samples is very large. On the other hand, a very significant clinical difference may not be statistically significant if the sample is too small. Many studies are not published because the results are not statistically significant even though they are clinically important.11 From this study obtained 77 samples from the total sampling that have met the inclusion and exclusion criteria. There are many complicating factors experienced by researchers so that the number of samples obtained is too small. Thus, other methods in determining the number of research samples, such as using a probability formula with a high confidence interval, can be an alternative for the next research to obtain maximum research results.

Discussion: There was no relationship between NLR, and outcome based on GOS 6 months of traumatic brain injury patients. Further research is needed with a larger sample size to obtain optimal results.

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