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Inflammatory and Metabolic Markers in Acute Stroke Patients: Diagnostic Associations of NLR and GPR

Akut İnme Hastalarında İnflamatuar ve Metabolik Belirteçler: NLR ve GPR'nin Tanısal İlişkileri

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Abstract: The neutrophil-to-lymphocyte ratio (NLR) and glucose-to-potassium ratio (GPR) are simple, readily available markers reflecting inflammatory and metabolic responses in acute stroke. However, their diagnostic value in emergency department (ED) presentations remains uncertain. This study evaluated the association of NLR and GPR with stroke among patients presenting with stroke-like symptoms. This retrospective study included 475 participants (286 stroke, 189 controls). Demographic, clinical, and laboratory data were analyzed. Independent predictors were identified using multivariable logistic regression, and diagnostic performance was assessed with receiver operating characteristic (ROC) analysis. Stroke patients were older than controls (59 vs. 43 years, $p<0.001$) and had higher prevalences of hypertension, diabetes mellitus, and coronary artery disease (all $p<0.05$). NLR, GPR, and C-reactive protein levels were higher (all $p<0.001$), while lymphocyte counts ($p=0.015$) and albumin levels ($p=0.018$) were lower. Age was an independent predictor of both ischemic and hemorrhagic stroke ($p<0.001$). GPR was independently associated with ischemic stroke (OR=1.08, 95% CI: 1.05–1.12, $p<0.001$). In hemorrhagic stroke, both NLR (OR=1.40, 95% CI: 1.20–1.65, $p<0.001$) and GPR (OR=1.13, 95% CI: 1.06–1.21, $p<0.001$) remained significant. Hypertension showed the strongest association with hemorrhagic stroke ($p<0.001$). ROC analysis demonstrated moderate discrimination (AUC: 0.636 for NLR; 0.729 for GPR). NLR and GPR were elevated in stroke and showed moderate diagnostic performance. GPR was associated with ischemic stroke, whereas both markers were linked to hemorrhagic stroke, suggesting complementary pathophysiological roles.

Keywords: Children, diabetic ketoacidosis, immature granulocytes

Özet: Nötrofil-lenfosit oranı (NLR) ve glukoz-potasyum oranı (GPR), akut inmede inflamatuvar ve metabolik yanıtları yansıtan, basit ve kolay erişilebilir belirteçlerdir. Ancak, acil servis (AS) başvurularındaki tanısal değerleri belirsizliğini korumaktadır. Bu çalışma, inme benzeri semptomlarla başvuran hastalarda NLR ve GPR'nin inme ile ilişkisini değerlendirmeyi amaçlamıştır. Bu retrospektif çalışmaya toplam 475 katılımcı (286 inme, 189 kontrol) dahil edilmiştir. Demografik, klinik ve laboratuvar verileri analiz edilmiştir. Bağımsız belirleyiciler çok değişkenli lojistik regresyon analizi ile belirlenmiş, tanısal performans ise alıcı işletim karakteristiği (ROC) analizi ile değerlendirilmiştir. İnme hastaları kontrol grubuna kıyasla daha yaşlıydı (59 vs. 43 yıl, $p<0.001$) ve hipertansiyon, diyabetes mellitus ve koroner arter hastalığı prevalansları daha yüksekti (tümü $p<0.05$). NLR, GPR ve C-reaktif protein düzeyleri daha yüksek bulunurken (tümü $p<0.001$), lenfosit sayıları ($p=0.015$) ve albümin düzeyleri ($p=0.018$) daha düşüktü. Yaş, hem iskemik hem de hemorajik inme için bağımsız bir belirleyici olarak saptandı ($p<0.001$). GPR, iskemik inme ile bağımsız olarak ilişkiliydi (OR=1.08, %95 GA: 1.05–1.12, $p<0.001$). Hemorajik inmede ise hem NLR (OR=1.40, %95 GA: 1.20–1.65, $p<0.001$) hem de GPR (OR=1.13, %95 GA: 1.06–1.21, $p<0.001$) anlamlılığını korudu. Hipertansiyon, hemorajik inme ile en güçlü ilişkiyi gösterdi ($p<0.001$). ROC analizi, orta düzeyde ayırt edici performans gösterdi (AUC: NLR için 0.636; GPR için 0.729). NLR ve GPR inme hastalarında yüksek bulunmuş ve orta düzeyde tanısal performans göstermiştir. GPR iskemik inme ile ilişkiliyken, her iki belirteç de hemorajik inme ile ilişkili bulunmuş olup, tamamlayıcı patofizyolojik rollere işaret etmektedir.

Anahtar Kelimeler: Glikoz-potasyum oranı, inflamasyon, metabolik düzensizlik, nötrofil-lenfosit oranı, inme

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1. Introduction

Disruptions to the brain's blood flow, caused by strokes, encompass various conditions and potentially lead to neurological impairments. Among these, stroke is a leading global cause of death and long-term disability (1, 2). The worldwide impact of stroke is substantial (3), presenting major challenges for healthcare and society (4). Improved strokes diagnostic and therapeutic strategies require a thorough understanding of the mechanisms, risk factors, and emerging biomarkers involved (5).

Genetic, environmental, and lifestyle factors, alongside ischemic and hemorrhagic mechanisms, all play a role in the multifaceted pathogenesis of strokes. A blockage in a blood vessel supplying the brain, from thrombosis or embolism, causes the majority (85%) of strokes, which are classified as ischemic.(6). A ruptured blood vessel causing brain bleeding characterizes hemorrhagic strokes, which constitute about 15% of stroke cases (7). Increased intracranial pressure, tissue damage, and neurological deficits arise from the sudden escape of blood into brain tissue or the subarachnoid space.

Recent findings highlight the crucial role of inflammation and immune responses in the development of ischemic and hemorrhagic strokes (8). A stroke launches a brain inflammatory cascade: microglia activation, peripheral leukocyte infiltration, and pro-inflammatory cytokine release (9). While initially protective, this neuroinflammatory process causes further neuronal damage, impacting stroke results (10).

The neutrophil-to-lymphocyte ratio (NLR), a readily available and inexpensive marker of systemic inflammation, has emerged (11). This is computed by taking the absolute neutrophil count and dividing it by the absolute lymphocyte count; these are standard admission blood tests. A high NLR signifies heightened inflammation due to an imbalance between neutrophils and lymphocytes in the immune response. The prognostic significance of NLR in cardiovascular disease, cancer, and infections has been shown in multiple studies (12, 13, 14, 15). Larger infarct size, more severe neurological impairment, and worse functional outcomes in strokes patients are associated with higher NLR on admission (11, 16). In the study of Lattanzi et al. (17) elevated NLR independently correlated with negative outcomes in patients experiencing acute ischemic stroke. Scientists are actively investigating its potential as a predictor of acute ischemic stroke (18).

Acute stroke patients, including those without diagnosed diabetes, often present with hyperglycemia (19). Stress-caused high blood sugar can worsen nerve damage in several ways, such as by increasing oxidative stress, lactic acidosis, and disrupting the blood-brain barrier (19). On the other hand, potassium is vital for cellular function, and an imbalance can result in cardiac and neurological complications (20). The glucose-potassium ratio (GPR) is a proposed combined marker reflecting metabolic disorders (21). Higher GPR levels might be linked to higher death rates in critically ill patients (22, 23), but more research is needed to understand its role in stroke outcomes Improved stroke diagnosis and patient outcomes may result from advancements in our understanding of inflammatory and metabolic biomarkers such as NLR and GPR (24).

In the emergency department setting, the clinical applicability of biomarkers is largely determined by their rapid availability, low cost, and routine use at admission. Although inflammatory mediators such as C-reactive protein or interleukin-6 have demonstrated associations with stroke-related inflammation, their use in acute decision-making is often limited by delayed turnaround times and restricted availability in routine emergency practice (8, 10). In contrast, both NLR and GPR can be readily derived from standard laboratory tests obtained at presentation and represent two complementary biological domains: systemic inflammation and metabolic stress. Accordingly, these markers were selected to explore their diagnostic associations in patients presenting with acute stroke symptoms in a real-world emergency department setting.

With the significant morbidity and mortality rates associated with strokes, there is an immediate need for reliable and easily measurable biomarkers that can support risk classification, early detection, and prediction (25). Despite the promise of individual markers NLR and GPR, their combined use for predicting acute stroke outcomes requires further study. The goal of this study is to determine the relationship between NLR and GPR with clinical outcomes among patients exhibiting strokes symptoms.

2. Materials and Methods

Data from stroke patients and a control group treated at Konya Hospital's Emergency Medicine Clinic

from March 1, 2025, to July 1, 2025, were collected using a retrospective cross-sectional analysis. Following ethics committee approval at Necmettin Erbakan University University (Approval number: 2025/5535), a retrospective assessment of patient files was conducted.

Emergency department patients exhibiting symptoms including headache, confusion, motor deficits, aphasia, visual disturbances, balance problems, and numbness and diagnosed with stroke via cranial imaging (magnetic resonance imaging and/or computerized tomography) were included in the study. Inclusion criteria were patients aged ≥18 years with a diagnosis of stroke confirmed by cranial imaging (coputed tomography or magnetic resonance imaging) and complete laboratory data available at admission. Exclusion criteria were the presence of acute infection, malignancy, chronic inflammatory disease, use of immunosuppressive therapy, or incomplete medical records. Both ischemic and hemorrhagic strokes were eligible for inclusion without stratification. Data were collected from electronic medical records, including demographic variables (age, sex), comorbidities (hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, and heart failure), laboratory parameters (neutrophil count, lymphocyte count, NLR, glucose, potassium, GPR, albumin, C-reactive protein, blood urea nitrogen [BUN], and creatinine), hospitalization details (length of stay, hospitalization type, thrombolytic therapy, and mechanical thrombectomy), and patient outcomes (discharge, mortality, unauthorized departure). Controls were ED patients without stroke, matched by admission time, who underwent laboratory testing for non-neurological complaints. Length of stay data were not available for control patients as they were not hospitalized.

Given the biological differences between ischemic and hemorrhagic stroke, subtype-specific multivariable models were constructed, allowing assessment of NLR and GPR across stroke phenotypes.

Statistical analysis

Data management, visualization, and reporting were facilitated by R version 4.4.2 and its various packages for statistical analysis.

A Shapiro-Wilk test was conducted to evaluate the normality of the numerical data. Mean and standard deviation (SD) summarized the parametric data. Medians, minimum and maximum, and described the non-parametric data. The categorical data summary included observation counts (n) and percentage frequencies (%).

Group differences and relationships were analyzed using inferential statistics. Test selection considered data normality (Shapiro-Wilk test) and assumption fulfillment. Normally distributed numerical data used t-tests (two groups) and ANOVA (three or more groups) for comparison. For non-normally distributed data, the Wilcoxon rank test (two groups) or Kruskal-Wallis test (multiple groups) was applied. Categorical data analysis used Chi-square tests when cell counts exceeded 5; Fisher's exact test was used for smaller samples. Agreement between two categorical variables was evaluated using Kappa analysis.

Independent predictors of stroke were identified using multivariable logistic regression. Due to potential collinearity and differing biological domains, NLR and GPR were evaluated in separate multivariable logistic regression models. Variables entered into the multivariable model included age, sex, hypertension, diabetes, coronary artery disease, creatinine, CRP, and albumin. Multicollinearity was assessed using VIF and was within acceptable limits. Odds ratios (OR) with 95% confidence intervals (CI) were determined using binary logistic regression to analyze the relationship between stroke and clinical and laboratory variables. Given the biological and clinical differences between ischemic and hemorrhagic stroke, we performed sensitivity analyses for subtypes. Subtype-specific predictors of ischemic and hemorrhagic stroke were evaluated using multivariable logistic regression models incorporating either NLR (Model A) or GPR (Model B). Model fit was evaluated using Omnibus tests, Nagelkerke R^2, and Hosmer–Lemeshow goodness-of-fit.

The diagnostic ability of NLR and GPR to predict stroke was evaluated via receiver operating characteristic (ROC) curve analysis. The discriminative power of these markers was assessed by calculating the area under the curve (AUC). Results with p-values below 0.05 were deemed statistically significant.

3. Results

Four hundred seventy-five people participated; 286 had stroke, while 189 were controls. The mean age of participants was 55 years (18-67 years), and 215 (43.5%) were female. Median NLR and GPR were 2.6 (0.5–31.5) and 26.2 (2.2–141.4), respectively. Among the stroke cohort, 37 patients had hemorrhagic stroke. Mortality was absent from the control group but present in 17 participants (6%) of

the stroke group. Compared to the control group, the stroke group had a much larger male percentage (64.3% vs. 40.2%, p<0.001) and older age (59 vs. 43 years, p<0.001). Coronary artery disease, hypertension, diabetes mellitus, and a history of cerebrovascular diseases (CVDs) were all significantly more common in the stroke group (p<0.001 for each). Table 1 and Supplementary Table 1 displays the demographic, clinical, and laboratory characteristics of patients and controls. Significantly higher systolic and diastolic blood pressure (p<0.001), neutrophil counts (p<0.001), NLR (p<0.001), glucose levels (p<0.001), GPR (p<0.001), and C-reactive protein (p<0.001) were observed in stroke patients. In contrast, lymphocyte counts (p=0.015) and albumin levels (p=0.018) showed a significant decrease in the stroke group.

A comparison of variables for participants with and without prior CVD diagnoses, stratified by stroke diagnosis, is shown in Table 2 and Supplementary Table 2. Stroke patients with prior CVD showed significantly higher diastolic blood pressure (p=0.002) and neutrophil count (p=0.039), longer hospital stay (p<0.001) and lower potassium levels (p<0.001).

Kappa Analysis of GPR and NLR was showed in Table 3. When the agreement between NLR and GPR was evaluated, the kappa value was 0.092, indicating that the agreement between the two variables was at a very low level (p = 0.023).

In the multivariable logistic regression models for ischemic stroke, age emerged as a consistent independent predictor in both Model A (OR=1.10, 95% CI: 1.07–1.13, p<0.001) and Model B (OR=1.09, 95% CI: 1.06–1.12, p<0.001). In Model B, the GPR remained independently associated with ischemic stroke (OR = 1.08, 95% CI: 1.05–1.12, p<0.001). CRP was also significant in both models (Model A: OR=1.04, p=0.030; Model B: OR=1.04, p=0.010). Hypertension was significant only in Model B (OR=2.50, 95% CI: 1.36–4.67, p=0.003).

For hemorrhagic stroke, both inflammatory and metabolic markers demonstrated stronger associations. NLR was independently predictive in Model A (OR=1.40, 95% CI: 1.20–1.65, p<0.001), while GPR remained significant in Model B (OR=1.13, 95% CI: 1.06–1.21, p<0.001). Hypertension showed a particularly strong effect in hemorrhagic stroke (Model A: OR=20.2, 95% CI: 6.24–80.3, p<0.001; Model B: OR=9.32, 95% CI: 3.13–31.2, p<0.001).

ROC analysis of NLR and GPR in stroke and control groups is presented in Figure 1. The predictive ability of NLR and GPR in stroke diagnosis and mortality was demonstrated using ROC analysis. NLR and GPR achieved AUC values of 0.636 and 0.729, respectively. Optimally, NLR's threshold was 1.977, yielding 72.7% sensitivity and 51.9% specificity. GPR achieved its best performance with a threshold of 26.988, resulting in 61.1% sensitivity and 77.8% specificity. ROC analysis results for NLR and GPR in mortality cases are presented in Supplementary Figure 1. Both values yielded a moderately high AUC.

Table 1. Analysis of stroke and control cases

	Overall (n = 475), n (%)	**Control (n = 189), n (%)**	**Stroke (n = 286), n (%)**	**p value**
Sex (F/M)	215 (45.3) / 260 (54.7)	113 (60.0) /76 (40.2)	102 (35.7) / 184 (64.3)	**<0.001**
Age*	55 (18-67)	43 (18-66)	59 (21-67)	**<0.001**
Coronary Artery Disease	40 (8.4)	2 (1.1)	38 (13.3)	**<0.001**
Hypertension	180 (37.9)	29 (15.3)	151 (52.8)	**<0.001**
Diabetes Mellitus	98 (20.6)	17 (9.0)	81 (28.3)	**<0.001**
History of CVD	66 (13.9)	2 (1.1)	64 (22.4)	**<0.001**
SBP (mmHg)*	130 (80-250)	120 (80-200)	156 (85-250)	**<0.001**
DBP (mmHg)*	80 (40-173)	80 (40-110)	90 (50-173)	**<0.001**
NLR*	2.6 (0.5-31.5)	1.9 (0.5-20.8)	2.9 (0.8-31.6)	**<0.001**
GPR*	26.2 (2.2-141.4)	23.7 (2.2-47.7)	30.7 (13.4-141.4)	**<0.001**
Hospitalization Status				
In-patient			152 (53.2)	
ICU			107 (37.4)	
Out-patient			12 (4.2)	
Referral to another hospital			9 83.2)	
Thrombolytic Therapy				
Yes			47 (16.4)	
No			195 (68.2)	
Mechanical Thrombectomy			18 (6.3)	

	Overall (n = 475), n (%)	Control (n = 189), n (%)	Stroke (n = 286), n (%)	p value
Outcome				
Discharged			239 (83.6)	
Mortality			17 (6.0)	
Unauthorized departure			9 (3.2)	
Length of stay (Days)*			6 (1-120)	

**Numeric variables were presented as median (minimum–maximum) or mean ± SD.*
Abbreviations: *CVD: Cerebrovascular Diseases, DBP: Diastolic Blood pressure, F: female, GPR: Glucose-Potassium Ratio, ICU: Intensive Care Unit, NLR: Neutrophil-Lymphocyte Ratio, SBP: Systolic Blood pressure.*

Table 2. Comparison of variants according to cerebrovascular disease history status in patients with cerebrovascular events

	Overall (n = 286), n (%)	No History of CVD (n = 222), n (%)	History of CVD (n = 64), n (%)	p value
Age*	59 (21-67)	59 (21-67)	59 (26-67)	0.866
Gender (F/M)	102 (35.7) / 184 (64.3)	78 (35.1) / 144 (64.9)	24 (37.5) / 40 (62.5)	0.842
SBP (mmHg)*	156 (85-250)	150 (90-240)	170 (85-250)	0.074
DBP (mmHg)*	90 (50-173)	86 (50-150)	100 (53-173)	**0.002**
NLR*	2.9 (0.8-31.5)	2.8 (0.8-31.5)	3.9 (0.8-22.2)	**0.015**
GPR*	30.7 (13.4-141.4)	30 (13.4-141.4)	32.7 (19.1-137.1)	0.053
Hospitalization Status				
In-patient	152 (53.2)	127 (58.8)	25 (39.1)	
ICU	107 (37.4)	72 (33.3)	35 (54.7)	**0.018**
Out-patient	12 (4.2)	10 (4.6)	2 (3.1)	
Referral to another hospital	9 (3.2)	7 (3.2)	2 (3.1)	
Thrombolytic Therapy				**0.007**
Yes	47 (16.4)	43 (21.5)	4 (6.7)	
No	195 (68.2)	141 (70.5)	54 (90.0)	
Mechanical Thrombectomy	18 (6.3)	16 (8.0)	2 (3.3)	
Outcome				
Discharged	239 (83.6)	187 (91.2)	52 (86.7)	0.117
Mortality	17 (5.9)	10 (4.9)	7 (11.7)	
Unauthorized departure	9 (3.2)	8 (3.9)	1 (1.7)	
Length of stay (Days)*	6 (1-120)	5 (1-75)	8 (3-120)	**<0.001**

**Numeric variables were presented as median (minimum–maximum) or mean ± SD.*
Abbreviations: *CVD: Cerebrovascular Diseases, DBP: Diastolic Blood pressure, F: female, GPR: Glucose-Potassium Ratio, ICU: Intensive Care Unit, NLR: Neutrophil-Lymphocyte Ratio, SBP: Systolic Blood pressure.*

Table 3. Kappa Analysis of Glucose-Potassium Ratio and Neutrophil-Lymphocyte Ratio

		Glucose-Potassium Ratio Cut-off Group		Total	κ value	p value
		<= 26.99	> 26.99			
Neutrophil-Lymphocyte Ratio Cut-off Group	=< 1.98	107	151	258	0.092	**0.023**
	> 1.98	69	148	217		
Total		176	299	475		

Table 4. Predictors of stroke: Multivariable logistic regression (Model A: NLR; Model B: GPR)

	Predictors of ischemic stroke			
	p value	OR	95% CI	
			Lower	Upper
Model A: Neutrophil-Lymphocyte Ratio				
Sex (F:M)	**<0.001**	0.37	0.20	0.66
Age	**<0.001**	1.10	1.07	1.13
Neutrophil-Lymphocyte Ratio	0.077	1.09	1.00	1.20
C-reactive Protein	**0.030**	1.04	1.01	1.07
Creatinine	**0.030**	1.04	1.01	1.07
Hypertension	0.109	2.86	1.08	12.0
Model B: Glucose-Potassium Ratio				

Sex (F:M)	**0.003**	0.39	0.21	0.72
Age	**<0.001**	1.09	1.06	1.12
Glucose-Potassium Ratio	**<0.001**	1.08	1.05	1.12
C-reactive Protein	**0.010**	1.04	1.01	1.08
Creatinine	0.054	3.85	1.7	17.4
Hypertension	**0.003**	2.50	1.36	4.67
	Predictors of hemorragic stroke			
Model A: Neutrophil-Lymphocyte Ratio				
Sex (F:M)	**0.004**	0.14	0.04	0.53
Age	**0.001**	1.08	1.03	1.14
Neutrophil-Lymphocyte Ratio	**<0.001**	1.40	1.20	1.65
C-reactive Protein	0.253	0.97	0.91	1.02
Creatinine	0290	3.93	0.70	82.1
Hypertension	**<0.001**	20.2	6.24	80.3
Model B: Glucose-Potassium Ratio				
Sex (F:M)	0.007	0.20	0.06	0.61
Age	**0.032**	1.05	1.01	1.11
Glucose-Potassium Ratio	**<0.001**	1.13	1.06	1.21
C-reactive Protein	0.843	0.99	0.91	1.07
Creatinine	0.238	2.48	0.62	19.0
Hypertension	**<0.001**	9.32	3.13	31.2

Notes: *Sensitivity analysis was performed excluding hemorrhagic stroke cases. Model A includes NLR as the primary inflammatory marker, and Model B includes GPR. All models were constructed using multivariable logistic regression.*

Abbreviations: *CI: confidence interval, OR:odds ratio.*

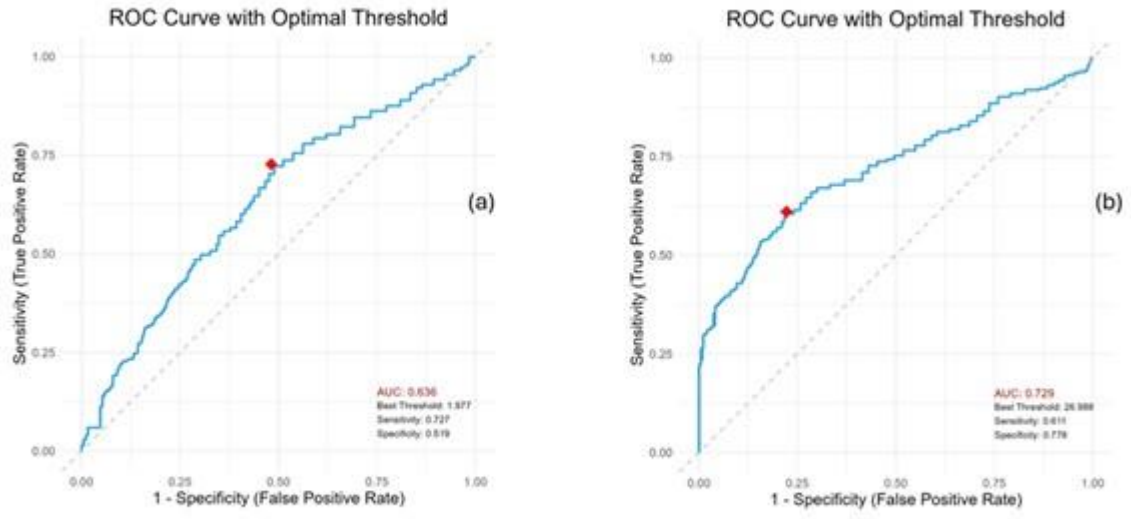

Figure 1. ROC Analysis of Stroke and Control Group According to Neutrophil-Lymphocyte Ratio (a) and Glucose-Potassium Ratio (b)

4. Discussion

This study investigated the demographic, clinical, and laboratory characteristics of stroke patients and controls, exploring the relationships between NLR, GPR, and stroke and its outcomes. In multivariable analyses, metabolic dysregulation reflected by GPR remained independently associated with ischemic stroke, whereas the independent contribution of NLR appeared weaker, suggesting that metabolic stress markers may outperform inflammatory ratios in diagnostic discrimination. In hemorrhagic stroke, both inflammatory and metabolic markers appeared to have particularly strong associations. NLR and GPR in the models. Notably, hypertension emerged as the most powerful risk factor, with markedly elevated odds ratios across both models, underscoring its central role in hemorrhagic stroke outcomes. In ROC analyses, both NLR and GPR demonstrated moderate discriminatory ability, with NLR showing higher sensitivity and GPR higher specificity for stroke diagnosis. A low level of agreement was observed between NLR and GPR, even with statistical significance. Consequently, it may be better to evaluate these variables independently. Moreover, older age and the presence of hypertension emerged as consistent clinical risk factors for stroke.

Older age and male sex were significantly more prevalent among stroke patients, aligning with findings from previous research (1, 3) demonstrating an increased stroke risk in these groups. High rates of hypertension, diabetes mellitus, and coronary artery disease in those who had a stroke confirm already known stroke risk factors. Endothelial dysfunction, atherosclerosis, and pro-thrombotic states are likely mechanisms by which these contribute to stroke pathophysiology (1, 2, 5).

Strokes, especially ischemic stroke, continue to be major causes of illness and death globally. Improving patient outcomes necessitates understanding the underlying pathophysiology and identifying reliable and easily measurable biomarkers that may support early diagnostic risk stratification in acute presentations (6). NLR—readily derived from the admission complete blood count—indexes systemic inflammation and was higher in stroke than in controls in our cohort. NLR exhibited only moderate discrimination for case–control status, and although prior work often links higher NLR to worse outcomes, effect sizes vary across cut-offs, case-mix, and settings (16, 17, 26, 27, 28, 29). An imbalance between innate (neutrophil activation) and adaptive (lymphopenia) immunity likely underlies these associations (8, 9, 29). Although previous studies have reported heterogeneous findings regarding the independent predictive value of NLR (16, 17, 26, 27, 28, 29), our results indicate that NLR retains significance when evaluated within an inflammation-focused multivariable model.

Acute stroke patients frequently experience metabolic disruptions, such as hyperglycemia and electrolyte imbalances, which correlate with poorer prognoses (19). Neuronal injury is amplified by hyperglycemia through processes like heightened lactate and oxidative stress; meanwhile, potassium is essential for maintaining neuronal excitability and vascular tone (30). GPR, a combination of these two parameters, gives a composite marker that might better indicate the level of metabolic disruption than either parameter used by itself (31). In our cohort, GPR was elevated in stroke patients, reflecting hyperglycemia and hypokalemia, both of which have been associated with adverse outcomes (19, 22, 31, 32). While studies specifically examining GPR in the context of stroke are limited, related research in critical care settings supports its potential utility (22, 31, 32). A study by Wu et al.(31) showed an AUC of 0.720 when predicting 90-day mortality. Our emergency department setting precluded the collection of long-term follow-up data. This study revealed a GPR AUC of 0.729 for case-control discrimination, indicating moderately clinical discriminatory power. The independent association of GPR with ischemic stroke suggests that readily available metabolic indices may offer clinically useful diagnostic support in emergency settings. Prior studies have similarly reported prognostic relevance of glucose-potassium imbalance in cerebrovascular and critical illness cohorts (21, 31).

Although NLR and GPR were higher in patients with stroke and demonstrated moderate discrimination on ROC analysis, sensitivity analyses excluding hemorrhagic cases suggested that these markers were not independently associated with stroke after multivariable adjustment. The observed diagnostic signal of NLR and GPR should also be interpreted in the context of structural group differences. Stroke patients were older and carried a higher vascular risk burden, which may partially explain biomarker elevations. Residual confounding remains possible despite multivariable adjustment, and future prospective studies with matched control cohorts are warranted. This pattern indicates that the observed diagnostic signal may be partly driven by structural differences between groups—particularly age and vascular risk burden. In contrast, age

remained the most consistent independent predictor, while hypertension and CRP showed independent associations in the NLR-based model. Although some laboratory parameters showed statistical significance, such as potassium (4.2 vs. 4.3 mmol/L), these small absolute differences may not be clinically meaningful. Previous studies reporting independent predictive roles for NLR or GPR often used different endpoints, patient populations, and adjustment strategies, which may account for these discrepancies (17, 21, 28, 29, 31). Our findings suggest that GPR may be a useful marker for diagnostic discrimination in acute stroke presentations; however, its prognostic implications cannot be established in the absence of functional and long-term outcome data. Because ischemic and hemorrhagic strokes differ substantially in inflammatory and metabolic responses, analyzing them together may have attenuated subtype-specific signals. This limitation should be considered when interpreting the moderate discriminative performance of NLR and GPR. The inflammatory response, glucose dysregulation, and potassium homeostasis differ substantially between these entities, and this heterogeneity may have contributed to the moderate discriminative performance observed for NLR and GPR. Future studies with larger, subtype-specific cohorts are required to validate the diagnostic utility of these biomarkers separately in ischemic and hemorrhagic stroke.

An important strength of the updated analysis is the subtype-specific evaluation of predictors. In hemorrhagic stroke, NLR showed a strong independent association, consistent with the more pronounced inflammatory activation observed in intracerebral hemorrhage. Conversely, GPR remained independently associated with ischemic stroke, highlighting the clinical relevance of metabolic stress responses, particularly hyperglycemia-related pathways, in acute ischemic events (10, 19, 32).

Stroke's progression and consequences are heavily influenced by the intricate relationship between inflammation and metabolism (6, 8, 9). Immune cell activity and glucose control are interconnected, with inflammation and metabolic disorders playing key roles (8, 10, 19, 30). Our discovery of high NLR and GPR levels underscores this two-way connection. Low concordance between NLR and GPR (κappa = 0.092) was a key finding, implying that these markers represent separate pathophysiological processes. The poor correlation emphasizes the multifaceted nature of stroke mechanisms, involving multiple pathways affecting its development and results. Targeting these interconnected pathways may offer therapeutic benefits. Treatment targeting inflammation (corticosteroids, cytokine inhibitors) and careful metabolic control might lessen secondary neuronal injury, leading to better patient outcomes (8, 10). However, to determine the effectiveness and safety of such combined therapies, clinical trials are needed.

The control group showed no deaths, but the stroke group had a 6% mortality rate in the present study. Both NLR and GPR have been linked to mortality in prior studies, and our ROC analysis confirmed their moderate predictive value, potentially due to its reflection of metabolic stress and nutritional status (17, 22, 26, 31). While showing some prognostic value, these markers' clinical utility appear limited unless included in more extensive risk models, according to these findings. The mortality subgroup included only 17 cases, leading to limited statistical power; therefore, the mortality-related results should be interpreted as exploratory.

The potential of NLR and GPR as readily available markers for early diagnostic assessment in emergency department presentations may have clinical implications. These inexpensive, easily accessible markers may improve early risk assessment, thus informing treatment choices and may support early triage and prioritization for imaging/workup, but should not be considered standalone decision tools. Future research should focus on multimodal approaches and validate optimal cutoffs in large prospective cohorts.

Limitations

There are several limitations to this study. First, the retrospective design could lead to selection bias. Secondly, our analysis lacked an assessment of dynamic NLR and GPR changes over time, potentially overlooking valuable prognostic information. The relationship between systemic inflammation, metabolic dysfunction, and stroke could have been better understood by evaluating additional inflammatory and metabolic markers (e.g., interleukin-6, hemoglobin A1c), which were omitted from this study. We had no data on patient compliance with antihypertensive or antidiabetic therapy, which could affect results. The control group consisted of heterogeneous ED patients, which may introduce selection bias and limit the generalizability of our findings. The absence of extensive follow-up data also limited our ability to analyze the prognostic impact of NLR and GPR.

Differences in age, sex, and vascular risk factors between groups may partially explain the observed biomarker differences. In addition, no formal power analysis was performed; thus, the study may be underpowered for some subgroup analyses. Groups were not matched; biomarker elevations may reflect baseline vascular risk rather than stroke itself. The hemorrhagic stroke subgroup included only 37 patients, which limited statistical power and may have resulted in unstable estimates; therefore, the main interpretation was based on ischemic stroke and sensitivity analyses excluding hemorrhagic cases.

5. Conclusion

Patients presenting with acute stroke symptoms showed elevated inflammatory and metabolic markers compared with controls. GPR demonstrated an independent diagnostic association with ischemic stroke, whereas NLR showed stronger relevance in hemorrhagic stroke, supporting the complementary inflammatory and metabolic signatures across stroke phenotypes. These findings suggest that NLR and GPR may serve as readily available, low-cost biomarkers to support early diagnostic risk stratification in emergency department presentations of suspected stroke. However, given the heterogeneity of stroke subtypes, baseline risk factor imbalances, and the limited number of mortality events, the results should be interpreted as exploratory and hypothesis-generating. Larger prospective, subtype-specific studies are required to clarify their clinical utility.

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