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Importance of Inflammatory Marker Ratio and Lipid Profile Ratio in Acute Ischemic Stroke

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Abstract

Background: *Acute Ischemic Stroke is a chronic inflammatory disease that is projected to be one of the leading causes of mortality affecting millions of people globally. It is essential to study the Platelet lymphocyte ratio (PLR), Neutrophil lymphocyte ratio (NLR) ratios and C reactive protein (CRP) in impacting the inflammatory status during stroke. It is also important that altered lipid metabolism could influence the inflammatory conditions associated with AIS. Hence analysing the relevance of lipid ratio and inflammatory ratio in the context of AIS is important to understand the pathophysiology of disease.* ***Methodology:*** *The blood was collected from the participants for biochemical and hematological analysis such as lipid profile, CRP and Complete blood count for the quantitation of NLR and PLR.* ***Results:*** *The groups involved in the study are AIS and healthy controls. The sample size for this study was n=151 in both AIS and control group. Inflammatory markers such as NLR, PLR, CRP and lipid profile ratio, TG/HDL-C and systolic & diastolic BPs where the parameters considered for comparison between control and AIS groups. The results revealed that there was significant differences in NLR, CRP, TG/HDL-C and BP between the study groups (p value<0.01). PLR value did not significantly altered between the groups (P=0.5).* ***Conclusion:*** *The result showed that inflammatory markers, lipid profile and blood pressure play vital role in the occurrence of acute ischemic stroke.*

Keywords: Inflammation, haematological, triglycerides, neutrophils, platelets.

INTRODUCTION

Stroke is projected to be the leading cause of mortality affecting millions of people across the globe irrespective of social and economic status. Despite a decrease in death rates, the burden remains high. [1] AIS occurs when blood flow to the brain is significantly reduced, leading to neuronal death. The penumbra, a zone of high risk, is vulnerable to CBF fluctuations and is affected by local and global factors like cerebral vasoreactivity and blood pressure. Blood pressure (BP) significantly impacts vascular function and organ perfusion, with abnormalities linked to vascular dysfunction, particularly in cerebral circulation. One of the most frequent phenomena seen in the early hours and days following the beginning of AIS is acute blood pressure increase, which may have a significant impact on clinical judgments and alter the likelihood of acute consequences [2]. Previous study shows that a significant number of patients with acute ischemic stroke experience early neurological improvement (ENI) within the first 24 hours post-intravenous thrombolysis [3, 4]. Various studies have shown that neuroinflammation is closely with pathophysiology of ischemic stroke [5–8].

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Recently, it has been revealed that the neutrophil to lymphocyte ratio (NLR) and the platelet to lymphocyte ratio (PLR) may be the novel biomarkers of the baseline inflammatory process and may be the excellent predictors of ischemic stroke patients [9, 10]. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are widely utilized hematological parameters, serving as reliable markers for systemic inflammation and stress across medical disciplines. Our analysis focuses on the dynamic changes of neutrophil granulocytes and lymphocytes and the platelet and lymphocyte ratio in circulation during systemic inflammation, with NLR and PLR reflecting the dynamic relationship between neutrophils and lymphocytes and platelets and lymphocytes in illness and pathological states [11]. PLR has been utilised as an indicator of inflammation in autoimmune and cardiovascular conditions [12] Goyal et al found on patient with stroke admission, NLR was found to be elevated [13]. Since NLR and PLR indicate inflammatory response during ischemic stroke, there is the possibility to project theses parameters as generalized biomarkers for stroke [14]. Dyslipidemia is a risk factor, and non-conventional lipid profiles, including non-HDL-C,TC/HDL-C,TG/HDL-C ratios, have been linked to cardiovascular disease but their association with stroke remains controversial [15]. The objective of this research was to examine the correlation between lipid ratios and composite inflammatory ratios in patients with AIS. Besides, the study intended to investigate the possibility of utilizing the inflammatory and lipid parameters as predictive biomarkers for the occurrence of stroke and related complications.

METHODS

Study Design and Participants

This study was designed as prospective comparative cross sectional study. The study involved a total of 302 participants (151 Healthy control and 151 AIS) in the age group between 40 and 70 years in a tertiary care hospital. Healthy control participants who were coming for healthy checkup in the same hospital and all the AIS patients were treated in this hospital in the event of acute ischemic stroke for the first time were involved in this study. This study was approved by the institutional ethics committee (NIMSUR/IEC/2022/368 dated 28.09.2022 and 28/23/IEC/JCMMC&RI dated02.03.2023). CT and MRI scans were analysed to clinically differentiate different forms of stroke.

Both males and females with comorbidities such as hypertension, smoking, neurological disorders, and vascular complications like atrial fibrillation and congestive heart failure were included in the study population. The study excluded people who had experienced a hemorrhagic stroke or were an anticoagulant or antiplatelet therapy. Extracerebral hemorrhage, transient ischemic attack, stroke with unknown etiology, subarachnoid hemorrhage, brain tumors, patients treated with intravenous thrombolytic therapy prior to onset, patients with insufficient clinical data, patients receiving antiplatelet and anticoagulation therapy, surgery, rheumatoid immune-related diseases, or malignancy were the other exclusion criteria. Before starting any antihypertensive medication, the patient's blood pressure was measured in the emergency department (ED) upon arrival. For every patient, the absolute difference between Systolic Blood Pressure and Diastolic Blood Pressure at admission was measured for all participants. Prior to starting anticoagulant medication, blood samples were taken from each participant upon admission. These samples included total leukocyte counts, neutrophil counts, lymphocyte counts, absolute lymphocyte numbers, and platelet counts.

The laboratory investigations were done in DxH 900 Beckman Coulter hematology fully automated analyzer to analyse Complete blood count and in DxC 700 AU Beckman Coulter biochemistry fully automated analyzer to analyse Lipid profile. NLR was determined by taking the total number of neutrophil count and dividing by the total number of lymphocyte count. PLR was computed as the platelet count divided by the total number of absolute lymphocyte count. TG/HDL was determined by taking triglycerides and dividing by High density lipoprotein. CRP was done by turbidimetry in BT 1500 Biotecnica Chemistry/Turbidimetry fully automated analyzer.

Statistics

IBM SSPS Statistics, Version 26.0, was used to statistically analyze the coded and inserted data into an excel sheet. For continuous variables, descriptive statistics were explained using means/standard deviations, medians/IQRs, and frequencies and percentages; for categorical variables, they took the form of percentages. Using the Shapiro-Wilk test was used to study the distribution of the variables. With continuously distributed data, group comparisons were performed using the relevant statistical tests. When comparing two groups, Mann-Whitney U tests were employed because the data was discovered to be non-normally distributed. Correlations were performed using bivariate Spearman's correlations. P value less than 0.05 ($p < 0.05$) was considered as statistically significant.

RESULT

Baseline characteristics of the study participants inclusive of age, gender and blood pressure were represented in Table 1. Confounding variables included smoking, diabetes mellitus, hypertension, and a history of cardiovascular disease. Upon admission, the patient's diastolic and systolic blood pressure readings were taken. Distribution of Age among groups were represented in Figure 1. Distribution of gender among groups were represented in Figure 2. Laboratory data and outcome parameters for all patients control and AIS were represented in Table 2. Comparison of Inflammatory markers and lipid ratio between Healthy Control and AIS were represented in Table 3.

The p-values for NLR and CRP are both less than 0.001, indicating statistically highly significant differences in these inflammatory markers between the AIS and control groups. In other words, the distributions of NLR and CRP values are significantly different between the two groups, suggesting that these markers may be useful in differentiating between AIS patients and control. The p-value for PLR is 0.500, which is greater than the typical significance level of 0.05. P value >0.05 in PLR value indicated no significance between the control and AIS groups. Comparison of NLR between Control and AIS were represented in Figure 3. Comparison of CRP between control and AIS were represented in Figure 4. Comparison of TG/HDL-C between Control and AIS were represented in Figure 5.

Table 1. Baseline characteristics, and in-hospital measures for all patients control and AIS

	Control		**AIS**		**PValue**
	Mean	***Median***	***Mean***	***Median***	
Age	47.09 ± 6.43		53.48 ± 7.09		
Gender					
Male (%) (n = 197)	99 (65.6%)		98(64.9%)		
Female (%) (n = 105)	52 (34.4%)		53 (35.1%)		
Systolic	120	110–120	150	130–180	< 0.001
Diastolic	80	80–80	80	80–100	< 0.001

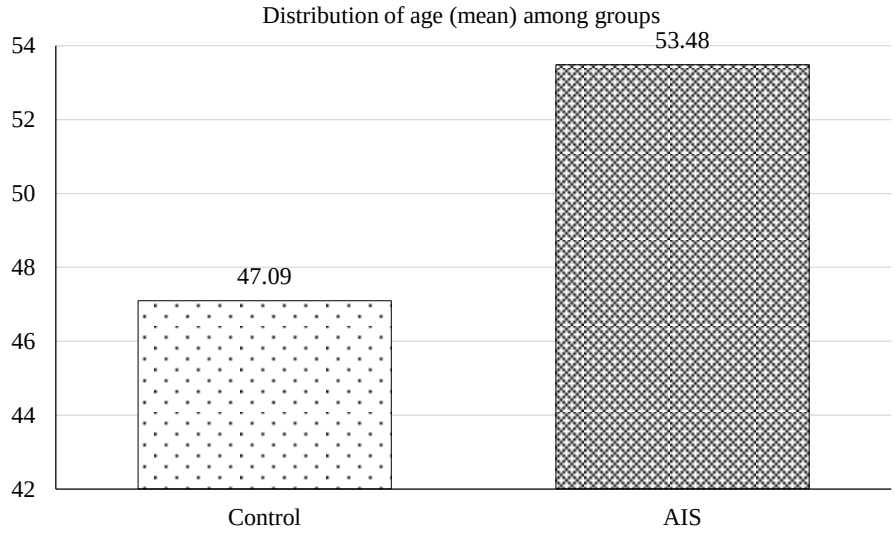

Figure 1. Distribution of Age among groups.

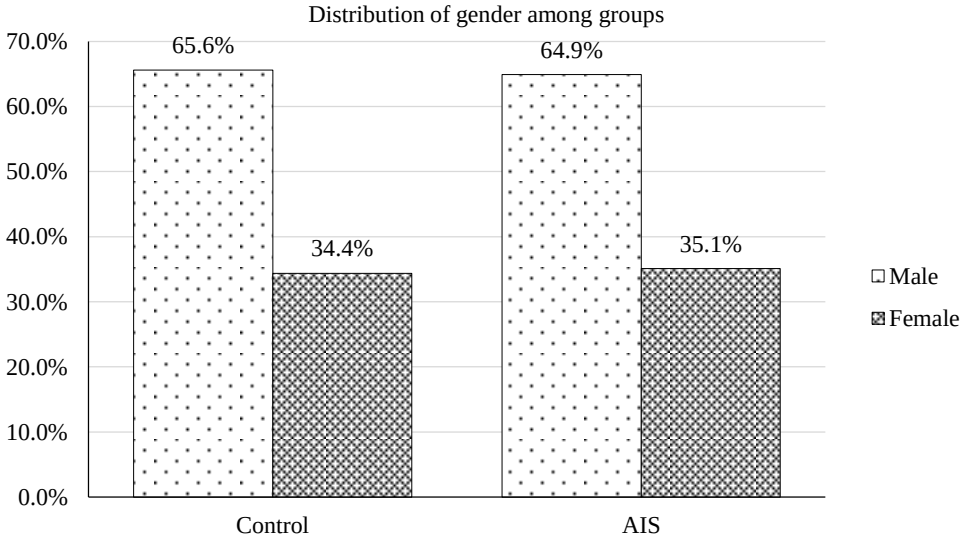

Figure 2. Distribution of gender among groups.

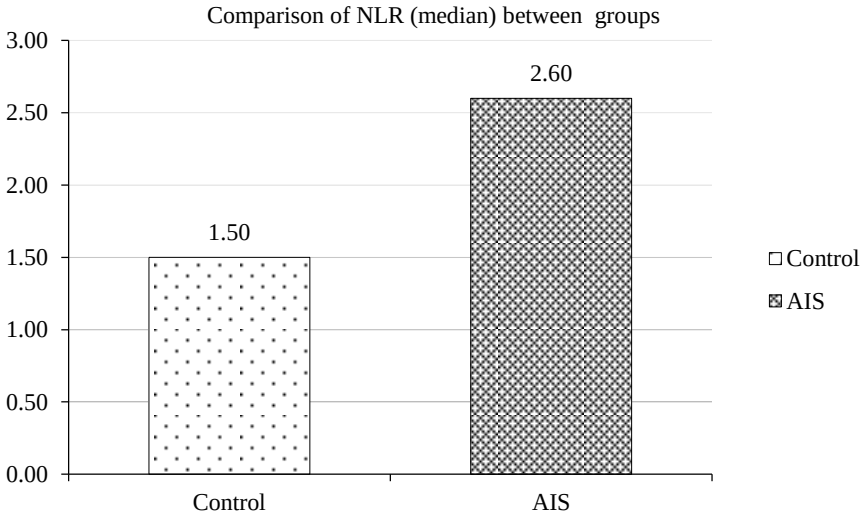

Figure 3. Comparison of NLR between Control and AIS.

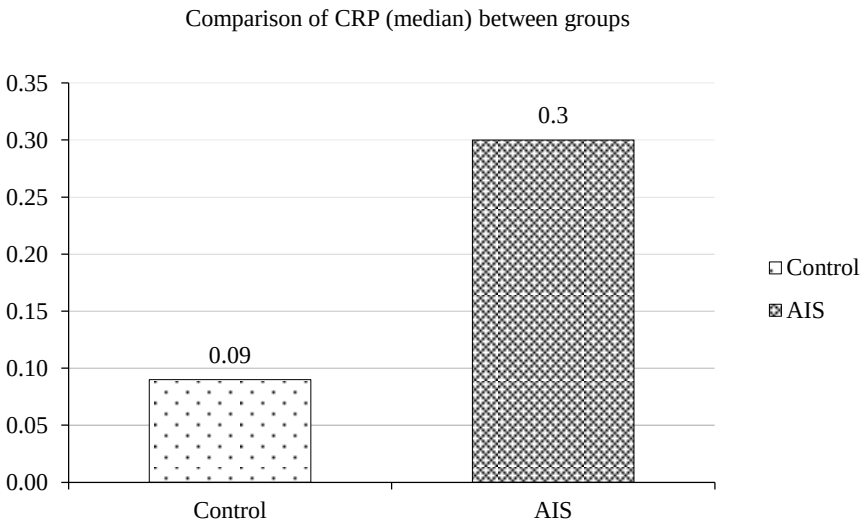

Figure 4. Comparison of CRP between Control and AIS.

Table 2. Laboratory data and outcome parameters for all patients control and AIS.

	Control		AIS		PValue
	Mean	***Median***	***Mean***	***Median***	
LaboratoryValues					
Neutrophil (%)	53.98	53	66.29	66	
Lymphocyte(%)	35.19	36	25.36	26	
NLR	1.50	1.28–1.82	2.60	1.82–4.18	<0.001*
TotalWBC(*10^3/L)	6.27	6.0	8.98	8.57	
Platelet(*10^5/L)	252.11	256	238.11	225	
AbsoluteLymphocyte	2.18	1.29	2.12	2.04	
PLR	114.34	94.21–139.81	110.29	87.9–143.39	0.500
CRP(mg%)	0.09	0.02–0.20	0.3	0.07–0.7	<0.001*
TG (mg%)	120.23	41	131.56	116	
HDL (mg%)	46.89	24	43.16	40	
TG/HDL	2.62	1.79–3.67	2.86	2.08–4.19	0.015*

Table 3. Comparison of Inflammatory markers and lipid ratio between Healthy Control and AIS.

Parameters	**Control**		**AIS**		**P-Value**
	Median	***IQR***	***Median***	***IQR***	
NLR	1.50	1.28–1.82	2.60	1.82–4.18	<0.001*
PLR	114.34	94.21–139.81	110.29	87.9–143.39	0.500
CRP	0.09	0.02–0.20	0.3	0.07–0.7	<0.001*
TG/HDL	2.62	1.79–3.67	2.86	2.08–4.19	0.015*

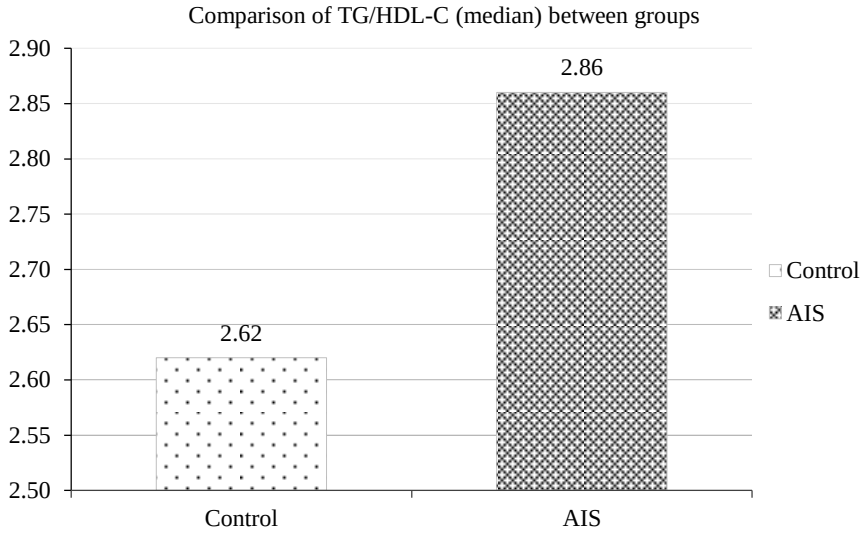

Figure 5. Comparison of TG/HDL-C between Control and AIS.

When the p-value is less than 0.05, it is deemed statistically significant, signifying a substantial difference between the control and AIS groups. While this difference is statistically significant, it's not as strong as the differences observed for NLR and CRP

The systolic and diastolic blood pressure p-values were both less than 0.001, suggesting that there were substantial differences between the AIS and control groups. This means that the distributions of systolic and diastolic blood pressure values were significantly different between the two groups. Comparison of Systolic BP between Control and AIS were represented in Figure 6. Comparison of diastolic BP between control and AIS were represented in Figure 7. Correlation of parameters of control and AIS shown in Table 4. Histogram of NLR in Control group were represented in Figure 8. Histogram of NLR in AIS were represented in Figure 9. Histogram of CRP in Control group were represented in Figure 10. Histogram of CRP in AIS group were represented in Figure 11. Histogram of TG/HDL-C in Control group were represented in Figure 12. Histogram of TG/HDL-C in AIS group were represented in Figure 13. Histogram of Systolic BP in control group were represented in Figure 14. Histogram of Systolic BP in AIS group were represented in Figure 15. Histogram of Diastolic BP in control group were represented in Figure 16. Histogram of Diastolic BP in AIS group were represented in Figure 17.

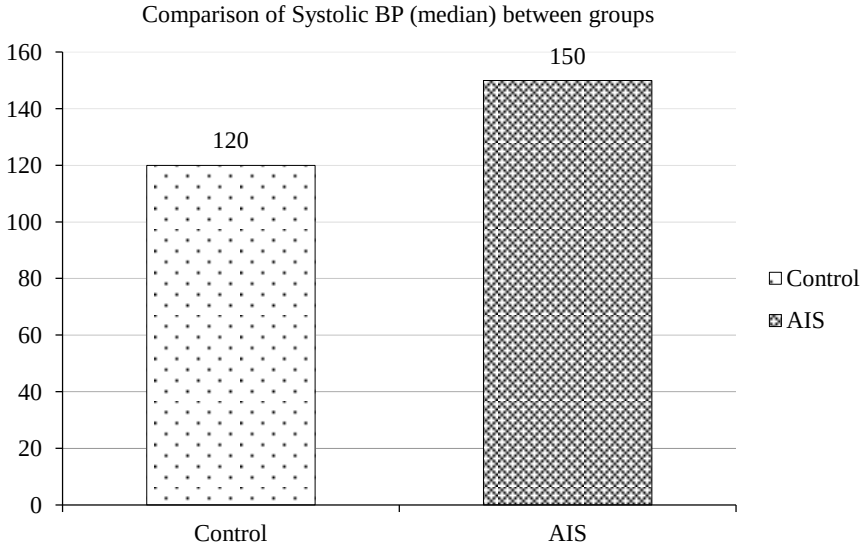

Figure 6. Comparison of Systolic BP between Control and AIS.

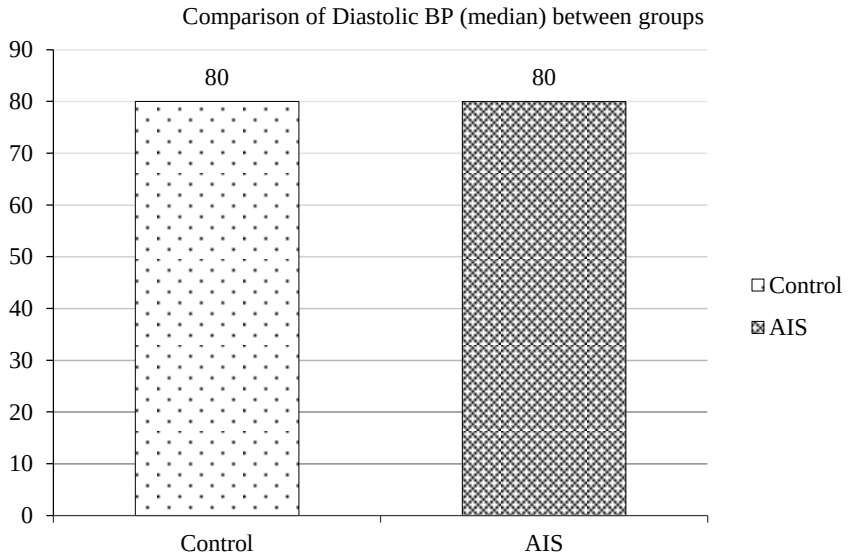

Figure 7. Comparison of Diastolic BP between Control and AIS.

Table 4. Correlation of parameters of Control and AIS

	Control		AIS	
Parameters	***Correlation coefficient***	***P-value***	***Correlation coefficient***	***P-value***
NLR vs.TG/HDL	-0.038	0.642	-0.109	0.184
PLR vs.TG/HDL	-0.142	0.081	-0.044	0.593
CRP vs.TG/HDL	-0.052	0.529	0.106	0.194

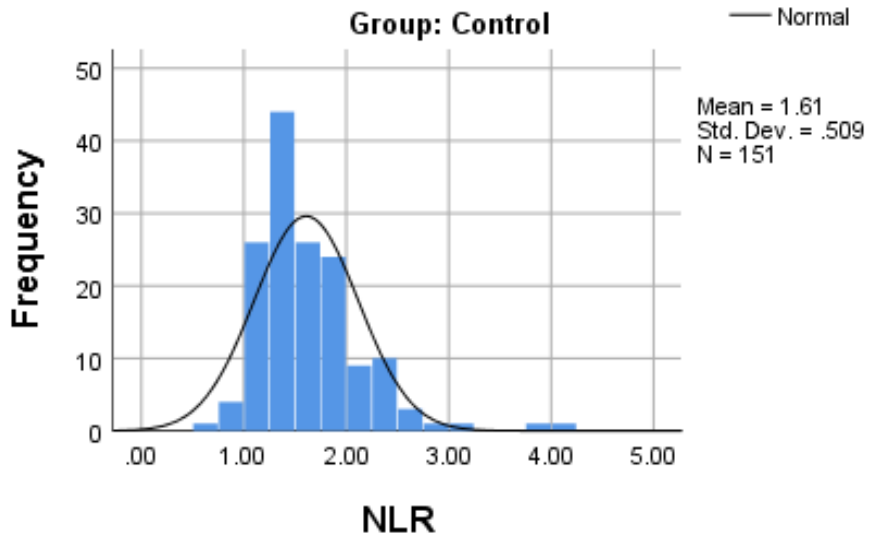

Figure 8. Histogram of NLR in Control group

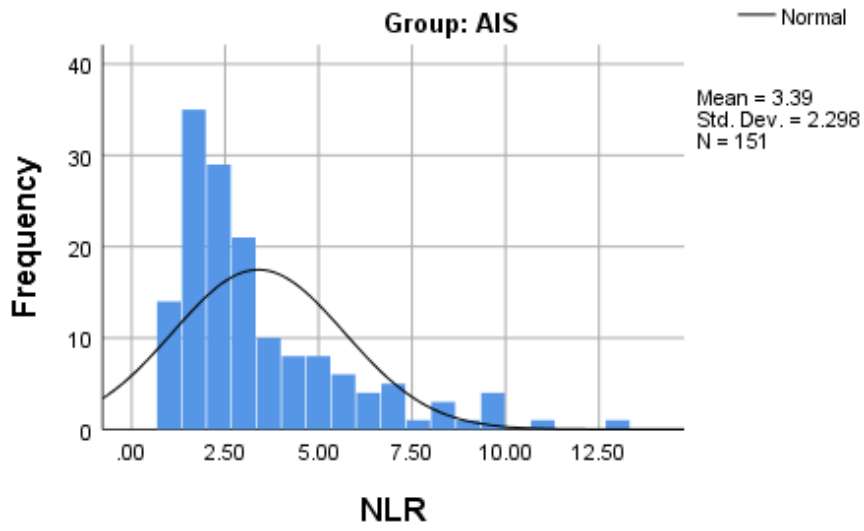

Figure 9. Histogram of NLR in AIS group.

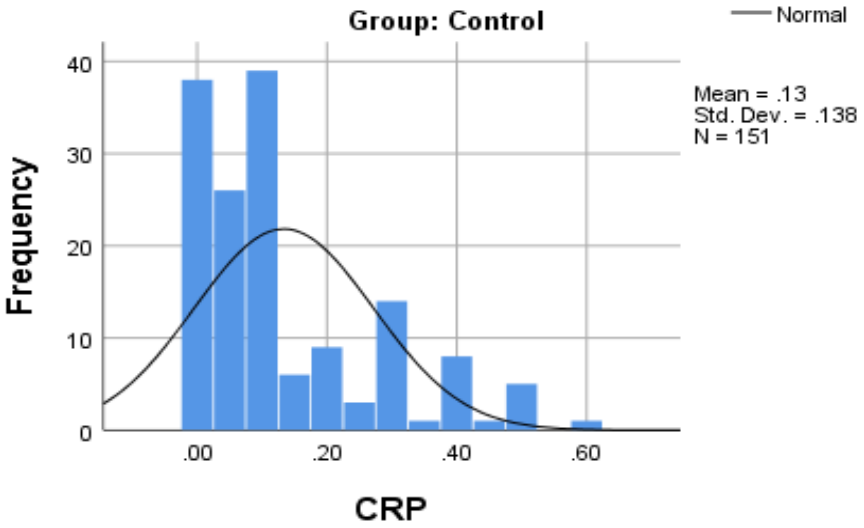

Figure 10. Histogram of CRP in Control group.

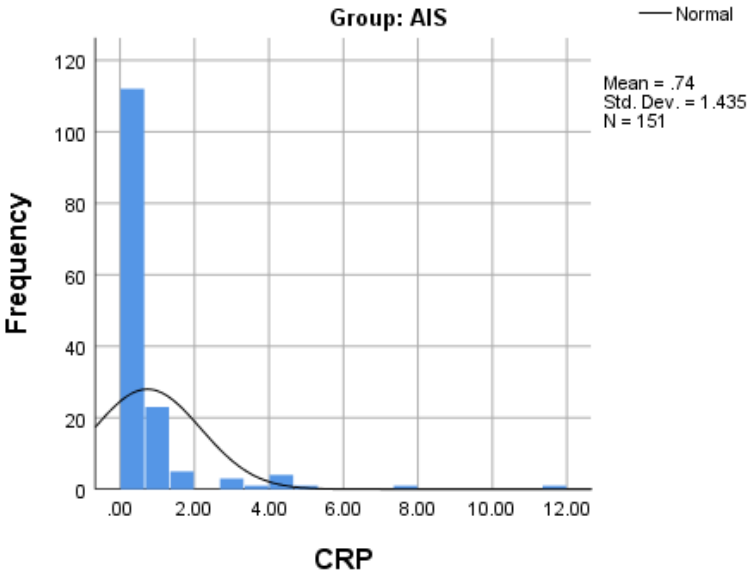

Figure 11. Histogram of CRP in AIS group.

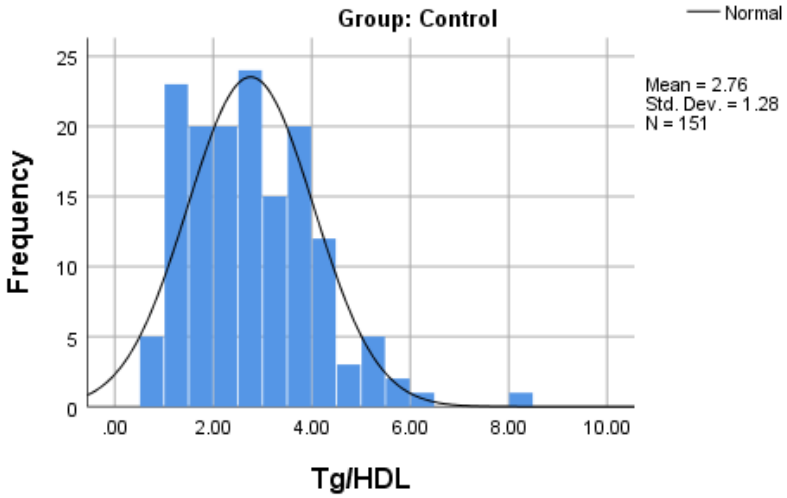

Figure 12. Histogram of TG/HDL-C in Control group.

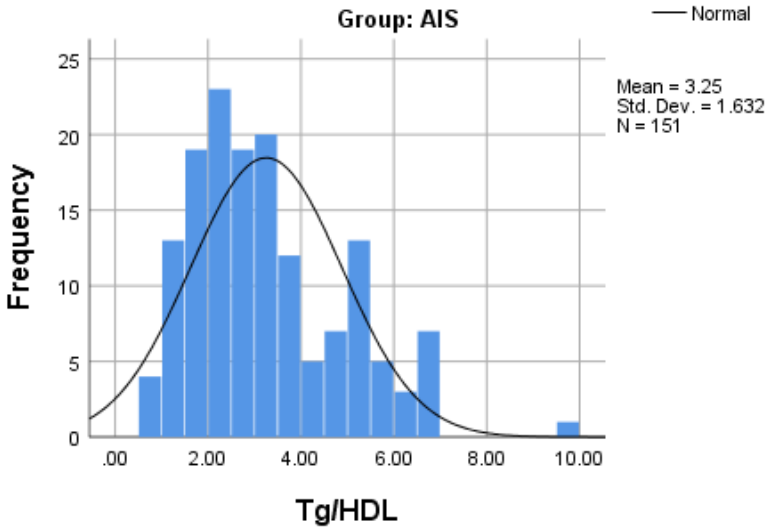

Figure 13. Histogram of TG/HDL-C in AIS group.

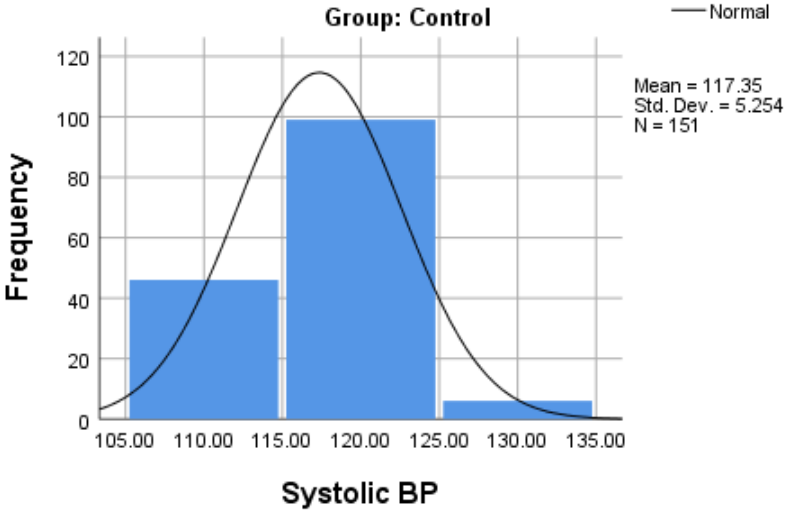

Figure 14. Histogram of Systolic BP in control group.

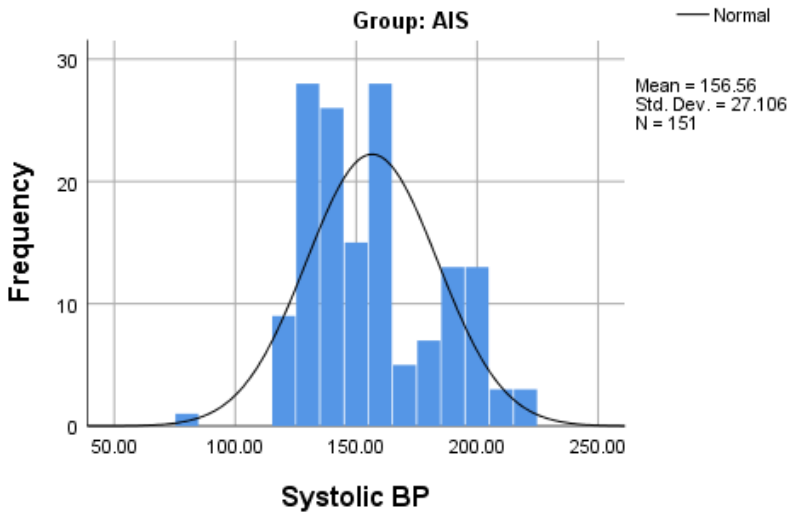

Figure 15. Histogram of Systolic BP in AIS group.

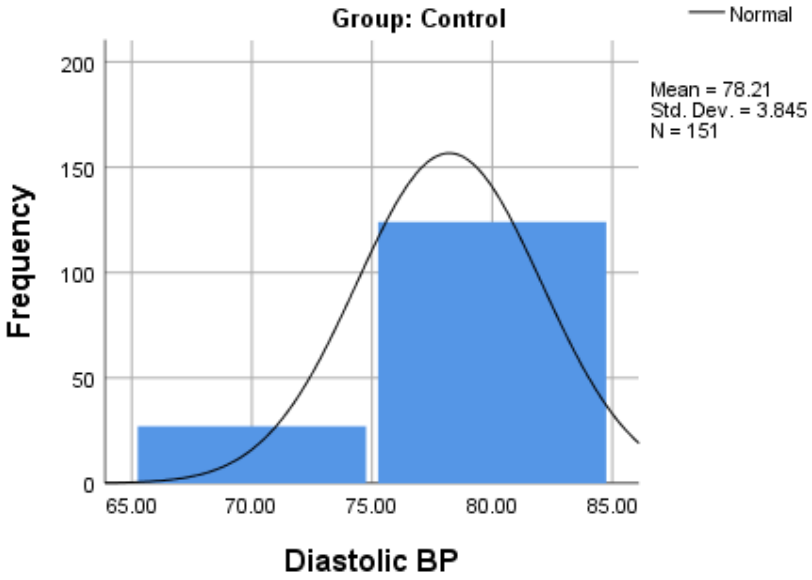

Figure 16. Histogram of Diastolic BP in control group.

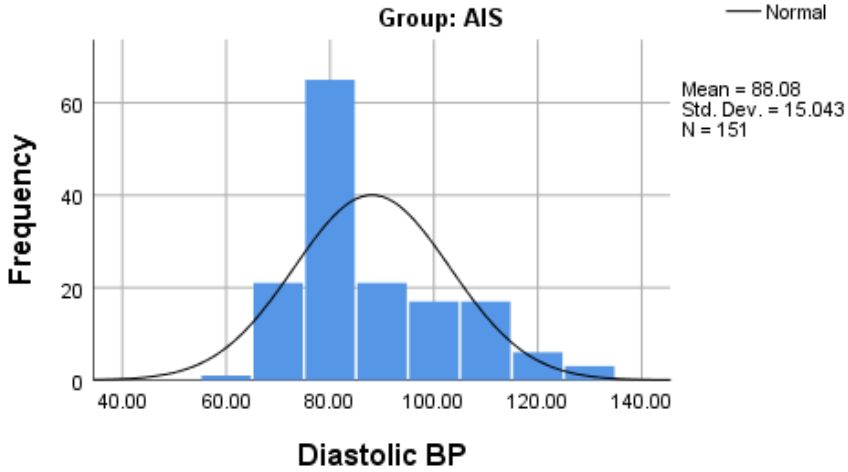

Figure 17. Histogram of Diastolic BP in AIS group.

DISCUSSION

Approximately 75% of patients experience an acute hypertensive response (AHR) during the acute phase of acute ischemic stroke, peaking within the first hours after stroke onset [16, 17]. Increased Neutrophil-to-lymphocyte ratio (NLR) and PLR are indicators of poor prognosis in acute ischemic stroke (AIS). In 5–10% of ischemic stroke patients, low blood pressure (BP) is associated with inferior functional outcomes [18, 19]. Blood pressure levels during stroke acute phase indicate collateral circulation effectiveness. Higher BP slows ischemic lesion growth, while lower BP may improve pial collateral recruitment. Higher BP improves cerebral blood flow, but sustained high BP may increase infarct growth [20–28]. The result of the present study revealed that classic inflammatory markers such as CRP and NLR were elevated during AIS. The findings undercomes the reference of inflammation in the occurrence of Ischemic stroke. Besides, the level of lipid profile ratio such as TG/HDL-C is elevated during AIS. The increased value of TG/HDL-C is an indication of the contributory role of lipid metabolites in the pathophysiology of stroke.

CONCLUSION

The combinatorial increase in both inflammatory markers and lipid profile markers during AIS could explain the importance of regulating inflammation and lipid metabolism during Ischemic stroke and alerting the clinicians for rationalizing dietary and therapeutic regimen.

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