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Neutrophil-Lymphocyte Ratio Related to Patients Outcome in Moderate Head Injury Patients with Intracerebral Hemorrhage

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ABSTRACT

Background. Head injury is still a major health problem that is a common cause of disability and death. Moderate head injuries are quite common with outcomes varying patient examination of neutrophils and lymphocytes is quite routinely carried out in health services and the combination of these two values has a stronger predictive value for assessing outcomes in patients because it describes an inflammatory reaction. The GOS is a commonly used scale for classifying patient outcomes. This study aimed to determine the relationship between the ratio of neutrophil-lymphocytes (RNL) to the Glasgow outcome scale (GOS) in moderate head injury patients with intracerebral hemorrhage. **Methods:** This study has a cross-sectional with samples from moderate head injury patients with CT scan images of intracerebral hemorrhage in Dr. M. Djamil Padang in 2021 and 2022. The data comes from medical records and observations of samples that meet the inclusion and exclusion criteria, 36 subjects participated in this study. **Results:** Most of the subjects (61.1%) were male. A total of 55.6% of subjects had RNL ≥ 7.35 with 44.4% of subjects having poor GOS. In this study, a statistically significant relationship was found between the ratio of neutrophil-lymphocytes in patients with moderate head injury with intracerebral hemorrhage and the Glasgow outcome scale (p-value = 0.005). **Conclusion:** RNL can predict outcomes in moderate head injury patients with intracerebral hemorrhage.

1. Introduction

Head injury is one of the major causes of disability and death in the world. Head injuries can cause cognitive and functional limitations so that the patient will suffer for the rest of his life.¹ The incidence of head injuries worldwide in 2010 was around 2.5 million cases and has resulted in an estimated economic cost burden of nearly 76.5 billion US dollars.² Every year in the United States there are 1.7 million cases of head injury with a death rate of 52,000 people. Head injuries are predicted to be the third leading cause of death in 2020.³ The proportion of head injury patients nationally

in 2018 was 11.9%, with the highest proportion in Gorontalo at 17.9% and the lowest in South Kalimantan at 8.6%. The proportion of head injuries in West Sumatra Province is 14.3%. In Indonesia, there have been several reports of head injuries, during June-December 2018 there were 118 cases of head injuries recorded at H. Adam Malik Hospital, North Sumatra with patient ages ranging from 18 years to 35 years and dominated by the male gender. man. Based on data from the Medical Record Installation of Dr. M. Djamil Padang, the number of head injury cases in

2017 was 356 cases and in 2018 there were 505 cases.⁴⁻⁶ It is estimated that about 20% of patients admitted to the hospital for head injuries are moderate with an incidence varying from 4-28%. Based on research on moderate head injury cases from 2007 to 2014, it was found that 1.9 million patients had head injuries with 7.6% being moderate head injuries. Most of the patients had moderate head injuries from falls (43%) and traffic accidents (34%).⁷⁻⁸

An important part of the pathophysiology of head injury is inflammation. The main role of this process is the number of immune mediators released within minutes after the primary injury. These mediators initiate subsequent events, including the expression of adhesion molecules, cellular infiltration, secretion of inflammatory molecules, and growth factors, leading to cell regeneration or death.^{9,10,11} Head injury causes microglial activation and release of proinflammatory cytokines and other neurotoxic products that produce free radical compounds. These free radical compounds cause tissue damage.¹¹ An increase in the number of leukocytes and neutrophils is usually considered a nonspecific indicator of infection, inflammation, tissue necrosis, bleeding, or stress conditions. One of the markers of inflammation that can be used is the ratio of neutrophils to lymphocytes (RNL). Neutrophil and lymphocyte levels were obtained from the type of leukocyte count which is one of the components of routine blood tests. Various studies have shown an increase in neutrophils and a decrease in lymphocytes immediately after tissue injury, including in patients with head injuries. The important role of neutrophils in ischemic-reperfusion injury has been suggested by several studies showing a close relationship between neutrophil accumulation and tissue injury.^{12,13}

Neutrophils are often viewed as proinflammatory cells and are rapidly recruited in the central nervous system after traumatic brain injury and then enter the meningeal vessels and the choroid plexus. Neutrophils can damage the blood-brain barrier by releasing metalloproteinases, proteases, TNF, and Reactive Oxygen Species (ROS). Neutrophils cause neuronal cell death by using the same mediators that destroy the blood-brain barrier. Within 24 hours after brain injury,

the number of circulating neutrophils was greatly increased compared to the uninjured control group.^{12,13} Neutrophil to Lymphocyte Ratio (RNL) is a predictor of prognosis in patients involving brain conditions. Other studies have shown that the neutrophil to lymphocyte ratio can be a useful predictor of outcome and mortality in patients with intracerebral hemorrhage after 1 year.¹⁴ Other studies have shown neutrophils, lymphocytes, and platelets as potential markers to indicate the severity of the head injury, the higher the value of the neutrophil to lymphocyte ratio and the platelet-to-lymphocyte ratio, the higher the severity of the head injury.¹ A study stated the ratio of neutrophils to lymphocytes to be one of the prognostic factors in morbidity and mortality from a head injury. An increase in the ratio of leukocytes to neutrophils correlates with a decrease in GCS.¹⁵

2. Methods

The design of this study was an analytic observational study with a cross-sectional approach to patients with moderate head injury with the intracerebral hemorrhage who were treated at RSUP Dr. M. Djamil Padang from January to February 2022. A total of 36 research subjects participated in this study, where the subjects met the inclusion criteria (moderate head injury patients with a diagnosis of intracerebral hemorrhage who came to the Emergency Unit of Dr. M. Djamil Padang Hospital 48 hours after the incident, patients with a history of head injury for the first time and were discharged from treatment, there were neutrophil and lymphocyte data on admission to the hospital). The exclusion criteria were patients who had a history of metabolic disease, multiple trauma patients, patients who had a history of stroke, brain tumor, inflammation or infection in the previous brain, patients indicated for surgery, moderate head injury patients with intracerebral hemorrhage accompanied by another intracranial bleeding (epidural hemorrhage), subdural hemorrhage and subarachnoid hemorrhage), immunocompromised patients, and confirmed COVID-19 patients.

The variable assessed in this study was the neutrophil-lymphocyte ratio (RNL). RNL is categorized

as less than 7.35 and more than equal to 7.35. The demographic characteristics of the subjects in the form of age and gender are also presented in this study. The outcome from a head injury was assessed by the Glasgow Outcome Score (GOS). Data analysis was performed with the help of SPSS version 25 software. Univariate analysis was performed to present the frequency distribution of the test variables. Bivariate analysis was conducted to assess the relationship between the dependent and independent variables with

the chi-square test with a probability value of 5% or 0.05.

3. Results

Table 1 shows the mean age of patients with moderate head injury with intracerebral hemorrhage is 40 years. The youngest age of the subject is 14 years old and the oldest is 76 years old. In addition, the table also describes the sex distribution with the proportion of male sex being more than female, namely 22 people.

Table 1. Characteristics of patients with moderate head injury with intracerebral hemorrhage by age and gender

Characteristics	Total	%
Age (years)		
Mean	40	
Min-max	14-76	
Gender		
Male	22	61.1
Female	14	38.9
Total	36	100

Table 2 shows more than half of patients with moderate head injury with intracerebral hemorrhage

had a neutrophil-lymphocyte ratio of ≥ 7.35 , as many as 20 people (55.6%).

Table 2. Overview of the neutrophil-lymphocyte ratio in patients with moderate head injury with intracerebral hemorrhage

Neutrophil Lymphocyte Ratio	N	%
< 7.35	16	44.4
≥ 7.35	20	55.6
Total	36	100

Table 3 shows that in patients with moderate head injuries accompanied by intracerebral hemorrhage, 21

people (58.3%) have good GOS and 15 people (41.7%) have poor GOS.

Table 3. Overview Glasgow outcome scale of patients with moderate head injury patients with intracerebral hemorrhage

Glasgow outcome scale	N	%
Good	21	58.3
Poor	15	41.7
Total	36	100

Table 4 shows that GOS is good, more dominant in patients with RNL values that are low, namely as many as 14 people (38.9%) while bad GOS, more occurring in patients with high RNL values, namely 13 people (36.1%). Table 4 also shows that there is a statistically

significant relationship between the ratio of neutrophil-lymphocytes in patients with moderate head injury with intracerebral hemorrhage and the Glasgow outcome scale (p-value = 0.005).

Table 4. Relationship between neutrophil-lymphocyte ratio in patients with moderate head injury with intracerebral hemorrhage with Glasgow outcome scale patients

Neutrophil-Lymphocyte Ratio	Glasgow Outcome Scale		*P-value
	Good n (%)	Poor n (%)	
< 7,35	14(38,9)	2(5.6)	0.005
≥ 7.35	7(19.4)	13(36.1)	

*Chi square test, p<0,05

4. Discussion

This study found a significant relationship between RNL in head injury patients and intracerebral hemorrhage and glasgow outcome scale with a p-value of 0.005. This suggests that an increased neutrophil to lymphocyte ratio is associated with outcomes in patients with moderate head injury with intracerebral hemorrhage. This is because the inflammatory response itself has an important role in brain tissue damage in head injury patients with intracerebral hemorrhage. The brain responds to head injury through the production of inflammatory mediators that cause the infiltration of various inflammatory cells (neutrophils and lymphocytes) into brain tissue. Another study showed using a cut-off RNL 7.35, the same as this study. In that study, it was found that a high RNL group was associated with poor short-term survival rates in patients with intracerebral hemorrhage. A high RNL is also associated with a lower GCS score.¹⁶⁻²¹

There is evidence to suggest that RNL is a significant predictor of patient morbidity and mortality. The neutrophil-lymphocyte ratio is a biomarker that provides important information about inflammatory activity and is a prognostic indicator in patients with ischemic stroke, hemorrhagic stroke, glial tumor, and status epilepticus.²² A previous study also found an association of RNL with GOS in patients with a moderate-to-severe head injury but with a cut-off of 6.05. The difference in RNL values is influenced by the

region and the research subject. Several days after the head injury, ROS production will decrease. Disruption of ROS production may be one of the mechanisms underlying the increased susceptibility of hospitalized trauma head injury patients to infection and will affect the outcome of head injury patients.²³ The RNL value is taken from the laboratory examination, the leukocyte count is a routine laboratory examination, it is easy to obtain and calculate and the cost is relatively cheap. RNL examination is also an objective examination to predict the outcome of head injury compared to the GCS which is commonly used to predict the outcome of head injury. Knowing the RNL value early can be an indicator for doctors for intensive care of head injury patients and predict outcomes.²⁴⁻²⁶

5. Conclusion

Neutrophil-lymphocyte ratio can predict *outcome* in moderate head injury patients with intracerebral hemorrhage.

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