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PREDICTIVE VALIDITY OF NEUTROPHIL TO PLATELET RATIO FOR RISK OF HEMORRHAGIC TRANSFORMATION IN ACUTE ISCHEMIC STROKE

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ABSTRACT

Background: Acute ischemic stroke is a major neurological emergency with significant morbidity and mortality. Haemorrhagic transformation (HT) is a serious complication that worsens outcomes. The neutrophil-to-platelet ratio (NPR) has emerged as a potential biomarker reflecting the balance between inflammation and haemostasis, which may help predict the risk of HT. Aims And Objectives: To study the correlation of neutrophil-to-platelet ratio with haemorrhagic transformation in patients with acute ischemic stroke. Methodology: This hospital-based cross-sectional study was conducted over 2 years at Department of General Medicine, Pacific Institute of Medical Sciences, Umarda, Udaipur, Rajasthan. A total of 70 patients with acute ischemic stroke were included. Clinical details, imaging findings, and laboratory parameters including NPR were recorded. Patients were evaluated for development of haemorrhagic transformation using CT/MRI. Statistical analysis was performed using appropriate tests, with $p < 0.05$ considered significant. **Results:** Among 70 patients, 64.3% were males and the mean age was 58.5 ± 10.66 years, with the majority (>60 years) comprising 60% of cases. Common comorbidities included hypertension (61.4%) and diabetes (52.9%). Haemorrhagic transformation occurred in 22.9% of patients. Severe stroke (NIHSS ≥21) showed a significant association with HT ($p = 0.002$). HT was more common in anterior circulation strokes compared to posterior circulation (31.3% vs 4.5%, $p = 0.01$). The median NPR was significantly higher in patients with HT (43.37) compared to those without HT (29.91) ($p = 0.008$). ROC analysis demonstrated that NPR had good predictive value for HT (AUC = 0.72, $p = 0.001$). **Conclusion:** Neutrophil-to-platelet ratio is a simple, cost-effective, and significant predictor of haemorrhagic transformation in acute ischemic stroke. Higher NPR values are associated with increased risk of HT and may aid in early risk stratification and clinical decision-making.

INTRODUCTION

Acute ischemic stroke is a neurological emergency caused by an abrupt reduction or complete cessation of blood flow to a specific region of the brain, most commonly due to arterial occlusion from thrombosis or embolism. [1] This sudden interruption in cerebral perfusion initiates a complex ischemic cascade beginning with cellular energy failure and depletion of adenosine triphosphate, leading to dysfunction of membrane ion pumps, neuronal depolarization, and excessive release of excitatory neurotransmitters such as glutamate. [2] The resultant influx of calcium ions triggers mitochondrial dysfunction, oxidative stress, and activation of apoptotic and necrotic pathways, culminating in irreversible neuronal injury and cell death. Within the affected brain tissue, a central infarct core develops where damage is permanent, surrounded by an ischemic penumbra that remains metabolically compromised yet structurally viable for a limited period. This penumbral zone represents the principal target for acute reperfusion therapies aimed at salvaging threatened tissue. [3] The severity of neurological deficits and final infarct volume are influenced by multiple factors, including the duration of ischemia, adequacy of collateral circulation, systemic physiological status, and the timeliness of reperfusion. Clinically, acute ischemic stroke manifests as sudden-onset focal neurological deficits such as hemiparesis, aphasia, visual disturbances, or altered consciousness, and prompt neuroimaging is essential to confirm the diagnosis, exclude intracranial haemorrhage, and guide appropriate acute management. [4]"

Within this pathophysiological framework, haemorrhagic transformation emerges as a frequent and potentially devastating complication of acute ischemic stroke. It is characterized by extravasation of blood into previously ischemic brain tissue and represents a pathological continuum ranging from small petechial haemorrhages to large parenchymal hematomas associated with mass effect and neurological deterioration. [5] The development of haemorrhagic transformation is closely linked to ischemia-induced disruption of the blood–brain barrier, resulting from endothelial cell injury, degradation of the extracellular matrix, and loss of tight junction integrity. These structural changes are driven by a combination of inflammatory mediators, oxidative stress, and activation of matrix metalloproteinases, which collectively weaken the cerebral microvasculature. [6] Reperfusion of ischemic tissue, whether spontaneous or achieved through thrombolysis or mechanical thrombectomy, may further amplify this risk by exposing already damaged vessels to sudden increases in blood flow and intravascular pressure. Several clinical and radiological factors have been consistently associated with haemorrhagic transformation, including large infarct size, severe neurological deficit at presentation, cardioembolic stroke etiology, hyperglycaemia, advanced age, and the use of reperfusion therapies. The occurrence of haemorrhagic transformation has major prognostic implications, as it is associated with worsening neurological outcomes, restrictions on secondary prevention strategies, and increased mortality. [7]

In this context, the neutrophil to platelet ratio has emerged as a simple yet informative inflammatory biomarker that reflects the dynamic balance between systemic inflammation and haemostatic function in acute ischemic stroke. Neutrophils are among the earliest immune cells recruited to ischemic brain tissue and play a pivotal role in secondary injury through the release of proinflammatory cytokines, reactive oxygen species, and proteolytic enzymes. These substances exacerbate endothelial damage and contribute directly to blood–brain barrier disruption. Platelets, conversely, are essential for maintaining vascular integrity and effective haemostasis, while also participating in complex interactions with leukocytes and endothelial cells that modulate thromboinflammatory responses. An elevated neutrophil to

platelet ratio therefore signifies a state of heightened inflammatory activity coupled with relative impairment of platelet-mediated vascular protection, suggesting increased vulnerability of the cerebral microvasculature to injury and bleeding. [8,9]

The predictive validity of the neutrophil to platelet ratio for assessing the risk of haemorrhagic transformation in acute ischemic stroke lies in its ability to capture this underlying inflammatory–haemostatic imbalance that drives post-ischemic vascular damage. [10] Elevated neutrophil to platelet ratios at admission have been shown to be independently associated with a higher incidence of haemorrhagic transformation, including symptomatic forms, particularly in patients undergoing reperfusion therapies. Excessive neutrophil activation promotes endothelial dysfunction and degradation of the basal lamina, while reduced platelet numbers or function compromise the capacity to maintain vascular integrity during reperfusion. Together, these mechanisms create a biological milieu conducive to blood extravasation into ischemic brain tissue. [11] As a readily available, inexpensive, and reproducible parameter derived from routine laboratory testing, the neutrophil to platelet ratio offers practical utility for early risk stratification in acute ischemic stroke. When integrated with established clinical, laboratory, and imaging predictors, it may aid in identifying patients at higher risk for haemorrhagic complications, informing therapeutic decisions, and guiding closer clinical monitoring. [12] Nevertheless, despite its promise, the neutrophil to platelet ratio should be interpreted cautiously, and further large-scale prospective studies are required to validate its predictive accuracy, establish standardized cutoff values, and clarify its role in personalized management strategies for acute ischemic stroke."

With this background the present study was planned to study the predictive validity of neutrophil to platelet ratio for risk of hemorrhagic transformation in acute ischemic stroke at a tertiary care hospital.

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted in the Department of General Medicine, Pacific Institute of Medical Sciences, Umarda over a period of two years following approval from the Institutional Ethics Committee. A total of 70 patients with newly diagnosed acute ischemic stroke were enrolled after obtaining written informed consent. Adult patients of either sex with radiologically confirmed ischemic stroke were included, while those with intracranial hemorrhage, central nervous system infections, malignancy, hematological disorders affecting platelet count, or active systemic infections were excluded. Detailed clinical history, demographic data, vascular risk factors, and neurological examination findings were recorded using a predesigned proforma. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS). All patients underwent neuroimaging (non-contrast computed tomography or magnetic resonance imaging) at admission to confirm diagnosis and detect hemorrhagic transformation; repeat imaging was performed on day 4 in selected cases. Blood samples were collected at admission for complete blood count, and the neutrophil-to-platelet ratio (NPR) was calculated. Patients were managed as per standard institutional protocols. Data were analyzed using SPSS version 25.0, with quantitative variables expressed as mean ± standard deviation and qualitative variables as proportions. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 70 patients with Acute Ischemic Stroke were analyzed and their Nutrophil to Platelet Ratio was calculated to check it's co relation with Hemorrhagic Transformation

Table 1. Distribution of patient according to Hemorrhagic Transformation

Haemorrhagic transformation	Frequency (n)	Percentage (%)
Present	16	22.9
Absent	54	77.1
Total	70	100

Table 1 show the distribution of patients according to haemorrhagic transformation. Haemorrhagic transformation of acute ischemic stroke was present in 16 (22.9%) patients in our study.

Table 2. Association between Gender and Hemorrhagic Transformation

Gender	Haemorrhagic transformation		p-value*
	Present n (%)	Absent n (%)	
Males	12 (26.7)	33 (73.3)	0.31
Females	04 (16)	21 (84)	
Total	16 (22.9)	54 (77.1)	

Table 2 shows the association between gender and haemorrhagic transformation. Haemorrhagic transformation was present in 12 (26.7%) male patients and four (16%) female patients, while it was absent in 33 (73.3%) male patients and 21 (84%) female patients. The association between gender and haemorrhagic transformation was not statistically significant (p = 0.31).

Table 3. Association between Age and Hemorrhagic Transformation

Age	Haemorrhagic transformation		p-value*
	Present n (%)	Absent n (%)	
18 to 30 years	00 (00)	02 (100)	0.63
31 to 45 years	01 (11.1)	08 (88.9)	
46 to 60 years	05 (29.4)	12 (70.6)	
> 60 years	10 (23.8)	32 (76.2)	
Total	16 (22.9)	54 (77.1)	

Table 3 shows the association between age and haemorrhagic transformation. Haemorrhagic transformation was present in one (11.1%) patients aged 31 to 45 years, five (29.4%) patients aged 46 to 60 years and 10 (23.8%) patients aged more than 60 years. It was absent in two (100%) patients in the age group of 18 to 30 years, eight (88.9%) patients aged 31 to 45 years, 12 (70.6%) patients aged 46 to 60 years and 32 (76.2%) patients aged more than 60 years. The association between age and haemorrhagic transformation was not found statistically significant (p = 0.63).

Table 4. Association between Severity of Stroke based on NIHSS score and Haemorrhagic Transformation

Severity of stroke based on NIHSS	Haemorrhagic transformation		p-value*
	Present n (%)	Absent n (%)	
Mild (1 to 4)	00 (00)	03 (100)	0.002
Moderate (5 to 15)	00 (00)	08 (100)	
Moderate to Severe (16 to 20)	01 (3.8)	25 (96.2)	
Severe (21 to 42)	15 (45.5)	18 (54.5)	
Total	16 (22.9)	54 (77.1)	

Table 4 shows the association between severity of stroke based on NIHSS score and haemorrhagic transformation. Haemorrhagic transformation was not present in any patient with mild stroke (NIHSS score 1 to 4) and moderate stroke (NIHSS score 5 to 15). It was present in one (3.8%) patient with moderate to severe stroke (NIHSS score 16 to 20) and 15 (45.5%) patients with severe stroke (NIHSS score 21 to 42). Among patients without haemorrhagic transformation, three (100%) had mild stroke, eight (100%) had moderate stroke, 25 (96.2%) had moderate to severe stroke and 18 (54.5%) had severe stroke. The association between severity of stroke based on NIHSS score and haemorrhagic transformation was found statistically significant (p = 0.002).

Table 5. Association between Location of ischemia and Haemorrhagic Transformation

Location of Ischemia	Haemorrhagic transformation		p-value*
	Present n (%)	Absent n (%)	
Anterior circulation	15 (31.3)	33 (68.8)	0.01
Posterior circulation	01 (4.5)	21 (95.5)	
Total	16 (22.9)	54 (77.1)	

Table 5 shows the association between location of ischemia and haemorrhagic transformation. Haemorrhagic transformation was present in 15 (31.3%) patients with anterior circulation ischemia and in one (4.5%) patients with posterior circulation ischemia. It was absent in 33 (68.8%) patients with anterior circulation involvement and 21 (95.5%) patients with posterior circulation involvement. The association between location of ischemia and haemorrhagic transformation was found statistically significant **(p = 0.01).**

Table 6. Association between Neutrophil-to-Platelet Ratio (NPR) and Haemorrhagic Transformation

Variable	Haemorrhagic transformation		p-value*
	Present (Median IQR)	Absent (Median IQR)	
NPR	43.37 17.99	29.91 15.66	0.008

Table 6 shows the association between neutrophil-to-platelet ratio (NPR) and haemorrhagic transformation. Since NPR was non-normally distributed, Mann Whitney U test was used. The median NPR was significantly higher among patients with haemorrhagic transformation (43.37 17.99) as compared to patients without haemorrhagic transformation (29.91 15.66). The difference between NPR among patients with haemorrhagic transformation and without haemorrhagic transformation was statistically significant (p = 0.008).

Table 7. ROC Analysis of NPR for Prediction of Haemorrhagic transformation

Parameter	Area under curve (AUC)	p-value*
NPR	0.72	0.001

**p-value < 0.05 statistically significant*

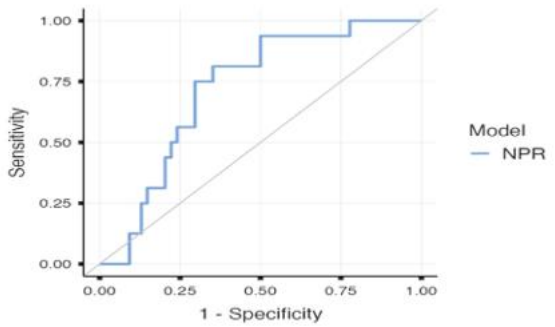

Figure. ROC Curve of NPR for Prediction of Haemorrhagic Transformation

Table 8. Statistical Analysis of NPR for Prediction of Haemorrhagic Transformation

Parameter	Sensitivity	Specificity	PPV	NPV	Accuracy
NPR	81.3 %	64.8 %	40.6 %	92.1 %	68.6 %

Tables 7, 8 and the figure above show the ROC analysis, statistical analysis and ROC curve for prediction of haemorrhagic transformation. The area under curve (AUC) was 0.72 and was statistically significant (**p = 0.001**). The sensitivity and specificity of NPR for prediction of haemorrhagic transformation was 81.3% and 64.8% respectively. The positive and negative predictive value of NPR were 40.6% and 92.1% respectively. The diagnostic accuracy of NPR for predicting haemorrhagic transformation of acute ischemic stroke was 68.6%."

DISCUSSION

Acute ischemic stroke remains one of the leading causes of mortality and long-term disability worldwide, posing a substantial burden on healthcare systems, particularly in developing countries. Despite advances in early diagnosis and management, haemorrhagic transformation continues to be a serious and potentially life-threatening complication of ischemic stroke. It not only worsens neurological outcomes but also limits the use of reperfusion therapies such as thrombolysis and anticoagulation. Therefore, early identification of patients at increased risk for haemorrhagic transformation is of paramount importance for optimizing management strategies and improving prognosis.

In recent years, there has been growing interest in the role of inflammatory and haematological markers in the pathogenesis and progression of acute ischemic stroke. Inflammation plays a central role in ischemic brain injury, contributing to blood–brain barrier disruption, endothelial damage, and increased vascular permeability, all of which predispose to haemorrhagic transformation. Among various biomarkers, the neutrophil-to-platelet ratio (NPR) has emerged as a novel and promising indicator, reflecting the balance between inflammatory response (neutrophils) and thrombotic activity (platelets). Being derived from routine blood investigations, NPR offers the advantage of being simple, cost-effective, and readily available in most clinical settings.

However, despite its potential utility, there is limited data evaluating the predictive value of NPR in the context of haemorrhagic transformation in acute ischemic stroke, particularly in the Indian population. Furthermore, the interaction of NPR with established clinical and radiological predictors such as stroke severity and infarct location remains inadequately explored. In this context, the present study was undertaken to evaluate the association between NPR and haemorrhagic transformation in patients with acute ischemic stroke. Additionally, the study aims to analyse various demographic, clinical, laboratory, and imaging parameters to identify high-risk patients and enhance early risk stratification, thereby facilitating timely and evidence-based clinical decision-making.

CONCLUSION

The present study highlights the neutrophil-to-platelet ratio (NPR) as a significant and clinically relevant biomarker for predicting haemorrhagic transformation in patients with acute ischemic stroke. A higher NPR was found to be strongly associated with an increased risk of haemorrhagic transformation, underscoring the pivotal role of systemic inflammation and platelet activation in the pathophysiology of ischemic brain injury and subsequent vascular disruption. The statistically significant elevation of NPR in patients who developed haemorrhagic transformation, along with its moderate diagnostic accuracy and high negative predictive value, suggests that NPR may be particularly useful as a screening tool to identify patients at lower risk and guide clinical vigilance in higher-risk groups.

In addition to NPR, stroke severity as assessed by NIHSS score and the location of ischemia were found to be important determinants of haemorrhagic transformation. Patients with severe stroke and those with anterior circulation involvement demonstrated a significantly higher risk, indicating that both the extent of neurological injury and vascular territory play crucial roles in influencing outcomes. In contrast, demographic variables such as age and gender did not show a statistically significant association, suggesting that biological and clinical factors may outweigh baseline characteristics in determining the risk of haemorrhagic conversion.

Taken together, these findings support the integration of NPR into routine clinical assessment as a simple, cost-effective, and readily available biomarker for early risk stratification in acute ischemic stroke. Its use in conjunction with established clinical and radiological parameters may enhance prognostic

accuracy, facilitate timely therapeutic decision-making, and ultimately contribute to improved patient management and outcomes.

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