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Correlation of Neutrophil-Lymphocyte Ratio with the Evidence of Stroke Haemorrhagic at Tertiary Hospitals

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Abstract

Stroke is the leading cause of death, disability, and morbidity in the world. Hemorrhagic stroke (HS) prevalence accounts for 10–20% of all strokes, whereas ischemic stroke accounts for 85 percent. Clinical manifestation and numerous biomarkers such as ferritin level, cholesterol level, and lately neutrophil-to-lymphocyte ratio have been suggested as a sign of HS prognosis. It's also used as a modality for differentiating ischemia from hemorrhagic. The purpose of this study is to assess if there is a link between NLR and HS evidence. A retrospective cross-sectional study was conducted among the medical reports of patients treated with stroke at Sanjiwani Hospital Bali through 2018–2020. The inclusion criteria were complete medical reports in adults≥ 18 years old. Data obtained from the medical record include demographic data, including age, gender, chief complaint, stroke diagnoses based on clinical manifestations, data of leucocytes, neutrophils, lymphocytes, NLR, and results of computed-tomography scanning of the head. Data were analyzed with the Chi-Square test for nominal data and Spearman Correlation test to evaluate the correlation of the leucocyte, neutrophil, lymphocyte, NLR, with the diagnoses. Ninety-six patients' medical records were evaluated in the current study. Age ≥ 50 years old (85.4%) with the oldest age was 91 years old. The top three chief complaints are hemiparesis (78.1%), a decrease of consciousness (7.3%), and facial palsy (5.2%). We also analyzed the correlation of inflammation parameters using the Spearman correlation test. There is a positive weak correlation between leucocyte count (r: 0.351; p<0.001) and NLR with evidence of HS (r = 0.371; p<0.001). The correlation between neutrophil counts and evidence of HS is a positive moderate correlation (r = 0.408, p<0.001). Lymphocyte count has a strong positive correlation with HS (r: 1.000, p = 0.017). The leucocyte, neutrophil, lymphocyte, and NLR are able to predict the evidence of hemorrhagic disease in resource-limited countries.

Keyword: Neutrophil-Lymphocyte Ratio, Hemorrhagic Stroke

INTRODUCTION

Stroke is the central cause of morbidity, mortality, and disability around the globe. (1) After ischemic heart disease (14.8 percent of all deaths), stroke was the second most common cause of death (11.8 percent of all deaths) and the third most prevalent cause of disability (4.5 percent of disability-adjusted life years, DALYs from all causes) in 2013. (1) Not only is the incidence rising due to population aging, but more young people in low-income countries have recently experienced a stroke. (2) The World Health Organization's (WHO) definition of stroke is "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin." (3) Strokes can either be ischemic (occlusion of a blood vessel) or hemorrhagic (rupture of a blood vessel). Among all strokes, hemorrhagic stroke represents approximately 10–20% versus 85% of ischemic stroke. (4) The pathogenesis of thrombotic cerebral infarction results from the atherosclerotic obstruction of large cervical and cerebral arteries. 5,6 This will cause ischemia in all or part of the territory of the occluded artery. On the other hand, hemorrhagic stroke is mainly due to the disruption of the vessel wall in arteriolar hypertensive disease and is rarely associated with a coagulation disorder. (5,6)

Stroke is defined as "rapidly developing clinical evidence of focal (or global)

impairment of brain function, with symptoms lasting 24 hours or more or leading to death, with no evident cause other than vascular origin," according to the World Health Organization (WHO). (3) Ischemic (blood vessel occlusion) or hemorrhagic strokes are the two types of strokes (a rupture of a blood vessel). Hemorrhagic stroke accounts for 10–20% of all strokes,4 whereas ischemic stroke accounts for 85% of all strokes. The atherosclerotic blockage of major cervical and cerebral arteries is the cause of thrombotic cerebral infarction. (5,6) Ischemia will occur in all or part of the blocked artery's area. On the other hand, a coagulation problem is only occasionally associated with hemorrhagic stroke, which results from the breakdown of the arterial wall in arteriolar hypertension. (5,6)

Intracerebral hemorrhage (ICH, or bleeding within the brain) and subarachnoid hemorrhage are two types of hemorrhagic strokes (SAH, bleeding between the inner and outer layers of tissue covering the brain within the subarachnoid space). (4) Although hemorrhagic stroke is less common, it is associated with higher rates of mortality and disability, and there are currently only a few effective therapy methods available. Early detection is critical for stroke patients in order to prevent complications and long-term damage. In inpatient care, however, recognizing the kind of stroke is crucial. Simple clinical symptoms are helpful in determining the kind of stroke, but diagnostic imaging is an unavoidable necessity. As a result, early stroke type identification is critical for stroke outcomes. Clinical manifestation and numerous biomarkers such as ferritin level 7, cholesterol level 8, and the recently described neutrophil-to-lymphocyte ratio as a sign of HS prognosis are the modalities for differentiating ischemia or hemorrhagic (9,10)

As one of the inflammatory markers in HS, the neutrophil-to-lymphocyte ratio may also differentiate ischemic stroke or HS; hence, the objective of the current study is to evaluate the correlation of NLR with the evidence of HS.

METHODS

A retrospective cross-sectional study was conducted among medical reports of patients treated with stroke at Sanjiwani Hospital Bali through 2018–2020. The inclusion criteria were a complete medical report for adults ≥ 18 years old. We excluded the incomplete medical report. Data obtained from the medical record include demographic data, including age, gender, chief complaint, clinical manifestations of the stroke, leucocyte, neutrophil, lymphocyte, and NLR. Diagnoses were based on clinician judgment based on the clinical manifestation and result of computed-tomography scanning of the head. The diagnosis of the patient is divided into ischemic or non-hemorrhagic stroke and hemorrhagic stroke. Data were analyzed with the Chi-Square test for nominal data and the Spearman correlation test to evaluate the correlation of the leucocyte, neutrophil, lymphocyte, and NLR with the diagnoses.

RESULTS

Ninety-six patients medical records were evaluated in the current study. Age < 60 years old represents 44.8% of the patients, with the oldest being 91 years old. There was no patient less than 30 years old, but there were 2 (2.08%) of the patients who were 31 years old. The top three chief complaints are listed in Table 1. Other chiefs complain of aphasia and speech involvement, which are as high as 3.1% and 2.1%, respectively. Vertigo and coma were also reported as the chief complaints, each in 1% of the samples. The majority of the patients (72.9%) were diagnosed with an ischemic stroke. Another symptom was aphasia, which accounts for 6/70 among ischemic strokes and 2/26 among HS (p = 1.000).

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Table 1 Basic characteristics of the samples

Variable	All samples (N=96)	Ischemic stroke (N=70)	Hemorrhagic stroke (N=26)	*p*
Age, mean (SD)	61.2 (12.06)	61.4 (12.17)	60.62 (11.97)	0.778[a]
Sex, N (%)				
Male	61 (63.5)	44 (62.86)	17 (65.38)	0.819[b]
Female	35 (36.5)	26 (37.14)	9 (34.62)	
Chief complain (%)				
Hemiplegia	75 (78.1)			
Decrease of consciousness	7 (7.3)			
Facial palsy	5 (5.2)			
Sign and symptoms, N (%)				
Hemiplegia	90 (93.8)	66 (94.75)	24 (92.3)	0.661[c]
Facial palsy	19 (19.8)	16 (22.86)	3 (11.54)	0.262[c]
Headache	25 (26)	11 (15.71)	14 (53.85)	<0.001[b]
Speech involvement	24 (25)	17 (24.29)	7 (26.92)	0.791[b]
Vomiting	21 (21.9)	10 (14.29)	11 (42.31)	0.003[b]
Paresthesia	12 (12.5)	10 (14.29)	2 (7.69)	0.503[c]
Risk factors, N (%)				
Hypertension	64 (66.67)	42 (60)	22 (84.62)	0.018[c]
Diabetes	12 (12.5)	11 (15.71)	2 (76.92)	0.171[c]
Heart disease	15 (15.63)	12 (17.14)	3 (11.54)	0.753

[a]Unpaired *t* test, [b] Chi Square test, [c]Fisher Exact test

Other risk factors were history of stroke previously, dyslipidemia, and high uric acid, and none of those risk factors were associated with the stroke (p = 1.000; p = 1.000; p = 0.271). We analyzed the correlation of inflammation parameters such as white blood cells, neutrophil count, lymphocyte count, NLR, hematocrit, and platelet count with the evidence of HS.

Table 2 Laboratory finding

Variable	All samples (N=96)	Ischemic stroke (N=70)	Hemorrhagic stroke (N=26)	*p*
White blood cell, mean (SD)	8.45 (2.53)	7.81 (2)	10.16 (3.01)	0.001[A]
Neutrophil count, median (IQR)	5.02 (1.8-14.36)	4.71 (1.8-8.9)	7 (6.9-14.36)	<0.001[B]
Lymphocyte count, median (IQR)	1.8 (0.8-6.25)	44 (62.86)	17 (65.38)	0.819[B]
NLR, median (IQR)	2.82 (0.75-12.11)	26 (37.14)	9 (34.62)	<0.001[B]
Hemoglobin, mean (SD)	13.51 (1.36)	13.59 (1.33)	13.31 (1.46)	0.410[A]
Hematocrit, mean (SD)	39.6 (3.93)	39.72 (3.72)	39.26 (4.51)	0.644[A]
Platelet count, mean (SD)	219.28 (66.8)	213.59 (63.75)	234.58 (73.52)	0.205[A]

[A] Independent *t* test, [B] Mann Whitney test

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The result of Spearman correlation test reported in table 3. Parameter of the inflammatory response that significantly correlates with the evidence of HS are white blood cell count, neutrophil count, lymphocyte count, and NLR, with the strongest correlation is shown by lymphocyte count (r=1.000). There is a positive, weak correlation between the level of white blood cells and NLR with the evidence of HS. The correlation between neutrophil counts and evidence of HS is a positive, moderate correlation.

Tabel 3 Result of Spearman correlation test

Variables	r	*p*
White blood cell, mean (SD)	0.351	<0.001
Netrophil count, median (IQR)	0.408	<0.001
Lymphocyte count, median (IQR)	1.000	0.017
NLR, median (IQR)	0.371	<0.001
Hemoglobin, mean (SD)		0.410
Hematocrit, mean (SD)	1.000	0.629
Platelet count, mean (SD)	1.000	0.113

DISCUSSION

The goal of this study was to see if there was a link between NLR and the presence of HS in acute stroke patients. Age, race, sex, family history of stroke, and genetics are all non-modifiable stroke risk factors; hypertension, diabetes, dyslipidemia, arrhythmia, cardiac diseases, obesity, smoking, physical inactivity, alcohol, hormone replacement therapy, hyperhomocysteinemia, and hypercoagulable state are all modifiable stroke risk factors. 5, 6 Evidence of atherosclerosis rises with age, subsequently increasing the risk for ischemic stroke. (11) Unfortunately, the current study found the prevalence of stroke among middle-aged adults was high, accounting for 44.8%, or almost half of the sample. The results are in line with those of another study, which showed that young people are more likely to experience stroke, particularly in low- and middle-income countries. (2) The findings of the study could be related to the role of additional stroke risk factors such as hypertension (4–11%), hypercholesterolemia (12–21%), diabetes (4–7%), smoking (5–16%), and obesity (4-9 percent).(12)

In this study, we found a significant difference between the mean white blood cell count in ischemic stroke and hemorrhagic stroke (p = 0.001). The mean difference in WBC count is 2.35 x 103/µL, and HS has a higher count of WBC. Acute leukocytosis or white blood cells may contribute to post-stroke inflammation, induce further vascular injury by releasing pro-inflammatory mediators, and result in a more severe stroke or hemorrhagic stroke. A well-known reaction to intracerebral bleeding is leukocytosis. Higher leukocyte counts on admission were linked to a lower risk of hematoma expansion (Odds Ratio for 1000 Cells Increase [OR] 0.91, 95 percent Confidence Interval [CI] 0.86–0.96, p = 0.001). (13) The fact that we used a retrospective study design and did not evaluate hematoma expansion may help to explain the discrepancy in study results. The findings were similar to those of another study, which found that WBC levels were higher among people who had a hemorrhagic stroke. (14)

Neutrophils are blood cells that act as inflammatory cells by secreting pro-inflammatory cytokines. We found a significantly higher neutrophil count in HS patients (p<0.001). The study finding also did not match the previous study result, which found the hematoma expansion was inversely associated with neutrophil count (OR 0.90, 95% CI 0.85–0.96, p = 0.001). 13 The reason for the difference in study results may be associated with different study methods, where our retrospective study method did not evaluate the progression of the HS.

In our study, the median difference in NLR was 17, with the NLR being larger among ischemic stroke patients. In patients with various forms of stroke, there is a strong link between neutrophil-to-lymphocyte ratio (NLR) and death. The

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relationship between the NLR and HS is still unknown. At admission, there was no significant difference in NLR between patients with acute intracerebral hemorrhage who survived (2.39±1.75) and those who did not survive (3.09±2.16, p=.065). However, the next morning after admission, NLR was significantly higher in those who died (12.53±9.33) compared to those who survived (5.53±4.68) (p<.001). (9)

The current study used the admission NLR, and this finding is incongruent with the previous study. The incongruence may be explained by our study methods, in which we did not evaluate the progression of the HS in the patients.

We found a slight positive association between WBC (r: 0.351; p<0.001) and NLR (r: 0.371, p<0.001) counts and HS, as well as a moderate positive correlation between neutrophil (r: 0.408, p<0.001) counts and HS. Finally, the number of lymphocytes in the blood has a strong relationship with the presence of HS (r: 1.000, p = 0.017). All of these blood cells have been extensively examined as predictors of ischemic stroke progression, a bad prognosis of ischemic stroke, ischemic stroke progression to HS, and a poor HS result. (10,14–20)

The study limitations are the study methods, the low sample number, and the lack of data on other inflammatory markers of stroke such as C-reactive protein (CRP), SAA, and cytokines for analysis.

In conclusion, WBC, neutrophil count, lymphocyte count, and NLR are the cheaper predictors of HS to use in resource-limited countries.

CONFLICT OF INTEREST

The authors declare no conflict of interest

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