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Efficacy of novel haemogram parameters in the evaluation of inflammation in acute ischemic stroke

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Abstract

Objective: Inflammation in ischemic brain tissue is the primary factor contributing to the pathogenesis of acute ischemic stroke (AIS). This study aimed to investigate the role of new inflammatory parameters—immature granulocyte count (IGc) and the systemic immune-inflammation index (SII)—in determining the presence of inflammation and the subtype, severity, and prognosis of AIS. *Methods:* This retrospective study was conducted using data from 124 patients with AIS and 126 healthy controls. The severity at stroke onset and the functional outcome after at least 3 months of follow-up were determined. Patients with AIS were subdivided into subgroups according to aetiology. The following haemogram parameters were compared between the AIS and control groups: haemogram parameters; white blood cell (WBC) count, haemoglobin (Hgb), haematocrit (HCT), mean platelet volume (MPV), platelet count (PLT), PCT (plateletcrit), lymphocyte and neutrophil count, RDW-CV (red cell distribution width coefficient of variation), neutrophil/lymphocyte ratio (NLR), MPV/PLT ratio, PLT/lymphocyte ratio (PLR), WBC/MPV ratio (WMR), IGc and IG percentage (IG%), and SII values. *Results:* The parameters WBC, IGc, IG%, RDWCV, neutrophil count, NLR, WMR, and SII values were significantly higher in the AIS group than in the control group. We found significant correlations between high SII value and high clinical NIHSS scores at stroke onset, mRS obtained after at least a 3-month follow-up period.
Conclusion: IGc and SII may be new parameters to evaluate the presence of inflammation in patients with AIS. A higher SII was associated with higher stroke severity, and it may be useful for predicting adverse clinical outcomes.

Keywords: stroke, immature granulocyte, inflammation, systemic immune-inflammation index

INTRODUCTION

İschemic stroke is the most common type of stroke and is seen in 80–90% of patients who experience strokes.[1] Understanding the underlying mechanisms of ischemic stroke is important because of the high rate of long-term disability and mortality of the disease. Inflammation plays an important role in the pathophysiology of acute ischemic stroke (AIS).[1] The brain's response to ischemic injury is an acute and prolonged inflammatory process that is characterized by the production of proinflammatory mediators and the release of various types of inflammatory cells (neutrophils, monocytes/macrophages, various subtypes of T cells, and other cells) into the ischemic brain tissue. Together, these cellular events contribute to ischemic brain damage.[2] Patients with stroke who have systemic inflammation show worse clinical outcomes.[3,4] Therefore, the role of immune responses in AIS recovery has attracted the attention of clinical researchers, and many studies have been conducted to identify new diagnostic and prognostic biomarkers after cerebral infarction. Haemogram parameters, such as the neutrophil–lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR), have recently been defined as classic haematological markers of systemic inflammation that can sensitively reflect the inflammatory response.[5]

Although the immature granulocyte count (IGc) is poorly recognised by most clinicians, it is an

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indicator of local and systemic inflammation and can be measured in the peripheral blood using an automatic blood cell analyser. In recent years, studies have demonstrated that IGc is useful in predicting sepsis, acute appendicitis, and pancreatitis complications and long-term mortality in AIS.[5-9]

The systemic immune-inflammation index (SII), consisting of lymphocyte, neutrophil, and platelet counts, is a new index that is a potential indicator of poor outcomes in patients with cancer, ischemic heart disease, and AIS.[10-13]

Our study evaluated the effectiveness and predictive value of the novel systemic inflammation haemogram markers IGc and SII in determining the subtype, severity, and prognosis of acute ischemic stroke.

METHODS

This retrospective study included 124 patients between ages 26 and 68 years who were diagnosed with AIS at the emergency department of Prof. Dr. Mazhar Osman Educational and Research Hospital between December 2021 and January 2024, along with 126 healthy controls with age and gender compatibility. The medical history and clinical characteristics of all participants were recorded. AIS diagnosis was confirmed as an acute infarction in diffusion magnetic resonance imaging (MRI). Smoking was defined as taking more than one cigarette per day for 6 months. Alcohol consumption was identified as an average intake of 1 U/d for females or 2 U/d for males. Hyperlipidaemia was defined as a low-density lipoprotein cholesterol (LDL-C) level of ≥140 mg/dL. The severity and functional outcome of stroke is determined by The National Institutes of Health Stroke Scale (NIHSS) at stroke onset and the Modified Rankin Score (mRS) after at least 3 months of follow-up and stroke onset.[14] A mild stroke was defined as an NIHSS score below 6, whereas moderate to severe strokes were defined as those with NIHSS scores of ≥6.[15] The subtypes of AIS were categorised by the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification.[16] Clinical and laboratory data were collected on admission within 48 h from stroke onset. An unfavourable functional outcome was defined as an mRS ≥3 at least 3 months after AIS.

Patients with the following characteristics were not included in the study: age under 18 years; current pregnancy; myeloproliferative disease; chronic inflammatory liver or kidney disease; chronic obstructive pulmonary disease, asthma; chronic alcoholism; the use of sedatives or muscle relaxants; malignancy; the use of granulocyte colony-stimulating factors, immunosuppressive agents, or steroids; the use of antithrombotic, anticoagulant, or antiseizure medications; and the existence of uncontrolled hypertension (blood pressure>140/90 mm Hg under medical treatment) or diabetes (HBA1c level of >8% under medical agents), acute inflammation, or infection. Fasting blood samples were taken from the peripheral venous blood at admission. The recorded parameters were platelet (PLT) count, plateletcrit (PCT), neutrophil and lymphocyte count, haemoglobin (HGB), haematocrit (HCT), IGc and Ig%, mean platelet volume (MPV), red cell distribution width coefficient of variation (RDWCV); the calculated values were NLR, PLR and MPV/PLT, and the WBC/MPV ratio (WMR). The systemic immune-inflammation index (SII) was defined as the peripheral platelet count × the neutrophil/lymphocyte count.[10] All haemogram parameters were calculated using an automated blood analyser (Hematologic Analyzer, Beckman Coulter Inc., Brea, CA, USA). Our study was conducted in accordance with the Helsinki Declaration upon approval from the local ethics committee (decision date: November 6, 2023; number 21/08). All participants were informed about the study and gave written consent.

Statistical analyses were performed using SPSS Statistics for Windows, version 25 (SPSS Inc., Chicago, IL, USA). Frequency and percentage values are presented for qualitative variables. Quantitative variables with a normal distribution are expressed as the mean ± the standard deviation (SD), whereas median, minimum, and maximum values are presented for variables that do not have a normal distribution. The normality of the distribution was examined using the Shapiro–Wilk test. Chi-square tests were used for comparisons between two qualitative variables. In comparisons between two-category qualitative variables and quantitative variables, the independent samples t-test was used if the data conformed to a normal distribution, and the Mann–Whitney U test was used if the data did not conform to a normal distribution. For comparisons between qualitative variables with more than two categories and quantitative variables, one-way analysis of variance (ANOVA) was used if the data conformed to a normal distribution, and the Kruskal–Wallis H test was used if the data did not conform to a normal distribution. If the result of one-way ANOVA differed significantly from that of the Kruskal–Wallis H test, categories were compared

using post hoc analysis. The ability of biomarkers to distinguish patients with AIS was examined using receiver operating characteristic (ROC) analysis. The existence of a relationship between two quantitative variables was examined with Spearman correlation. In all analyses, $p < 0.05$ was accepted as statistically significant.

RESULTS

A total of 250 participants—124 patients with AIS and 126 healthy controls—were included in the study. Ninety three of the 124 patients had comorbid diseases; such as controlled hypertension (n:73), diabetes mellitus (DM) (n:37), cardiac diseases (n:10), thyroid disease (n:3), mild obstructive sleep apnea syndrome (n:4), hyperlipidaemia (n:86).

Table 1 summarises the descriptive and laboratory statistics of the variables compared between patients with AIS and the control group. As seen in Table 1, the groups did not differ significantly in terms of their median age ($p = 0.321$) or gender ($p = 0.613$). The differences between the patients with AIS and the control group in the WBC, IGc and IG%, RDWCV, and neutrophil count and the NLR, WMR, and SII values were significant ($p < 0.05$). All of these values were higher in patients with AIS than in controls.

Table 1: Explanatory statistics and comparison of variables in AIS and control groups

	Control n (%)	**AIS patients n (%)**	**Total n (%)**	**Chi-square**	**p**
Female	65 (51,6)	60 (48,4)	125 (50)	0,256[K]	0,613
Male	61 (48,4)	64 (51,6)	125 (50)		
	Control $\overline{x}$ ± SS / Med (min-max)	AIS Patient $\overline{x}$ ± SS / Med (min-max)	Total $\overline{x}$ ± SS / Med (min-max)	Z/t	p
Age	50 (24-68)	52 (26-68)	51 (24-68)	-0,993[Z]	0,321
Hgb	13,6 (10,3-17,3)	13,8 (8,3-17,5)	13,7 (8,3-17,5)	-0,010[Z]	0,992
Hct	41,85 (33,2-52,3)	41,3 (26,4-54,9)	41,65 (26,4-54,9)	-1,052[Z]	0,293
WBC	7,06 (3,26-11,8)	7,935 (4,42-14,9)	7,44 (3,26-14,9)	-4,432[t]	<0,001*
PLT	250 (147-447)	258,5 (94-442)	252 (94-447)	-0,981[Z]	0,326
MPV	10,2 (7,7-13,8)	10,5 (7,1-13,2)	10,3 (7,1-13,8)	-0,535[Z]	0,593
IGc	0,01 (0-0,1)	0,02 (0-0,35)	0,02 (0-0,35)	-5,306[t]	<0,001*
IG %	0,2 (0-0,7)	0,3 (0-2,8)	0,2 (0-2,8)	-4,715[t]	<0,001*
PCT	0,26 (0,16-0,49)	0,27 (0,11-0,43)	0,26 (0,11-0,49)	-0,987[Z]	0,323
RDWCV	13,4 (10,5-16,3)	13,6 (11,8-18,9)	13,5 (10,5-18,9)	-2,373[t]	0,018*
Lymphocyte	2,14 (0,58-4)	2,23 (0,57-6,89)	2,19 (0,57-6,89)	-0,180[Z]	0,857
Neutrophil	3,92 (1,88-9,34)	4,8 (1,83-13,8)	4,42 (1,83-13,8)	-4,859[t]	<0,001*
NLR	1,85 (0,83-5,13)	2,24 (0,39-18,9)	1,98 (0,39-18,9)	-3,677[t]	<0,001*
MPVPLT	0,04 (0,02-0,09)	0,04 (0,02-0,14)	0,04 (0,02-0,14)	-0,647[Z]	0,517
PLR	118,25 (60,74-291,38)	120,41 (33,96-452,11)	119,21 (33,96-452,11)	-0,544[Z]	0,586
WMR	0,69 (0,27-1,28)	0,79 (0,39-1,62)	0,74 (0,27-1,62)	-4,099[t]	<0,001*
SII	452,28 (200,97-1307,71)	591,41 (81,34-5652,33)	498,30 (81,34-5652,33)	-3,787[Z]	<0,001*

*p<0,05 | [K]: Chi-square test | [Z]: Mann-Whitney U test [t]: Independent samples T test

Abbreviations: HGB: Hemoglobin; HCT: Haematocrit; PCT: Plateletcrit; PLT: Platelet; PLR: Platelet to Lymphocyte Ratio; WBC: White Blood Cell; RDW: Red Cell Distribution Width; NLR: Neutrophil to Lymphocyte Ratio; WMR: White Blood Cell to Mean Platelet Volume Ratio; SII: Systemic Immune-Inflammation Index, AIS:Acute ischemic stroke; min: minimum; max: maximum;med: median

Table 2: Diagnostic performance of laboratory markers in AIS patients

	AUC	SE	p	95% CI	Cut-off	Sensitivity	Spesificity
WBC	0,662	0,034	<0,001*	0,595-0,729	≥7,865	0,540	0,706
IGc	0,686	0,033	<0,001*	0,62-0,751	≥0,025	0,484	0,817
IG %	0,668	0,034	<0,001*	0,602-0,735	≥0,25	0,548	0,722
RDWCV	0,587	0,036	0,018*	0,516-0,657	≥14,25	0,282	0,873
NEUTR	0,678	0,034	<0,001*	0,611-0,744	≥4,515	0,629	0,675
NLR	0,635	0,035	<0,001*	0,565-0,704	≥2,370	0,476	0,794
WMR	0,65	0,035	<0,001*	0,582-0,718	≥0,829	0,444	0,841
SII	0,639	0,035	<0,001*	0,569-0,708	≥784,8	0,395	0,881

*p<0,05

Abbreviations: AUC: Area under the curve; SE: Standard Error; CI: Confidence Interval. WBC: White Blood Cell; RDW: Red Cell Distribution Width; NLR: Neutrophil to Lymphocyte Ratio; WMR: White Blood Cell to Mean Platelet Volume Ratio; SII: Systemic Immune-Inflammation Index

The results of the ROC curve analysis performed to evaluate the diagnostic performance of laboratory parameters in patients with AIS were as follows: WBC ($p < 0.001$, cut-off ≥ 7,865), IGc ($p < 0.001$, cut-off ≥ 0,025), IG% ($p < 0.001$, cut-off ≥ 0,25), RDWCV ($p = 0.018$, cut-off ≥ 14,25), neutrophil count ($p < 0.001$, cut-off ≥ 4,515), NLR ($p < 0.001$, cut-off ≥ 2,370), WMR ($p < 0.001$, cut-off ≥ 0.829), SII ($p < 0.001$, cut-off ≥ 784,8) markers were found to be significant (Table 2).

As a result of the assessment made by the ROC curve analysis, it was determined that the WBC, IGc, NLR, neutrophil count, RDWCV, WMR, and SII parameters had significant diagnostic value in AIS. The ROC curves are presented in Figure 1.

The results of the comparison of quantitative variables between sub-groups in AIS patients are provided in Table 3. Patients in the large and small vessel groups were older ($p < 0.001$) and had stroke at older age than cardioembolic and cryptogenic stroke groups ($p < 0.001$);

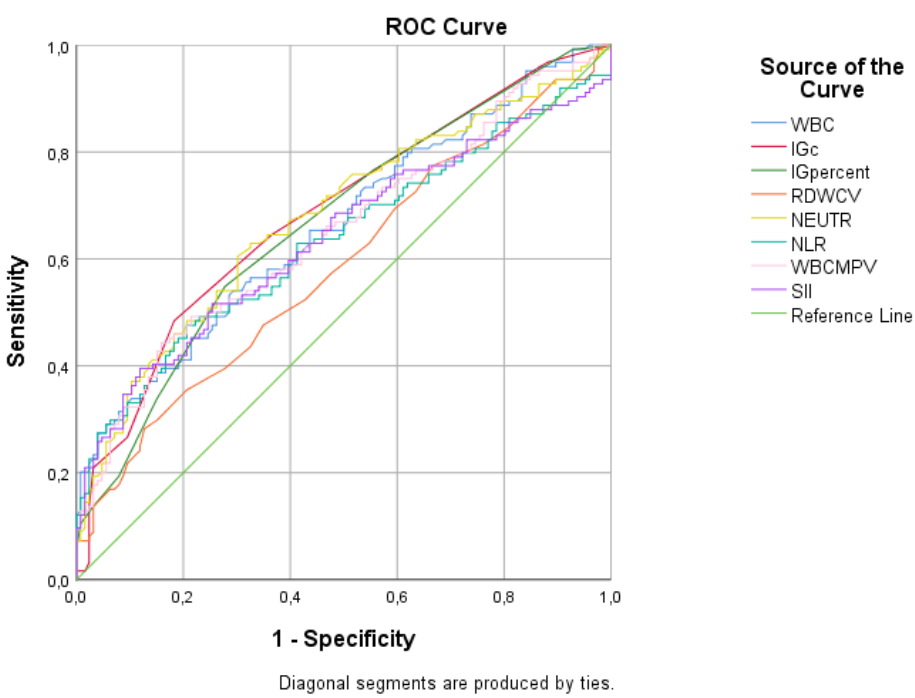

Figure 1. ROC curve analysis of haemogram variables in the diagnosis of acute ischemic stroke.

Table 3: Comparison of clinical and laboratory variables of patients in AIS subgroups according to etiology

	Cardioembolic (A) n: 11 Med (min-max)	Large vessel (B) n: 42 Med (min-max)	Cryptogenic (C) n: 42 Med (min-max)	Small vessel (D) n: 29 Med (min-max)	F/H	p	Difference
Age	46 (34-67)	58 (33-68)	47 (26-67)	57 (32-68)	18,641[H]	<0,001*	B,D>C
Age at stroke	46 (34-66)	57,5 (33-68)	46,5 (24-67)	57 (32-67)	20,462[H]	<0,001*	B,D>C
Follow-up time (month)	11 (3-18)	4 (3-24)	4 (3-24)	4 (3-24)	7,327[H]	0,062	-
NIHSS at stroke onset	2 (0-12)	3 (0-17)	2 (0-16)	2 (0-14)	2,100[H]	0,552	-
mRS at follow-up	0 (0-3)	0 (0-6)	0 (0-3)	0 (0-3)	1,400[H]	0,706	-
Mrs at stroke onset	0 (0-4)	1 (0-5)	1 (0-4)	1 (0-4)	0,895[H]	0,827	-
Hgb	12,3 (10,8-15,4)	14,15 (10,5-16,9)	13,3 (8,3-17,3)	14,6 (8,5-17,5)	15,340 [H]	0,002*	D>A,C
Hct	38,3 (32,6-45,2)	42 (33,4-51,2)	40,3 (26,4-50,2)	42,7 (26,5-54,9)	12,685[H]	0,005*	D>A
WBC	7,32 (5,98-12,09)	8,165 (5,3-14,9)	7,925 (4,42-14,6)	7,55 (4,68-13,97)	3,390[H]	0,335	-
PLT	269,73±68,7	272,9±82,82	265,17±74,05	244,52±51,67	0,937[F]	0,425	-
MPV	10,6±0,74	10,26±1,21	10,47±1,05	10,19±1,23	0,626[F]	0,599	-
IGc	0,01 (0,01-0,06)	0,03 (0-0,35)	0,02 (0-0,09)	0,02 (0-0,09)	5,003[H]	0,172	-
IG %	0,1 (0,1-0,9)	0,3 (0,1-2,8)	0,3 (0-1,1)	0,3 (0,1-1,1)	4,712[H]	0,194	-
PCT	0,29 (0,13-0,37)	0,265 (0,13-0,43)	0,275 (0,11-0,4)	0,24 (0,13-0,32)	7,902[H]	0,048*	-
RDWCV	13,9 (11,8-15,9)	13,55 (12,3-18,9)	13,55 (12,3-17,9)	13,6 (12,2-17,2)	0,295[H]	0,961	-
Lymphocyte	1,65 (1,1-2,94)	2,49 (0,57-5,58)	2,03 (0,6-4,22)	2,32 (0,71-6,89)	8,129[H]	0,043*	-
Neutrophil	4,74 (2,84-10,32)	5,155 (1,83-11,3)	4,65 (2,22-13,8)	4,97 (1,97-9,79)	1,037[H]	0,792	-
NLR	3,15 (1,06-7,82)	2,23 (0,46-8,42)	2,43 (1,06-18,9)	2,11 (0,39-5,17)	2,134[H]	0,545	-
MPVPLT	0,04 (0,03-0,09)	0,04 (0,02-0,14)	0,04 (0,03-0,13)	0,04 (0,02-0,08)	1,254[H]	0,740	-
PLR	155,36 (67,61-226,52)	108,76 (48,33-294,74)	131,76 (44,76-409,59)	118,51 (33,96-452,11)	8,598[H]	0,035*	-
WMR	0,7 (0,54-1,26)	0,85 (0,43-1,62)	0,79 (0,39-1,57)	0,76 (0,41-1,31)	3,420[H]	0,331	-
SII	834,18 (247,47-2337,64)	503,62 (138,02-2448,88)	603,37 (99,37-5652,33)	488,21 (81,34-1659,25)	4,630[H]	0,201	-

*p<0,05; F: One Way Anova test; H: Kruskal Wallis H test
Abbreviations: HGB: Hemoglobin; HCT: Haematocrit; PCT: Plateletcrit; PLT: Platelet; PLR: Platelet to Lymphocyte Ratio; WBC: White Blood Cell; RDW: Red Cell Distribution Width; NLR: Neutrophil to Lymphocyte Ratio; WMR: White Blood Cell to Mean Platelet Volume Ratio; SII: Systemic Immune-Inflammation Index

patients in the small vessel group had the highest HGB values (p = 0.002), and patients in the cardioembolic group had lower HCT values than patients in the small vessel group (p = 0.005). No significant difference was found between the etiologic subgroups in terms of follow-up period (p = 0.062), NIHSS at stroke onset (p = 0.552), follow-up mRS value (p = 0.706), mRS at stroke onset (p = 0.827), WBC (p = 0.335), IGc (p = 0.172), IG% (p = 0.194), RDWCV (p = 0.961), neutrophil count (p = 0.792), NLR (p = 0.545), MPVPLT (p = 0.740), WMR (p = 0.331), SII (p = 0.201) values. Regarding the PLR value (p = 0.035), although one-way ANOVA showed that the p-value was less than 0.05, it was determined that there was no significant difference between the groups after post hoc comparisons.

As a result of the comparisons between the existence of comorbid diseases and IGc, it was determined that patients with DM (p < 0.001) had higher IGc values. No significant relationship was found between the IGc value and the presence of HT (p = 0.433), smoking (p = 0.806), alcohol use (p = 0.434), hyperlipidaemia (p = 0.465), and the existence of comorbid disease (p = 0.136) in patients with AIS. Significant relationships between the SII value and non-smoking (p = 0.033) and the absence of hyperlipidaemia (p = 0.043) were found (Table 4). It was thought that this result may be related to the presence of other comorbidities in AIS patients who are non-smokers and do not have hyperlipidemia.

We found a significant correlation between increased SII value and the high clinical scores of NIHSS at stroke onset (p = 0.006) and mRS obtained after at least 3 months of follow-up (p = 0.022) (Tables 5, 6).

DISCUSSION

Several studies showed that the inflammatory response to focal cerebral ischemia is a key determinant of acute functional outcome and long-term prognosis.[2] Emerging data suggest that inflammatory cells play complex and multistage roles after ischemic stroke, and most of these cell types not only exert beneficial effects, but also contribute to ischemic brain damage.[2,17,18]

Thus, a growing body of evidence indicates that most of these proinflammatory cells play a dual role in the early and late stages of stroke.[2] For instance, MMP-9 (matrix metalloproteinase-9) has been shown to contribute to early ischemic brain injury but also support brain regeneration and neurovascular remodelling at later stages.[17,18] Therefore, a thorough understanding of the time-dependent course of inflammatory cells following focal cerebral ischemia and how these cells exert beneficial and adverse effects is critical for the development of effective therapeutic interventions for AIS.

Some studies have shown that inflammation

Table 4: Associations between clinical history and IGc, SII variables in AIS patients

Clinical History		IGc Median (min-max)	Z	p	SII median (min-max)	Z	p
HT	No	0,02 (0-0,35)	-0,784	0,433	601,19 (81,34-3409,92)	-0,312	0,755
(n:73)	Yes	0,03 (0-0,12)			561,07 (92,04-5652,33)		
DM	No	0,02 (0-0,35)	-4,276	<0,001*	591,41 (81,34-5652,33)	0,733	0,463
(n:37)	Yes	0,03 (0,01-0,12)			600,45 (138,02-2016,52)		
Smoking	No	0,02 (0-0,12)	-0,246	0,806	655,86 (81,34-5652,33)	-2,064	0,033*
(n:62)	Yes	0,02 (0-0,35)			501,32 (99,37-3409,92)		
Alcohol	No	0,02 (0-0,35)	-0,782	0,434	591,41 (81,34-5652,33)	-0,203	0,839
(n:8)	Yes	0,03 (0,01-0,08)			549,22 (325,9-1093,92)		
Hyperlipid.	No	0,02 (0-0,07)	-0,730	0,465	667,83 (99,37-3409,92)	-2,024	0,043*
(n:86)	Yes	0,03 (0-0,35)			520,94 (81,34-5652,33)		
Comorb.	No	0,02 (0,01-0,06)	-1,491	0,136	809,65 (359,2-2117,35)	-1,803	0,071
(n:93)	Yes	0,03 (0-0,35)			524,53 (81,34-5652,33)		

*p<0,05 | Z: Mann-Whitney U test value
HT:Hypertension; DM:Diabetes Mellitus; Hyperlipid: Hyperlipidemia; Comorb:Comorbid disease

Table 5: Correlation between clinical scores and IGc, SII values in AIS patients

		IGc	SII
NIHSS at stroke onset	rho	0,027	0,174
	p	0,766	0,053
mRS at stroke onset	rho	0,098	0,201*
	p	0,278	0,025
Follow-up m*RS value*	rho	0,099	0,217*
	p	0,274	0,016

*p<0,05 | rho: Spearman correlation coefficent

after ischemic stroke increases atherothrombosis, and with the migration of immune mediators and cytokines, the permeability of the blood–brain barrier is impaired, which results in neuronal damage, cerebral oedema, and increased infarct volume.[19,20]

Clinical studies have confirmed that neutrophils accumulate extensively at sites of cerebral infarction within 30 min to a few hours, and their levels peak in the first 3 days; this accumulation is correlated with larger final infarct volumes, increased stroke severity, and poor prognosis after ischemic stroke.[21,22] However, the pathogenic role of neutrophils in ischemic stroke remains uncertain.

Although earlier studies have suggested that lymphocyte recruitment plays a role in the later stages of ischemic brain injury[23,24], more recent studies have shown that T cells accumulate in the ischemic brain within the first 24 h after focal cerebral ischemia.[25,26] However the differential roles of different subtypes of T cells and lymphocytes in response to cerebral damage has demonstrated, the time course of the recruitment of these cells into the ischemic brain is unclear.[23-25]

High neutrophil count and low lymphocyte count were regarded as important factors of poor clinical outcomes in AIS.[27] In addition, several studies have confirmed that platelets play a pivotal role in thrombogenesis and inflammation and cause brain injury following ischemic stroke.[28,29] Many studies have investigated the effectiveness of hemogram parameters, such as MPV, RDW, NLR, and PLR, in evaluating the aetiology, prognosis, and recurrence risk of stroke.

In our study we found that the WBC, IGc and IG%, RDWCV, neutrophil count and the NLR, WMR, SII values were significantly higher in the AIS group than in the control group. In the sub-group analysis of patients with AIS, only SII increased in parallel with the severity of AIS and with poor outcomes.

It was determined that MPV predicts the risk of stroke in patients with a history of transient ischemic attack or stroke.[30] A high level of MPV has been identified as a predictor of a poor functional outcome in AIS.[31,32]

Xue *et al*. concluded that NLR was related to stroke severity, unfavorable functional outcome, and the recurrence of ischemic stroke in patients with AIS.[33] NLR could be a marker of short-term mortality in patients with AIS.[34] Furthermore, it was expressed that high PLR increased the infarct volume and the incidence of unfavourable prognosis in patients with AIS over 3 years of follow-up.[35] In another study, high levels of NLR and PLR (NLR ≥ 3.51, PLR ≥ 141.52) showed the highest risk of undesirable functional outcomes.[36] Several studies have found that high RDW is correlated with an increased risk of carotid atherosclerosis and have suggested that RDW is a prominent predictor of future risk of stroke.[37,38]

SII is a parameter comprising lymphocytes, neutrophils, and platelets levels and may be valuable to reflect the pathways of thrombus form*ation, inflammatory response, and adaptive immune response; furthermore, it can provide important information for the development of stroke and may be an underlying biomarker for prognosis. Several studies have reported SII

Table 6: Associations between follow-up mRS value, NIHSS at stroke onset and IGc, SII variables in AIS patients

Follow-up mRS value	**mRS <3** n:114	**mRS≥3** n:10	**Z**	**p**
IGc	0,02 (0-0,35)	0,02 (0,01-0,08)	-2,294	0,789
SII	549,98 (81,34-5652,33)	893,95 (472,84-1095,79)	-0,268	0,022*
NIHSS at stroke onset	**NIHSS scores <6** Mild (n:103)	**NIHSS scores ≥6** Moderate-severe (n:21)		
IGc	0,02 (0-0,12)	0,02 (0,01-0,35)	-2,741	0,722
SII	524,5333 (81,34-5652,33)	838,5542 (358,77-2448,88)	-0,355	0,006*

values in cerebrovascular diseases. It was shown that elevated SII is associated with an increased risk of stroke and mortality.[39] SII was suggested as a potential predictor of the poor prognosis of patients with acute/subacute cerebral venous sinus thrombosis.[40] Higher SII are correlated with a greater risk of stroke severity and could be useful for predicting adverse clinical outcomes after AIS.[41,42] A recent study showed that increased SII may be a predictor for a high risk of early neurological deterioration and poor functional outcomes 90 days after intravenous tissue plasminogen activator (ıv-rtPA).[43] Similar to literature we found that SII value was significantly higher in the AIS group than in the control group. In the sub-group analysis of patients with AIS, increased level of SII value was correlated with the severity of AIS and poor outcomes.

Several recent studies have recommended IGc as a new indicator of systemic inflammation, and its prognostic and predictive role has been demonstrated in many diseases.[44-47] The increased level of IGc is an early marker of bone marrow activation before the onset of leukopoiesis, which may indicate a response to inflammatory conditions or pregnancy.[48-50] IGc and IG% are easily detected automatically with new-generation haemogram devices, but this new parameter has not been used sufficiently by many physicians, and its areas of usage have not been clearly revealed.

In several studies it was suggested that high IGc values can indicate disease severity and mortality in patients with acute pancreatitis [51], and IG values had higher sensitivity and specificity in predicting inflammatory response in patients with serious bacterial infections.[50] High IGc levels were significantly associated with poor 30-day prognosis and short-term mortality in cases with in AIS.[5,52] Bedel *et al.* found a correlation between mortality and high IGc in patients with acute coronary syndrome.[7] In our study we found IGc and IG% values were significantly higher in the AIS group than in the control group, however no statistically significant relationship was found between these parameters and disease severity and prognosis.

The results of our study were compatible with some studies in the literature but not with others. Inconsistencies in results across studies may be due to various factors, such as study design, exclusion criteria, sample size, and the genetic heterogeneity of the study population. As emphasized in some studies in the literature, one of the strengths of our study is the careful exclusion of AIS patients with comorbidities such as previous stroke and those using medications that would affect hemogram parameters, such as antithrombotic therapy. However, our study has some limitations. First, the sample size could not be very large. Second, the time from the onset of symptoms to the time of sampling has not been precisely determined, and inflammatory biomarkers were not studied for each day of admission as these were acquired as part of routine care. Although patients with AIS are typically comprehensively assessed, peak values and dynamic changes in haemogram parameters cannot be monitored.

In conclusion, the results of our study showed that IGc and SII haemogram parameters are new and simple acute inflammatory clinical markers in patients with AIS. SII can be a useful parameter in determining the disease severity and poor functional outcome.

Multicentre studies are needed to demonstrate whether IG and SII can be used as prognostic and disease severity biomarkers for AIS. Clinicians can use serial haemogram parameters, including these measurements, in further studies.

DISCLOSURE

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