Blantika: Multidisciplinary Jornal
Volume 2 Number 4, February, 2024
p- ISSN 2987-758X e-ISSN 2985-4199

COMPARISON OF NEUTROFIL-LYMPHOCYTE RATIO TO SEVERITY OF STROKE ISCHEMIC BASED OF VASCULAR TERRITORY ASSESSED BY CT-SCAN

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ABSTRAK

Diagnosing severity of the stroke requires a NIHSS score which is a graded neurological examination. However, despite its successes, there are problems with the NIHSS. The scale contains items with poor reliability and has been criticized for its redundancy and complexity may not capture the full range of stroke severity, particularly in those with very mild or severe symptoms. Over the last 10 years, the evaluation of the NLR as an emerging marker of diseases has become a compelling field of bio-medical research. However, the value of NLR in predicting the poor prognosis of stroke patients is still controversial. Patients of stroke ischemic from July to December 2023 at Royal Prima Hospital were studied to analyze the correlation between NLR to severity of stroke regarding vascular territory. Our investigation reveals no correlation between those two variables.

Keywords: Stroke Ischemic, CT Scan, NLR

INTRODUCTION

Stroke is the second leading cause of death worldwide, with 80–87% of strokes being ischemic(Feigin et al., 2017). Stroke is a major cause of disability and death characterized by neurological deficit. It is classified as ischemic stroke and hemorrhagic stroke, and even though a report from American Health Organization shows that the prevalence of ischemic stroke is higher, deaths from hemorrhagic stroke demonstrate a bigger number. Meanwhile, according to data from the Ministry of Health's 2018, the prevalence of stroke in Indonesia has reached 10.9 per million, or in other words, there are 11 stroke incidents for every 1000 people. It is interesting to note that the tendency of stroke survivors, which had previously been in the older age range, has changed to be in the younger age range. This disease began to increase in the age of 10-14 years. In North Sumatera, particularly in Medan, exhibits a same trend. This high prevalence needs serious attention because in addition of it reducing the quality of life, it burdens the nation's economy, and threatens the vision of Indonesia Gold 2045.

Diagnosing severity of the stroke requires a NIHSS (National Institutes of Health Stroke Scale) score which is a graded neurological examination assessing consciousness, eye movements, visual fields, motor and sensory impairments, ataxia, speech, cognition, and inattention. The scale was developed as a communication tool and has since been used in stroke trials (Brott et al., 1989). Though other scales have been evaluated, the NIHSS is arguably the most frequently used deficit scale for stroke patient evaluations (Kasner et al., 1999). The NIHSS' reliability, coupled with its ability to predict patient outcome, has helped to foster its use in both clinical and academic arenas. However, despite its successes, there are problems

with the NIHSS. The scale contains items with poor reliability, and has been criticized for its redundancy and complexity, may not capture the full range of stroke severity, particularly in those with very mild or severe symptoms (Wityk et al., 1994). This can result in floor or ceiling effects, where a person scores the minimum or maximum score on some or all items, which limits the ability of the NIHSS to capture change over time. Another downside is the lessened weighting for posterior circulation strokes, a problem for nearly all neurological deficit scales. Therefore, it is important to seek another alternative biomarker to predict the prognosis of patients with stroke (Gur et al., 2007).

Over the last 10 years, the evaluation of the NLR (neutrophil-to-lymphocyte ratio) as an emerging marker of diseases has become a compelling field of bio-medical research. Although the value of NLR in predicting the poor prognosis of stroke patients is still controversial, some studies show that NLR had no obvious effect on mortality, while some studies demonstrated that a high NLR was an independent predictor of poor clinical outcomes in patients with stroke (Zhang et al., 2021). Thus, by using NLR as a robust prognostic biomarker we hope to overcome NIHSS limitation.

On the other hand, Brain imaging tools, notably CT scan, are typically used to diagnose strokes, whether they are ischemic or hemorrhagic. Although the severity of brain ischemic shown in CT scan doesn't reveal the correlation with NLR, the correlation with vascular territories in the brain should be explored

Therefore, this study aims to compare the NLR levels with the severity of ischemic stroke across distinct vascular territories as assessed by CT-scan. By elucidating potential associations between NLR and stroke severity within specific vascular territories, our findings may contribute to a more nuanced understanding of the inflammatory response in ischemic stroke and aid in refining risk stratification and treatment strategies tailored to individual patients.

RESEARCH METHOD

The design for this research is an analytical observational study with a cross-sectional study approach. Amount of data were 74 collected from stroke ischemic patients those treated at Royal Prima Hospital from July to December 2023. The patients included in study must have CT scan and completed blood work. Patients those have other diseases such as infection or other neurological diseases were excluded

Patient's medical record included patient CT scan images which explained the lesion region in brain and blood test which showed the numbers of neutrophil and lymphocyte. The lesion region in ischemic stroke patient divided into 3 parts: Anterior Cerebral Artery (ACA), Middle Cerebral Artery (MCA), and Posterior Cerebral Artery (PCA).

After the data was collected, analysis using statistic tests was conducted. Normality data was firstly tested using Kolmogorov-Smirnov with a result of p-value <0.001 which is less than 0,05. This shows that the data was not normally distributed ($p<0,05$). Thus, the analysis was done using Mann-Whitney test to determine the correlation between CT scan images of ischemic stroke patients and NLR.

This study was ethically approved by the Health Research Ethics Committee University of Prima Indonesia No 008/KEPK/UNPRI/VI/2023.

RESULTS AND DISCUSSION

Results

Table 1 Distribution of Patient Characteristics by Age

Usia	n	%
30-50 Years	7	9,5
>50 Years	67	90,5
Total	74	100

Table 1 describes patient characteristics based on age. There are 74 patients in total, with 7 patients within the age of 30-50 years with a percentage of 9,5% and 67 patients within the age of >50 years with a percentage of 90,5%.

Table 2 Distribution of Patient Characteristics by Sex

Sex	n	%
Male	47	63,5
Female	27	35,5
Total	74	100

Table 2 describes the characteristics of patients based on sex, 47 patients with a percentage of 63.5% which is of male sex, and 27 patients with a percentage of 35.5% which is of female sex, with a total of 74 patients.

Tabel 3 Patient Characteristics Based on The Severity of The Stroke

Severity	n	%
1 Region affected	36	48,6
2 Regions affected	27	36,5
3 Regions affected	11	14,9
Total	74	100

Table 3 describes patient characteristics based on the number of regions affected, patients with 1 region affected as many as 36 patients with a percentage of 48.6%, patients with 2 regions affected as many as 27 patients with a percentage of 36.5% and patients with 3 regions affected as many as 11 patients with a percentage of 14.9% of the total 74 patients.

Tabel 4 Data sample distribution based on neutrophil, lymphocyte and NLR counts

	Neutrophil	Lymphocyte	NLR
Mean	71,78	18,68	8,27
Median	73,15	17,35	4,29

Based on table 4 above, it can be explained that the average value of the neutrophil count is 71.78%, the average of the lymphocyte count is 18.68% and the average ratio of neutrophil lymphocytes (RNL) is 8.27%. Then, it can also be seen that the median value of the neutrophil

count is 73.15, the median value of the lymphocyte count is 17.35 and the median value of the NLR is 4.29.

Tabel 5 NLR Relationship Test to The Severity of Stroke

NLR Against Number of Lesions	Mean ± SD	Sig (*P-Value*)
NLR to 1 Region Affected	7,277 ± 12,982	0,002
NLR to 2 Regions Affected	3,544 ± 6,945	0,013
NLR to 3 Regions Affected	1,777 ± 3,608	0,133

Table 6 explains the results of research on the relationship between NLR and the severity of Stroke. From the results of the research that has been done, results were obtained for NLR with 1 region affected having an average value of 7.277 and a standard deviation of 12.982 with a significance value of 0.002 < 0.05 which shows that NLR is associated with 1 region affected.

The results for NLR with 2 regions affected had a mean value of 3.544 and a standard deviation of 6.945 with a significance value of 0.013 < 0.05 indicating that NLR was associated with 2 regions affected.

The results for NLR with 3 regions affected had a mean value of 1.777 and a standard deviation of 3.608 with a significance value of 0.133 > 0.05 indicating that NLR was not associated with 3 regions affected.

Tabel 6 Mann – Whitney Test Results

Group	Sig
1 Region Affected with 2 Regions Affected	0,555
1 Region Affected with 3 Regions Affected	0,633
2 Regions Affected with 3 Regions Affected	0,936

Based on table 8 above, it is known that the Asymptotic Significance value for the patient group with 1 region affected with 2 regions affected is 0.555 > 0.05, which means there is no significant difference in NLR values between 1 region affected with 2 regions affected, then for the patient group with 1 region affected with 3 regions affected the Asymptotic Significance value is 0.633 > 0.05, which means there is no significant difference in NLR values between 1 region affected with 3 regions affected, and for the patient group with 2 regions affected with 3 regions affected the Asymptotic Significance value is 0.936 > 0.05, which means there is no significant difference in NLR values between 2 regions affected with 3 regions affected.

Discussion

Based on the data obtained it can be concluded that the age group that most often suffered from ischemic stroke was the group with an age range of >55 years, which was 67 patients (90.5%), which was then followed by the group with an age range of 30-50 years, which was 7 people (9.5%). This further proves the research previously conducted by (Yousufuddin & Young, 2019), which showed that about 3/4 cases of stroke occurred in the group with the age of ≥65 years. Other previous research has also shown that the incidence of stroke will increase 2-fold after the age of 55 years (Soto-Cámara et al., 2020). In this study, the sex group that most often suffered from ischemic stroke was the group with the male sex, which was 47 people (63.5%). This is in accordance with previous research which states that most ischemic stroke events occur more in men compared to women (Gibson, 2013). One of the reasons that men are more likely to be diagnosed with ischemic stroke is because there is usually a delay in diagnosis for women. It is reported that women delay three times longer than men in seeking care when stroke symptoms have already appeared (Gibson, 2013). Another reason is because of the

differences in the sex steroid hormones, mainly the estrogen hormone. This explanation is reinforced by sex differences in ischemic stroke in animal models (Haast et al., 2012). In addition, the hormone, estradiol in females has strong dilation effects on the vascular endothelial and promotes blood flow, whereas testosterone hormone in males has opposite effects that constrict the endothelial and decrease blood flow (Krause et al., 2006). Other reasons like genetic and anatomic factors may also contribute to sex-related differences in stroke epidemiology, pathophysiology, and clinical outcomes.

Sizes of arteries, heart and body size are smaller in women in comparison to men which leads to an enlarged left atrium, particularly in humans, and is associated with an increased risk for the start of a stroke (Abhayaratna et al., 2006).

Differences in the lifestyles such as the status of physical activities, types of food intake, social communications, and cigarette smoking can be a risk factor for stroke and might independently or together contribute to the occurrence of stroke.

With most patients being 1 region affected as many as 36 patients with a percentage of 48.6%, followed by patients with 2 regions affected as many as 27 patients with a percentage of 36.5% and lastly patients with 3 regions affected as many as 11 patients with a percentage of 14.9%.

It is to be noted that patients with region affected are classified by how many cerebral arteries are affected by using CT scan results of the brain, which then will be used to define the degree of severity based on the branches affected. There are three primary branches of arteries which is the anterior, medial, and posterior branch. It can be concluded that one region affected could also means only one branch of the central arteries are affected. For the highest degree of severity, we could see the involvement of all three primary arteries.

As to comparison with the NIHSS scoring system, same results were produced. According to NIHSS scoring what classifies as minor stroke was a score of lower than 5. This follows other works that stated TIA (transient ischemic attack) accounted for 30% of all acute ischemic cerebrovascular events, which is then followed by TIA combined with minor stroke which is 65% of all acute ischemic cerebrovascular events. Minor events are the most common type in ischemic cerebrovascular disease and may constitute a larger proportion than previously reported (Bushnell et al., 2018). The average number of neutrophils in the sample was 71.78%, which was a slight increase from normal neutrophil levels (40-60%). This increase in the number of neutrophils may occur due to the presence of infection or inflammatory processes (Riley & Rupert, 2015). It can also be seen that the average number of lymphocytes in the sample is 18.68% which is a slight decrease from normal levels of 20-40%.

In previous studies, it was stated that lymphocyte levels in ischemic stroke patients tended to decrease. This decreased lymphocyte level is associated with the patient's prognosis which will be poor later As for the average NLR in the sample was 8.27% which means higher than the normal level of around 0.78-3.53. Previous research has shown that elevated RNL levels are associated with an increased risk of short-term death and poor functional outcomes. NLR was not associated with 3 regions affected but was shown to be associated with 1 and 2 regions affected.

From the results of the research that has been done, NLR with 1 region affected having an average value of 7.277 and a standard deviation of 12.982 with a significance value of $0.002 < 0.05$ which shows that NLR is associated with 1 region affected.

NLR with 2 regions affected had a mean value of 3.544 and a standard deviation of 6.945 with a significance value of $0.013 < 0.05$ indicating that NLR was associated with 2 regions affected and NLR with 3 regions affected had a mean value of 1.777 and a standard deviation of 3.608 with a significance value of $0.133 > 0.05$ indicating that NLR was not associated with 3 regions affected.

Neuroinflammation after stroke can have a detrimental effect on the early-stage progression of ischemic brain injury. This neuroinflammation is mediated by the disruption of

the blood–brain barrier, which leads to brain edema and secondary ischemic brain damage (Kim et al., 2014).

NLR, which reflects the combined activities of neutrophils and lymphocytes, is an indicator of the inflammatory status of ischemic stroke patients. A higher NLR is associated with a more severe degree of inflammation, which may result in poorer functional outcomes as stated but our research shows a different outcome, with 3 regions affected or 3 branches of arteries affected showing a lower NLR values in contrast to 1 or 2 regions affected producing a higher NLR values.

The results further proves that there is no significant difference between NLR values with the severities of stroke. Thus, it can be said that the NLR values in regions 1, 2 and 3 are the same.

Much further proven again by the test which shows that there is no significant difference of NLR values between 1 region affected with 2 regions affected, 1 region affected with 3 regions affected, and 2 regions affected with 3 regions affected, which means that the NLR values increase alongside stroke ischemic in general not specifically with the arteries affected. This might be due to the lack of specification on our data about the onset of stroke, whether it has progressed in later stages, or it is on recent stages.

The present study has several limitations, including its observational and cross-sectional design, which only documents data at a single point of time, that makes it not suitable to follow stroke progression over time. Inclusion of patient only from a single hospital might also have resulted in a sampling bias. In addition, the data obtained did not specify the onset of stroke in patients, so whether it has progressed further or occurred was not known, which may help to better understand the relationship between inflammation and ischemic stroke. Furthermore, the NLR value was only measured at the time of hospital admission, the changes in NLR which reflects the time progress of neuroinflammation were not evaluated. The continuation in NLR measurement during their time in the hospital may help in overcoming this problem. Finally, since research regarding NLR varies and is relatively recent, more data might be required with different approach concerning this topic.

CONCLUSION

In conclusion, this study highlights the complex relationship between social media usage and adolescents' mental health. While social media platforms offer numerous benefits, including social connection and self-expression, excessive use can have detrimental effects on adolescents' psychological well-being. The prevalence of cyberbullying, social comparison, and fear of missing out (FOMO) underscores the importance of addressing the negative consequences of social media on mental health. Moreover, individual differences and socio-cultural factors significantly influence how adolescents perceive and engage with social media, emphasizing the need for personalized interventions. Moving forward, promoting digital literacy, fostering positive online behaviors, and providing adequate support systems are essential steps in mitigating the adverse impact of social media on adolescents' mental health.

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