Journal of Institute of Medicine Nepal
Institute of Medicine, Kathmandu, Nepal

OPEN ACCESS

Original Article

JIOM Nepal. 2025 Aug;47(2):11-16.

Neutrophil-to-Lymphocyte Ratio in Predicting Outcomes of Patients with Aneurysmal Subarachnoid Hemorrhage in a Tertiary Care Hospital in Nepal

Deepika Rijal, Sujan Paudel, Prajjwol Luitel, Bishwa Deepak Rijal, Gopal Sedain, Sushil Krishna Shilpakar, Mohan Raj Sharma

Author(s) affiliation

Department of Neurosurgery, Maharajgunj Medical Campus, Tribhuvan University Teaching Hospital, Institute of Medicine, Kathmandu, Nepal

Corresponding author

Deepika Rijal, MBBS, MS
deepika.rijal91@gmail.com

ABSTRACT

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH), caused by a ruptured intracranial aneurysm, results in high mortality and disability rates. The Neutrophil-to-lymphocyte ratio (NLR), a simple yet effective marker, holds potential as a valuable prognostic tool, especially in the context of low and middle income countries. The primary aim of study was to predict the outcomes of aSAH patients by modified Rankin Scale (mRS) in 3 months based on admission NLR.

Methods

This observational study was conducted at Tribhuvan University Teaching Hospital from June 2022 to August 2023. Patients with aSAH presenting to the Emergency Department within 72 hours of symptoms were included. Hematological investigations and non-contrast computed tomography of the head were performed. Outcomes were assessed using the mRS after three months.

Results

A total of 51 patients were included. The mean age of the study population was 54.1±13.4 years (Range 25 to 80 years). The most common age group was 50-59 years. Female-to-male ratio was 2.9:1 Patients with poor outcomes had significantly higher admission NLR (7.1±4.7) compared to those with good outcomes (3.7±1.9) (p=0.001). Elevated NLR was significantly associated with worse outcomes at three months (p = 0.001). NLR ≥ 3.63 predicted poor prognosis with 87.5% sensitivity.

Conclusion

This study highlights the utility of NLR in predicting outcomes in aSAH, providing an easy-to-access prognostic marker for risk stratification. The findings are relevant in developing countries, where financial and logistical constraints limit access to advanced neuroimaging and continuous monitoring.

Keywords

Aneurysmal subarachnoid hemorrhage; modified Rankin scale; neutrophil-to-lymphocyte ratio; outcome

DOI
10.59779/jiomnepal.1397

Submitted
May 31, 2025

Accepted
July 30, 2025

INTRODUCTION

Aneurysmal subarachnoid hemorrhage (aSAH), resulting from the rupture of an intracranial aneurysm, representing nearly 80% of nontraumatic subarachnoid hemorrhages (SAHs) is a severe cerebrovascular disease accounting for approximately 25% of stroke deaths.[1] The global incidence of spontaneous SAH varies between 2 to 20 cases per 100,000 individuals, with the United States exhibiting an incidence of approximately 10 per 100,000 individuals annually.[2]

Prior studies have demonstrated that bleeding in the subarachnoid space can trigger systemic inflammatory reactions, leading to leukocytosis and lymphopenia in about 60% cases. This immune activation is often accompanied by platelet activation, which contributes to early brain damage, rebleeding, vasospasm, and delayed cerebral ischemia.[3-7] Elevated neutrophil and diminished lymphocyte counts observed at the time of admission have been correlated with the onset of delayed cerebral ischemia and poor clinical outcomes in patients with aSAH. The neutrophil-to-lymphocyte ratio (NLR) has emerged as a significant prognostic marker in this context.[8]

The neutrophil-to-lymphocyte ratio (NLR), calculated by dividing absolute neutrophil count (ANC) by the absolute lymphocyte count (ALC), is a novel, simple, and cost-effective biomarker of systemic inflammation. It has demonstrated superior prognostic value compared to leukocyte count alone in various conditions like cancer, cardiac disease, stroke, and sepsis.[3,9,10] In the context of aneurysmal subarachnoid hemorrhage (aSAH), several studies have reported that an elevated NLR at admission is associated with higher modified Rankin Scale (mRS) scores and poor prognosis at three months. However, other studies have found no significant correlation between elevated NLR and clinical outcomes.[9,10,11] This inconsistency underscores the need for further research to clarify the prognostic role of NLR in aSAH which is the primary objective of present study.

METHODS

This prospective observational study conforms to the ethical guidelines of the Declaration of Helsinki 2013 and has been reported in line with the Strengthening the reporting of cohort studies in surgery (STROCSS) criteria.

This study was conducted at the Department of Neurosurgery of Tribhuvan University Teaching Hospital, Kathmandu, a tertiary level referral center in, Nepal.

Data collection spanned from June 2022 to August 2023, with approval from the Institutional Review Committee of the IOM (IRC Reference no: 483 (6-11)E2 078/079). Prior informed consent was obtained from all participants.

Patients over 18 years of age, regardless of gender, ethnicity or geographic location who presented to the emergency department within 72 hours of symptoms onset and underwent surgical or interventional management for subarachnoid hemorrhage secondary to ruptured intracranial aneurysm, were included. Exclusion criteria compromised patients with traumatic SAH, a history of infection or stroke within preceding eight weeks, underlying malignancy, severe renal or hepatic disease, or a known auto-immune or hematologic disorder. Additionally individuals who declined to provide informed consent and lost to follow up within three months were left out of the study.

Sample size of 51 was calculated using formula

$$n = z^2pq/d^2$$

with p=22%, q=100-22 = 78, Z at 90% C.I.= 1.96, d=10% and drop out of 10%. Prevalence of NLR (6 and above) was taken as 22% from the previous study.[13]A consecutive sampling method was utilized to select the required sample.

Upon arrival at the Emergency Department (ED), patients were assessed for vital functions and level of consciousness using the Glassgow Coma Scale (GCS). Initial stabilization included interventions such as rapid sequence intubation (RSI), fluid resuscitation, and administration of vasopressors as needed. Following stabilization, baseline laboratory investigations including hematological and biochemical profiles were performed along with the non-contrast Computed Tomography (NCCT) of head which confirmed the aneurysmal subarachnoid hemorrhage, prompting hospital admission.

Blood pressure was managed in accordance with American Heart Association (AHA) and the American Stroke Association (ASA) guidelines, aiming for 160/90 mmHg using intravenous antihypertensive medications. Intracranial pressure (ICP) control was implemented for patients with reduced consciousness or signs of cerebral herniation. Management strategies included head elevation, sedation, administration of mannitol or hypertonic saline, and neuromuscular blockade. In refractory cases barbiturates were employed, and hyperventilation was used temporarily to reduce ICP.

Deep Vein thrombosis (DVT) prophylaxis with low-dose low molecular weight heparin was initiated after ruling out any active bleeding or significant risk of hemorrhage. Seizure prophylaxis was administrated in patients with clinical or electrographic seizures. Surgical interventions included placement of External ventricular drain (EVD) or decompressive craniectomy with aneurysm clipping.

ICU and hospital stay durations were recorded, and patients were followed up at 3 months either through out-patient visits or telephonic interviews. Functional outcomes were assessed using the modified Rankin Scale (mRS) based on semi-structured interviews with patients or their caregivers.In this study patient was said to have poor prognosis if they met any of the following criterias;[14]

a. mRS score ≥ 3 at three months, indicating moderate to severe disability or death,
b. mortality within 30 days of admission or during hospital stay,
c. requirement of prolonged mechanical ventilation (>7 days) or ICU stay,
d. development of severe complications such as rebleeding, vasospasm,multiorgan failure

Also favourable outcome is defined as mRS score of 0-2 indicating full recovery or slight disability but independent in daily activities. Unfavorable outcome is defined as mRS score of 3–6, reflecting moderate to severe disability or death.

Study Variables

Data were systematically collected and entered into the pro forma. The surgical resident documented all the data in a patient proforma, which was later aggregated into a Microsoft Excel spreadsheet (Microsoft Corporation, Redmond, USA). Both continuous and categorical variables were evaluated, encompassing age, sex, GCS upon admission, ANC, ALC, NLR, and mRS at 3 months post-intervention.

Patients were categorized according to their prognosis at 3 months for the purpose of analysis (mRS score 0–2 versus mRS score 3–6). Categorical variables were represented as numbers and percentages and analyzed using the Chi square or Fisher's exact test. Continuous variables were presented as mean±standard deviation (SD) or median with interquartile range (IQR) and analyzed through the Mann-Whitney U test. Independent predictors of aSAH prognosis were identified via univariate analysis alongside multivariate logistic regression analysis.

In order to identify the independent predictors correlated with adverse outcomes at three months, variables exhibiting $p<0.05$ in the univariate analysis were included into the multivariate logistic regression model. In the concluding multivariate model, a predictive variable demonstrating $p<0.05$ was considered to have a significant correlation. Furthermore, the relationship between NLR and adverse outcomes in aSAH was assessed utilizing a receiver operating characteristics curve (ROC), with the optimal cut-off value for prognostic prediction determined. Analyses were conducted utilizing SPSS version 24.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 54 patients were enrolled in the study. Three patients were lost to follow up and subsequently excluded leaving 51 patients for final analysis.

The mean age of the study population was 54.1±13.4 years (Range 25 to 80 years). The most common age group was 50-59 years. Female-to-male ratio was 2.9:1. The most common presenting complaint

Table 1. *Patient characteristics*

Characteristics		Total (n=51)	mRS score at 3 months		p-value
			0-2 (n=27)	3-6 (n=24)	
Age (years)		54.1±13.4	51.9 ± 11.7	56.5 ± 15	0.23
Sex	Female	38 (74%)	19 (70.4%)	19 (79.2%)	
	Male	13 (26%)	8 (29.6%)	5 (20.8%)	
Clinical Data	Hypertension	17 (33.34%)	10 (37%)	7 (29.2%)	0.55
	Co-morbidities	19 (37.26)	12 (44.4%)	7 (29.2%)	0.26
Laboratory investigations	Neutrophils (10^2 cells/mm^3)	74.4 ±10.1	69.7 ±10.8	79.7± 7.0	0.003*
	Lymphocytes (10^2 cells/mm^3)	19.3 ± 9.8	15.25 ± 8.8	15.25 ± 8.8	0.004*
	NLR		3.7±1.9	7.1±4.7	0.001*
GCS score	3-8	3 (5.88%)	1 (3.7%)	2 (8.3%)	0.006*
	9-12	10 (19.61%)	1 (3.7%)	9 (37.5%)	
	13-15	38 (74.5%)	25 (92.6%)	13 (54.2%)	

was severe headache in 92% of patients, vomiting in 59%, and loss of consciousness in 49% (Table 1). The majority of patients had aneurysmal rupture involving the anterior communicating artery(37%), followed by the middle cerebral artery in 27% of cases. Less commonly involved vessels included the anterior cerebral and posterior cerebral arteries. Of the total, 49 patients underwent craniotomy with microsurgical clipping of the aneurysm. One patient underwent endovascular coil embolization, and another deferred surgical intervention despite repeated counseling. The duration of ICU stay ranged from 3 to 70 days. Common complications observed included ventilator-associated pneumonia, sepsis, urinary tract infection, pressure sores, and ventilator-dependent syndrome. Four patients required tracheostomy due to prolonged ventilator dependency and four patient expired during treatment in the hospital.

The group with bad outcomes compared to good outcomes had significantly higher ANC (79.7 vs 69.7) 10^2 cells/mm^3, lower ALC (15.25 vs 22.89) 10^2 cells/mm^3, NLR (7.1 vs 3.7) and lower GCS (Table 1). Mean age, sex, comorbidities were not significantly different among those with good (52%) and bad outcomes (48%).

Given that neutrophils and lymphocytes were related to the NLR, these variables were excluded from the multivariable logistic regression model. Following adjustment, a high NLR upon admission was identified as an independent predictor of poor prognosis in patients with aneurysmal subarachnoid hemorrhage (aSAH) (OR 1.43, 95% CI 1.06-1.9; p=0.02).

In the ROC curve, NLR of 3.63 was identified as the best cut-off value for distinguishing 3 months favorable and unfavorable outcomes [area under the curve (AUC) 0.778, sensitivity 87.5%, specificity 59.3%] (Figure 1).

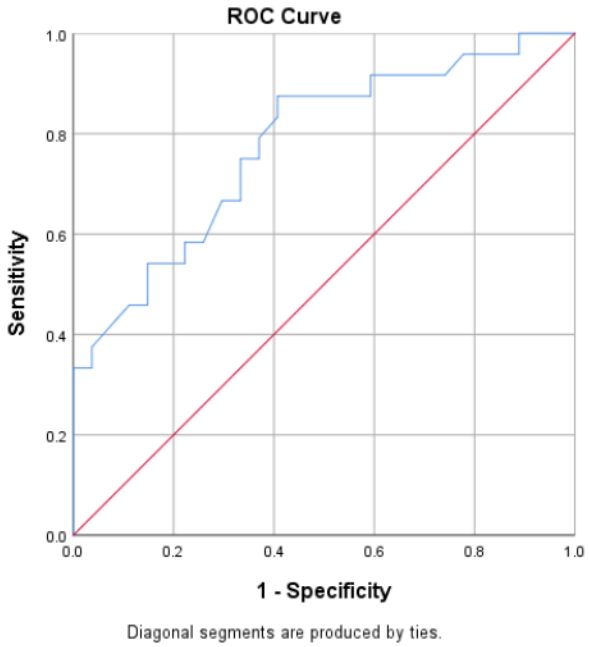

Figure 1. *Receiver operating characteristics (ROC) curve analysis for best cut off value of neutrophil-to-lymphocyte ratio (NLR) on functional outcome in patients with aneurysmal subarachnoid hemorrhage*

DISCUSSION

Our findings demonstrated that patients with poor outcomes during the 3-month follow-up (mRS >3) had a higher admission NLR values (7.1 ± 4.7) compared to those with good outcomes (3.7 ± 1.9). However, a higher NLR showed no association with lower GCS at admission , contrary to previous studies[15,16,17]. Lymphocytes, as key regulator of chronic inflammation, typically decline at the acute phase of aSAH and subsequently rise in response to increasing neutrophil levels. Lymphocytopenia resulting from aSAH-induced immunosuppression may predispose patients to infectious complications and contribute to poorer prognosis.[18]

aSAH triggers leukocytosis and and rapid neutrophil aggregation at the microvascular endothelium occurring within minutes of hemorrhage onset. This cascade damages the blood-brain barrier and promotes secondary brain injury through the release of reactive oxygen species, cathepsin, matrix metalloproteinases, and NETs.[19,20] Such inflammatory response have been implicated in aneurysm progression and rupture, with histological evidence linking leukocytosis with thinning of aneurysm wall.[11] These findings highlight the potential of targeted therapies aimed at inhibiting neutrophil activity and modulate T lymphocyte function and reduce neuroinflammation to improve patient outcomes following aSAH.[19]

Compared to neutrophil, thrombocyte, or lymphocyte counts, NLR offers a more comphrensive reflection of both proinflammatory and immunosuppressive states. It offers greater prognostic utility than traditional hematological and demonstrates superior stability, being less influenced by factors such as overhydration, dehydration, or variability in blood specimen handling.[21] Elevated NLR levels have been shown to correlate with greater neurological injury severity, including higher modified Fisher Scale scores and presence of intraventricular hemorrhage in patients with NLR values exceeding 7.05.[1,10,19,22] Notably, unlike earlier research, our study did not find a significant association between higher NLR and lower Glasgow Coma Scale (GCS) scores at admission.[14] The ROC analysis of our study demonstrated the sensitivity of 87.5% and a comparable specificity of 59.3% which is among the highest sensitivities reported in existing literature,

reinforcing NLR as an independent predictor of poor outcomes at 3 months post-aSAH.[19]

Furthermore combining NLR with additional parameters such as the modified Fisher score or the platelet-to-lymphocyte ratio (PLR), may enhance the predictive accuracy of for clinical outcomes in aSAH. This multimodal approach could improve both the sensitivity and specificity of prognostication tools, thereby increasing their clinical relevance.[19]

However, several limitations must be considered when interpreting our findings. The study was limited by a relatively small sample size and an imbalance in outcome groups with fewer patients experiencing poor outcomes. Propensity score matching was not applied to adjust for potential confounding variables. As a single-center study, results may subject to select and institutional bias. Additionally, variability in the definition of "elevated NLR" across studies due to ethnic variation and comorbid conditions pose a challenge in establishing a universally accepted cutoff value. Conditions like hypertension and diabetes mellitus can affect NLR, though we minimized bias by incorporating these factors into multiple regression models. Therapeutic drugs like nimodipine and vasopressors may also influence NLR values. However, despite these limitations, our findings remain aligned with prior research that supports NLR as an independent predictor of poor outcomes in aSAH patients.

CONCLUSION

Patients with poor outcomes demonstrated significantly higher absolute neutrophil counts, lower absolute lymphocyte counts, higher neutrophil-to-lymphocyte ratio, and lower Glasgow Coma Scale scores during admission compared to those with favorable outcomes. Receiver Operating Characteristic (ROC) analysis revealed that NLR had highest sensitivity (87.5%) and a comparable specificity (59.3%) supporting its role as an independent predictor of adverse outcomes at 3 months.This study thus highlights the utility of NLR in predicting outcomes in aSAH, providing an easy-to-access prognostic marker for risk stratification. The incorporation of NLR into routine practice offers a practical tool for early identification of high-risk patients and more efficient allocation of limited healthcare resources.

FINANCIAL SUPPORT

The author(s) did not receive any financial support for the research and/or publication of this article.

CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

Study concept and design: NO, BK, SP, RB. Data collection: NO, BK, SP, RB, AG, AS. Analysis and interpretation of data: NO, SP, AG. Drafting of the manuscript: NO, SP, AG. All the authors read and approved the final manuscript.

REFERENCES

1. Guo Y, Liu J, Zeng H, et al. Neutrophil to lymphocyte ratio predicting poor outcome after aneurysmal subarachnoid hemorrhage: A retrospective study and updated meta-analysis. Front Immunol. 2022;13. doi:10.3389/fimmu.2022.962760.
2. Abraham MK, Chang WTW, et al. Subarachnoid hemorrhage. Emerg Med Clin North Am. 2016;34(4):901–16. doi:10.1016/j.emc.2016.06.011.
3. Wang JY, Zhang XT, Wang JQ, et al. Admission neutrophil–lymphocyte ratio predicts rebleeding following aneurysmal subarachnoid hemorrhage. World Neurosurg. 2020;138:e317–22. doi:10.1016/j.wneu.2020.02.112.
4. Schievink WI, Wijdicks EFM, Parisi JE, et al. Sudden death from aneurysmal subarachnoid hemorrhage. Neurology. 1995;45(5):871–4. doi:10.1212/wnl.45.5.871.
5. Lattanzi S, Brigo F, Trinka E, et al. Neutrophil-to-lymphocyte ratio in acute cerebral hemorrhage: a system review. Transl Stroke Res. 2019;10(2):137–45. doi:10.1007/s12975-018-0649-4.
6. Yun S, Yi HJ, Lee DH, et al. Systemic inflammation response index and systemic immune-inflammation index for predicting prognosis of patients with aneurysmal subarachnoid hemorrhage. J Stroke Cerebrovasc Dis. 2021;30(8):105861. doi:10.1016/j.jstrokecerebrovasdis.2021.105861.
7. Srinivasan A, Aggarwal A, Gaudihalli S, et al. Impact of early leukocytosis and elevated high-sensitivity C-reactive protein on delayed cerebral ischemia and neurologic outcome after subarachnoid hemorrhage. World Neurosurg. 2016;90:91–5. doi:10.1016/j.wneu.2016.02.049.
8. Wu Y, He Q, Wei Y, et al. Association of neutrophil-to-lymphocyte ratio and delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage: possible involvement of cerebral blood perfusion. Neuropsychiatr Dis Treat. 2019;15:1001–7. doi:10.2147/NDT.S190477.
9. Al-Mufti F, Amuluru K, Damodara N, et al. Admission neutrophil–lymphocyte ratio predicts delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. J Neurointerv Surg. 2019;11(11):1135–40. doi:10.1136/neurintsurg-2019-014759.
10. Giede-Jeppe A, Reichl J, Sprügel MI, et al. Neutrophil-to-lymphocyte ratio as an independent predictor for unfavorable functional outcome in aneurysmal subarachnoid hemorrhage. J Neurosurg. 2020;132(2):400–7. doi:10.3171/2018.9.JNS181975.
11. Lai X, Zhang W, Ye M, et al. Development and validation of a predictive model for prognosis in aneurysmal subarachnoid hemorrhage. J Clin Lab Anal. 2020;34(12):e23542. doi:10.1002/jcla.23542.
12. Mathew G, Agha R, Albrecht J, et al. STROCSS 2021: Strengthening the reporting of cohort, cross-sectional and case-control studies in surgery. Int J Surg. 2021;96:106165. doi:10.1016/j.ijsu.2021.106165.
13. Tao C, Wang J, Hu X, et al. Clinical value of neutrophil to lymphocyte and platelet to lymphocyte ratio after aneurysmal subarachnoid hemorrhage. Neurocrit Care. 2017;26(3):393–401. doi:10.1007/s12028-016-0332-0.
14. Banks JL, Marotta CA, et al. Outcomes validity and reliability of the modified Rankin scale: Implications for stroke clinical trials. Stroke. 2007;38(3):1091–6. doi:10.1161/01.STR.0000258355.23810.c6.

15. Jamali SA, Turnbull MT, Kanekiyo T, et al. Elevated neutrophil-lymphocyte ratio is predictive of poor outcomes following aneurysmal subarachnoid hemorrhage. J Stroke Cerebrovasc Dis. 2020;29(4):104631. doi:10.1016/j.jstrokecerebrovasdis.2019.104631.
16. Kasius KM, Frijns CJM, Algra A, et al. Association of platelet and leukocyte counts with delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage. Cerebrovasc Dis. 2010;29(6):576–83. doi:10.1159/000306645.
17. Tam AKH, Ilodigwe D, Mocco J, et al. Impact of systemic inflammatory response syndrome on vasospasm, cerebral infarction, and outcome after subarachnoid hemorrhage: exploratory analysis of CONSCIOUS-1 database. Neurocrit Care. 2010;13(2):182–9. doi:10.1007/s12028-010-9402-x.
18. Sarrafzadeh A, Schlenk F, Meisel A, et al. Immunodepression after aneurysmal subarachnoid hemorrhage. Stroke. 2011;42(1):53–8. doi:10.1161/STROKEAHA.110.594705.
19. Cai L, Zeng H, Tan X, et al. Role of the blood neutrophil-to-lymphocyte ratio in aneurysmal subarachnoid hemorrhage. Front Neurol. 2021;12. doi:10.3389/fneur.2021.671098.
20. Hanhai Z, Bin Q, Shengjun Z, et al. Neutrophil extracellular traps promote microglia inflammation and contribute to poor outcome in subarachnoid hemorrhage. Aging (Albany NY). 2021;13(9):13108–23. doi:10.18632/aging.202993.
21. Balta S, Ozturk C, et al. Platelet-lymphocyte ratio: a simple, inexpensive and rapid prognostic marker for cardiovascular events. Platelets. 2015;26(7):680–1. doi:10.3109/09537104.2014.979340.
22. Chang JJ, Dowlati E, Triano M, et al. Admission neutrophil to lymphocyte ratio for predicting outcome in subarachnoid hemorrhage. J Stroke Cerebrovasc Dis. 2021;30(9):105936. doi:10.1016/j.jstrokecerebrovasdis.2021.105936.