DOI: 10.7860/JCDR/2026/85576.24180

Original Article

Internal Medicine Section

Prognostic Value of the Monocyte-to-HDL Ratio in Acute Ischaemic Stroke: A Prospective Cohort Study

BISHAL SWAIN[1], RANJAN KUMAR SEN[2], ABINASH SWAIN[3]

ABSTRACT

Introduction: The Monocyte-to-High-density lipoprotein cholesterol Ratio (MHR) has recently been identified as a novel inflammatory biomarker linked to atherosclerotic cardiovascular disease. Nonetheless, its predictive significance in Acute Ischaemic Stroke (AIS) remains insufficiently investigated.

Aim: To evaluate the correlation between MHR and stroke severity and prognosis in individuals with AIS.

Materials and Methods: This prospective observational cohort study was conducted at the Department of Medicine, Srirama Chandra Bhanja Medical College and Hospital (SCB) in Cuttack, Odisha, India, from 2023 to 2024. The study was designed and reported in accordance with STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines. A total of 200 consecutive patients aged 45 years or older with radiologically confirmed AIS who presented within 72 hours after onset were included. The monocyte count (five-part differential cell counter) and HDL-C level (fasting lipid profile) taken upon admission were used to calculate MHR. The National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS) were used to assess stroke severity and outcome (3 months). Statistical analyses were done by the Statistical Package for Social Sciences (SPSS) version 27.0, encompassing Spearman correlation, the Mann-Whitney U test, and ROC curve analysis

Results: The study included 200 patients (95 males and 105 females) with a mean age of 65.16±10.39 years. The median MHR was markedly elevated in patients with severe stroke {17.02 (IQR 3.26)} in contrast to those with moderate stroke {5.04 (IQR 1.55)}. There was a considerable positive relationship between MHR and both NIHSS (ρ=0.87, 95% CI: 0.80-0.92; p<0.001) and mRS (ρ=0.78, 95% CI: 0.70-0.85; p<0.001). The best MHR threshold for predicting a poor outcome was 9.24 (AUC 0.92, 95% CI: 0.88-0.96; sensitivity 80.2%, specificity 94.9%). In multivariable linear regression, MHR remained independently associated with admission NIHSS (B=1.38, p<0.001). In logistic regression analysis, MHR independently predicted poor 3-month functional outcome (OR=2.17, p<0.001).

Conclusion: An elevated MHR is independently correlated with heightened stroke severity and unfavourable functional outcomes. MHR could serve as an affordable and reliable predictor of prognosis in AIS.

Keywords: High-density lipoproteins, Inflammation, Ischaemic, Monocytes, Stroke

INTRODUCTION

Stroke remains one of the leading causes of mortality and long-term disability worldwide. The World Health Organisation (WHO) says that it is the second most common cause of death in the world and the most common cause of disability in adults [1]. In India, the projected annual incidence of stroke fluctuates between 119 and 145 per 100,000 individuals, equating to roughly 1.5 million new cases annually [2]. Even though there have been improvements in the treatment of acute stroke, especially thrombolysis and endovascular therapy, the outcome of AIS still depends a lot on the inflammatory response and vascular integrity at the time of presentation. In this context, the search for reliable and cost-effective biomarkers to predict stroke severity and prognosis is of significant therapeutic relevance. Experimental and clinical investigations have demonstrated that inflammatory cells, cytokines, and oxidative stress contribute to neuronal injury and blood-brain barrier disruption following ischaemia [3]. Monocytes, macrophages, and T-lymphocytes are essential mediators in this process. Monocytes invade the ischaemic brain early, stimulate the release of proinflammatory cytokines, and are involved in the creation and instability of atherosclerotic plaques [4,5]. Monocytes are classified into three principal subsets: classical (CD14++CD16–), intermediate (CD14++CD16+), and nonclassical (CD14+CD16++). Classical monocytes are predominantly proinflammatory, intermediate subsets exhibit both inflammatory and antigen-presenting functions, and nonclassical monocytes are primarily involved in anti-inflammatory and reparative processes [6]. During the early phase of stroke, classical monocytes swiftly travel to the damaged site, peaking between three and seven days, and differentiate into macrophages that modulate both tissue injury and healing [7]. High-Density Lipoprotein Cholesterol (HDL-C) demonstrates anti-inflammatory, antioxidant, and antithrombotic properties. It is essential for reverse cholesterol transfer, inhibits Low-Density Lipoprotein (LDL) oxidation, and stops endothelial dysfunction [8]. HDL-C also regulates monocyte activity by suppressing the production of adhesion molecules and cytokines, which helps keep blood vessels stable [9-11]. Because monocytes and HDL-C have opposite effects on vascular inflammation, the MHR has emerged as a composite biomarker that reflects the balance between proinflammatory and anti-inflammatory forces in atherosclerosis [12]. The predictive significance of MHR has been validated in several cardiovascular conditions, such as coronary artery disease and myocardial infarction; nevertheless, its function in AIS is insufficiently investigated. The current study is designed to analyse the correlation between MHR and stroke severity, as assessed by the NIHSS [13], and to determine whether increased MHR is associated with an unfavourable short-term prognosis, as indicated by the mRS [14]. Establishing such an association could enhance risk classification upon admission and help identify individuals who may require closer monitoring or more aggressive treatment.

MATERIALS AND METHODS

This was a prospective, observational cohort study carried out at the Department of Medicine at SCB Medical College and Hospital,

Cuttack, Odisha, India, from January 2023 to December 2024. The study was approved by the Institutional Ethics Committee of SCB Medical College (IEC Application number: 1215). All procedures involving human participants were performed in accordance with the ethical standards of the Institutional Ethics Committee and in compliance with the Declaration of Helsinki. No experimental animal procedures were conducted. Written informed consent was obtained from all participants or their legally authorised representatives.

Sample size calculation: The sample size was estimated based on the primary objective of evaluating the correlation between the admission Monocyte-to-High-Density Lipoprotein Cholesterol Ratio (MHR) and the National Institutes of Health Stroke Scale (NIHSS) score. Assuming an expected correlation coefficient (r) of 0.25, derived from a previous study by Algin A and Inan I [15], with a two-sided α error of 0.05 and a statistical power of 80%, the minimum required sample size was calculated to be 190 participants. To compensate for an anticipated dropout rate of approximately 5%, a total of 200 consecutive eligible patients were recruited.

Inclusion criteria: Consecutive patients aged 45 years or older with a first episode of acute ischaemic stroke, confirmed by CT or MRI of the brain, who presented within 72 hours of symptom onset, were included. Participants (or their legally authorised representatives) who provided written informed consent before enrollment were included.

Exclusion criteria: Patients with recurrent ischaemic stroke, haemorrhagic stroke, chronic liver or renal disease, cancer, connective tissue disorders, epilepsy, delayed presentation exceeding 72 hours, and previous statin therapy were excluded.

Study Procedure

Demographic information and medical histories, including vascular risk factors such as high blood pressure, diabetes, high cholesterol, smoking, drinking alcohol, and chewing betel, were collected. Stroke severity was assessed using the NIHSS at admission and again on day 7 [13]. Stroke severity was categorised as mild (NIHSS 0-4), moderate (NIHSS 5-20), and severe (NIHSS >20). Early neurological improvement or deterioration is defined as a change of ≥4 points from baseline [16]. The mRS was used to assess functional outcomes at three months. mRS was assessed during the outpatient follow-up visits at three months. Scores of 0-3 were considered good outcomes, whereas scores of 4-6 were considered poor outcomes [14]. Blood samples were collected upon admission before the initiation of statin or antiplatelet therapy. Absolute monocyte count was measured using an automated haematology analyser. A fasting lipid profile was used to get the High Density Lipoprotein Cholesterol (HDL-C) level. The MHR was calculated by dividing the absolute monocyte count by the HDL-C concentration measured at admission.

STATISTICAL ANALYSIS

Continuous variables were assessed for normality using the Kolmogorov-Smirnov test. Data that were normally distributed were shown as mean±Standard Deviation (SD), and skewed data were shown as median and Interquartile Range (IQR). The independent t-test or Mann-Whitney U test was used to compare groups, depending on the situation. Categorical variables were compared using the Chi-square test. Spearman's rho (ρ) was used to check for correlations. Multiple linear regression analysis was performed to evaluate the independent association between MHR and admission NIHSS score. Covariates entered were age, sex, systolic blood pressure, diastolic blood pressure, and random blood sugar. Adjusted regression coefficients (B) and Odds Ratios (OR) with 95% confidence intervals were reported. Receiver Operating Characteristic (ROC) analysis was performed to assess how well MHR distinguished between good and poor outcomes. The Area Under the Curve (AUC) was used as a measure of accuracy. No significant missing data were observed for the primary variables included in the analysis. Statistical significance was considered at $p<0.05$. All statistical analyses were performed using IBM SPSS version 27.0.

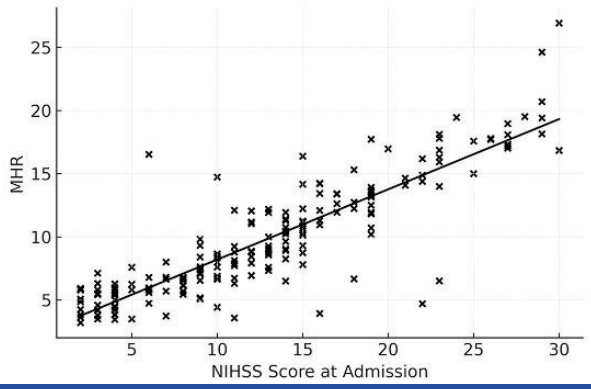
RESULTS

The baseline demographic and clinical characteristics of the study population are presented in [Table/Fig-1]. The cohort comprised 200 patients with a mean age of 65.16±10.39 years and a slight female predominance. Hypertension emerged as the most prevalent vascular risk factor, followed by diabetes mellitus, dyslipidaemia, smoking, alcohol consumption, and betel use. The majority of patients presented with motor or sensory deficits, while language disturbance and altered sensorium were also commonly observed. Of the 200 patients, 78 (39%) showed neurological improvement, 77 (38.5%) deteriorated, and the remaining 45 (22.5%) remained clinically stable during hospitalisation. According to the NIHSS categorisation, moderate stroke severity constituted the largest subgroup, with smaller proportions classified as mild and severe. Mean monocyte count at admission was 0.56±0.21 $\times 10^9$/L and was positively associated with stroke severity, whereas the mean HDL-C level was 41.3±10.8 mg/dL and was inversely associated. Admission MHR demonstrated a consistent significant stepwise increase across stroke severity categories. Patients with more severe neurological deficits exhibited substantially higher MHR values compared to those with milder presentations, indicating a progressive association between inflammatory-lipid imbalance and clinical severity. Correlation analyses demonstrated a strong positive association between MHR and admission NIHSS, supporting the relationship between inflammatory burden and acute stroke severity [Table/Fig-2]. A positive correlation was observed between admission MHR and 3 month mRS, indicating that elevated MHR at presentation was associated with poorer functional recovery [Table/Fig-3]. During hospitalisation, the early neurological course differed significantly according to admission MHR levels. Patients were categorised according to their early neurological course as improved (≥4-point decrease in NIHSS), deteriorated (≥4-point increase in NIHSS), or stable (<4-point change). Patients who experienced neurological deterioration had higher baseline MHR compared with those who improved [Table/Fig-4]. Multivariable regression analysis demonstrated that MHR remained independently associated with admission NIHSS after adjustment for age, gender, blood pressure, and metabolic parameters [Table/Fig-5]. In logistic regression analysis, admission MHR independently predicted poor 3-month functional outcome. Neither age nor gender was independently associated with outcome after multivariable adjustment. No significant association was observed between MHR and smoking status or alcohol consumption in the study population. ROC analysis demonstrated strong discriminative performance of MHR for predicting poor 3-month outcome [Table/Fig-6], supporting its potential prognostic utility in AIS.

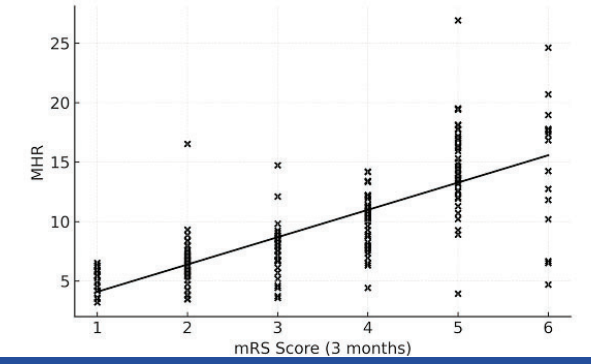
Variables	n (%)
Age (years), (mean±SD)	65.16±10.39
Gender	
Male	95 (47.5%)
Female	105 (52.5%)
Risk factors	
Hypertension	118 (59%)
Diabetes mellitus	51 (25.5%)
Dyslipidemia	46 (23%)
Smoking	17 (8.5%)
Alcohol consumption	16 (8.0%)
Betel use	54 (27%)
Presenting symptoms	
Motor/sensory deficit	184 (92%)
Language disturbance	114 (57%)

Altered sensorium	89 (44.5%)
Cranial nerve involvement	46 (23%)
Stroke severity (NIHSS at Admission)	
Mild (0-4)	36 (18%)
Moderate (5-20)	134 (67%)
Severe (>20)	30 (15%)

[Table/Fig-1]: Baseline demographic and clinical characteristics of the study population (N=200).
Continuous variables are expressed as mean±SD. Categorical variables are expressed as frequency and percentage. Stroke severity was categorised according to admission NIHSS score as mild (0-4), moderate (5-20), and severe (>20). NIHSS: National Institutes of Health Stroke Scale.



[Table/Fig-2]: Scatterplot showing the relationship between the Monocyte-HDL Ratio (MHR) and stroke severity at admission, measured by the NIHSS score. The fitted regression line demonstrates a significant positive correlation.
MHR: Monocyte-HDL ratio; NIHSS: National Institutes of Health Stroke Scale.



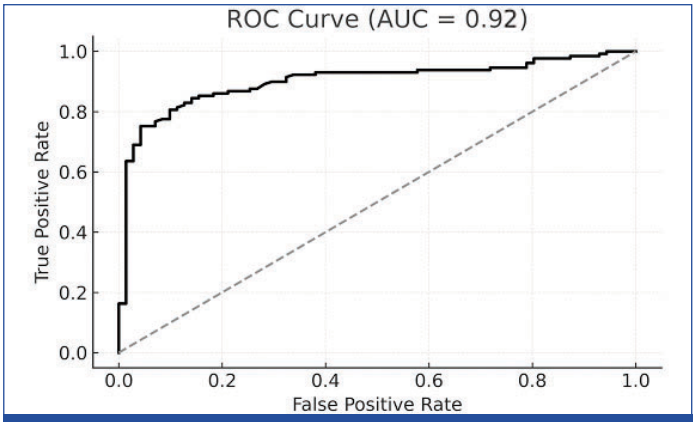
[Table/Fig-3]: Scatterplot showing the relationship between MHR and 3-month functional outcome measured by mRS. The regression line indicates a significant association between higher MHR and worse functional outcome.
MHR: Monocyte-HDL Ratio; mRS: modified Rankin Scale.

Early neurological course	n (%)	Median MHR (IQR)
Improved (≥4 NIHSS decrease)	78 (39%)	6.90 (2.85)
Deteriorated (≥4 NIHSS increase)	77 (38.5%)	11.95 (4.76)
Stable (<4 change)	45 (22.5%)	9.20 (3.30)

[Table/Fig-4]: Admission MHR according to early neurological changes during hospitalisation.
Early neurological course was defined as a ≥4-point change in NIHSS score from baseline during hospitalisation. Values are presented as median (interquartile range). Group comparisons were performed using the Mann-Whitney U test ($p < 0.001$). NIHSS: National Institutes of Health Stroke Scale; MHR: Monocyte-to-HDL cholesterol Ratio; IQR: Interquartile range

Outcome	Model type	Adjusted estimate	95% CI	p-value
NIHSS (Admission)	Multiple Linear Regression	B=1.38	1.27-1.49	<0.001
Poor 3-Month Outcome (mRS ≥4)	Binary Logistic Regression	OR=2.17	1.73-2.73	<0.001

[Table/Fig-5]: Multivariable regression analysis of MHR and clinical outcomes.
Multiple linear regression was performed to evaluate the independent association between admission Monocyte-to-HDL cholesterol Ratio (MHR) and NIHSS score at admission. Binary logistic regression was used to assess the independent association between admission MHR and poor 3-month functional outcome (modified Rankin Scale ≥4). Models were adjusted for age, sex, systolic and diastolic blood pressure, random blood sugar B: unstandardised regression coefficient; OR: Odds ratio; CI: Confidence interval; NIHSS: National Institutes of Health Stroke Scale; mRS: modified Rankin Scale



[Table/Fig-6]: Receiver Operating Characteristic (ROC) curve demonstrating the predictive value of the Monocyte-HDL Ratio (MHR) for predicting poor functional outcome (mRS ≥ 4) at 3 months. The Area Under the Curve (AUC) was 0.92 (95% CI: 0.88-0.96), reflecting strong prognostic performance.
MHR: monocyte-HDL ratio; mRS: modified Rankin Scale, AUC: Area under the curve

DISCUSSION

In the present study cohort of 200 patients with AIS, higher admission MHR was consistently associated with greater neurological deficit at presentation and poorer functional outcome at three months. The observed correlation between MHR and NIHSS suggests that systemic inflammatory burden at presentation parallels neurological deficit. Monocytes contribute to ischemic injury through cytokine release and endothelial activation, whereas HDL-C exerts anti-inflammatory and vasculoprotective effects [8-11]. The inverse relationship observed between HDL-C and stroke severity in this cohort supports the concept that reduced vascular protection may accompany heightened inflammatory activity during acute ischaemia.

In addition to its association with admission stroke severity, baseline MHR was significantly associated with the early neurological course during hospitalisation. Patients who experienced neurological deterioration had higher baseline MHR values than those who improved. This observation suggests that an elevated inflammatory state at presentation may contribute to ongoing ischaemic injury, impaired microvascular perfusion, and infarct progression. Our findings are consistent with previous reports. Algin A and Inan I demonstrated a significant correlation between MHR and NIHSS ($r \approx 0.52$), while Liu H et al., reported that higher MHR values were associated with increased stroke severity and unfavourable outcomes [15,17]. Similarly, Bolayir A et al., Li Y et al., and Oh SW et al., identified MHR as an independent predictor of poor functional outcome [18-20]. More recent investigations have further supported the prognostic value of MHR in AIS, highlighting its association with systemic inflammation and adverse clinical outcomes [21-24]. The strength of association observed in this cohort was higher than that reported in several prior studies. This may reflect the relatively high burden of hypertension and metabolic risk factors in our population, which could amplify systemic inflammatory activation at presentation. Such population-specific characteristics should be considered when interpreting the magnitude of effect. The adjusted OR observed in the present study reinforces the independent prognostic value of MHR after accounting for conventional risk factors. Although the discriminative performance of MHR was high in this analysis, caution is warranted. External validation in larger and more diverse cohorts is necessary before broad clinical adoption.

The findings of the present study suggest that the MHR may serve as a practical, readily available biomarker for early risk stratification in acute ischaemic stroke. Elevated MHR at admission could help identify patients at higher risk of severe neurological deficit, early neurological deterioration, and poor functional outcome. This may help clinicians prioritise closer monitoring, early intensive care, and timely therapeutic interventions. Additionally, MHR may complement established clinical scales such as the NIHSS, providing incremental

prognostic value from routinely available laboratory parameters. Future studies should explore integrating MHR with neuroimaging parameters, such as infarct volume, collateral status, and perfusion imaging, to improve prognostic accuracy. Combining MHR with other inflammatory biomarkers, such as the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Systemic Inflammatory Response Index (SIRI), may offer a more comprehensive assessment of stroke severity. Large multicentre studies are needed to validate these findings and determine whether incorporating MHR into clinical decision-making can enhance care for acute ischaemic stroke.

Limitation(s)

The present study was conducted at a single centre, and confounding cannot be entirely excluded. Additionally, outcomes were assessed at three months, and the longer-term prognostic effect remains to be determined. MHR is derived from routinely available laboratory parameters, which enhances its feasibility in clinical settings. However, this study did not perform a formal cost-effectiveness analysis. Serial measurements of MHR were not performed; therefore, dynamic changes in inflammatory status during hospitalisation could not be evaluated.

CONCLUSION(S)

In conclusion, the present study demonstrates that an increased monocyte-to-HDL ratio is significantly correlated with increased stroke severity and unfavourable short-term outcomes in patients with AIS. MHR appears to be a simple and potentially useful biomarker. Due to its simplicity and predictive value, MHR may complement existing clinical scales to improve risk stratification in AIS.

REFERENCES

[1] Government of India. Central Bureau of Health Intelligence. National Health Profile 2008. New Delhi (IN): Directorate General of Health Services; 2008. p. 102.
[2] National Stroke Registry-India. Burden of stroke in India [Internet]. Bengaluru (IN): National Centre for Disease Informatics and Research, Indian Council of Medical Research; 2025 [cited 2026 Mar 3]. Available from: https://stroke.ncdirindia.org/Burden.html.
[3] Jin R, Yang G, Li G. Inflammatory mechanisms in ischemic stroke: Role of inflammatory cells. J Leukoc Biol. 2010;87(5):779-89.
[4] Chiba T, Umegaki K. Pivotal roles of monocytes/macrophages in stroke. Mediators Inflamm. 2013;2013:759103.
[5] Jaipersad AS, Lip GY, Silverman S, Shantsila E. The role of monocytes in angiogenesis and atherosclerosis. J Am Coll Cardiol. 2014;63(1):01-11.
[6] Cormican S, Griffin MD. Human monocyte subset distinctions and function: Insights from gene expression analysis. Front Immunol. 2020;11:1070.
[7] Han D, Li R, Han Y, et al. The role of peripheral monocytes and macrophages in ischemic stroke. Neurol Sci. 2020;41(11):3087-95.
[8] Nagao M, Nakajima H, Toh R, Hirata K-I, Ishida T. Cardioprotective effects of high-density lipoprotein beyond its anti-atherogenic action. J Atheroscler Thromb. 2018;25(11):985-93.
[9] Murphy AJ, Woollard KJ, Hoang A, Mukhamedova N, Stirzaker RA, McCormick SP, et al. High-density lipoprotein reduces the human monocyte inflammatory response. Arterioscler Thromb Vasc Biol. 2008;28(11):2071-77.
[10] Assmann G, Gotto AM Jr. HDL cholesterol and protective factors in atherosclerosis. Circulation. 2004;109(1 Suppl 1):III-8-III-14.
[11] Hafiane A, Genest J. High density lipoproteins: Measurement techniques and potential biomarkers of cardiovascular risk. BBA Clin. 2015;3:175-88.
[12] Villanueva DLE, Tiongson MD, Ramos JD, Llanes EJ. Monocyte to high-density lipoprotein ratio (MHR) as a predictor of mortality and major adverse cardiovascular events among STEMI patients undergoing primary PCI: A meta-analysis. Lipids Health Dis. 2020;19(1):55.
[13] Brott T, Adams HP Jr, Olinger CP, Marler JR, Barsan WG, Biller J, et al. Measurements of acute cerebral infarction: A clinical examination scale. Stroke. 1989;20(7):864-70.
[14] van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke. 1988;19(5):604-07.
[15] Algin A, Inan I. The role of radiologic, clinical and biochemical parameters in prediction of stroke mortality. Neurosciences (Riyadh). 2019;24(2):110-14.
[16] Siegler JE, Martin-Schild S. Early Neurological Deterioration (END) after stroke: The END depends on the definition. Int J Stroke. 2011;6(3):211-12.
[17] Liu H, Liu K, Pei L, Gao Y, Zhao L, Sun S, et al. Monocyte-to-high-density lipoprotein ratio predicts the outcome of acute ischemic stroke. J Atheroscler Thromb. 2020;27(9):959-68.
[18] Bolayir A, Gokce SF, Cigdem B, Bolayir HA, Yildiz OK, Bolayir E, et al. Monocyte/high-density lipoprotein ratio predicts the mortality in ischemic stroke patients. Neurol Neurochir Pol. 2018;52(2):150-55.
[19] Li Y, Chen D, Sun L, Chen Z, Quan W. Monocyte/high-density lipoprotein ratio predicts the prognosis of large artery atherosclerosis ischemic stroke. Front Neurol. 2021;12:769217.
[20] Oh SW, Yi HJ, Lee DH, Sung JH. Prognostic significance of various inflammation-based scores in patients with mechanical thrombectomy for acute ischemic stroke. World Neurosurg. 2020;141:e710-e717.
[21] Xu Q, Wu Q, Chen L, Li H, Tian X, Xia X, et al. Monocyte to high-density lipoprotein ratio predicts clinical outcomes after acute ischemic stroke or transient ischemic attack. CNS Neurosci Ther. 2023;29(7):1953-64.
[22] Sharma D, Aravind S, Joseph S, Fagera N, Rajagopalan G. The role of monocyte to high-density lipoprotein cholesterol ratio in predicting the severity of acute ischemic stroke and its association with the NIHSS. J Assoc Physicians India. 2023;71(8):11-12.
[23] Wang J, Zheng G, Xu J. Association between monocyte to high-density lipoprotein cholesterol ratio and stroke prevalence in American adults: A cross-sectional NHANES Study. J Stroke Cerebrovasc Dis. 2026;35(3):108580.
[24] Huang Q, Li Y. Association between monocyte-to-high-density lipoprotein cholesterol ratio and stroke: A propensity score-matched cross-sectional study. Front Neurol. 2026;17:1721994.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Resident, Department of General Medicine, SCB MCH, Cuttack, Odisha, India.
2. Associate Professor, Department of General Medicine, SCB MCH, Cuttack, Odisha, India.
3. Assistant Professor, Department of Neurology, IMS&SUM Hospital II, Bhubaneswar, Cuttack, Odisha, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Ranjan Kumar Sen,
Associate Professor, Department of General Medicine,
SCB MCH, Cuttack-753007, Odisha, India.
E-mail: drranjansen@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Dec 17, 2025
- Manual Googling: May 09, 2026
- iThenticate Software: May 12, 2026 (10%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Nov 28, 2025**
Date of Peer Review: **Feb 12, 2026**
Date of Acceptance: **May 14, 2026**
Date of Publishing: **Aug 01, 2026**