

A Study to Predict Role of Monocyte to High-Density Lipoprotein Cholesterol Ratio in the Severity of Acute Ischemic Stroke and its Association with the NIHSS

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Abstract: ***Background:** Atherosclerosis, an underlying abnormality, plays a significant role in the progression of ischemic stroke. Inflammation, oxidative stress, platelet activation, endothelial dysfunction, and lipid abnormalities are the primary factors involved in the development of atherosclerosis. Monocytes, key contributors to chronic inflammation, actively participate in the development, progression, and rupture of atherosclerotic plaques within blood vessels. Therefore, the objective of this study is to investigate the monocyte to high-density lipoprotein cholesterol (HDL-C) ratio (MHR) in acute ischemic stroke (AIS) and its correlation with the National Institute of Health Stroke Scale (NIHSS) to predict the severity of the condition. **Materials and methods:** A prospective observational study was conducted on 100 AIS patients at a tertiary care hospital of Uttar Pradesh. Diagnostic methods included clinical examination, imaging, and laboratory tests. MHR was measured using a hematology analyzer and correlated with reference values and stroke severity. **Results:** The mean MHR of AIS patients were higher (14.12 ± 2.95) than controls (7.09 ± 1.48) ($p = 0.0001$). Besides, a statistically significant positive correlation was obtained between his MHR and NIHSS scores at admission and discharge. MHR values were significantly greater from a reference point in patients who deteriorated (18.48 ± 4.02) compared to significantly lower values in patients who improved (13.66 ± 2.44). **Conclusion:** In our study, the MHR shows an increased value in patients with AIS, and a linear correlation is found with the NIHSS score. Thus, the method is a pocket-friendly, easily available, and simple-to-use novel inflammatory marker that may predict the severity of a disease.*

Keywords: Cholesterol, AIS, NIHSS, HDL

1. Introduction

In recent decades, stroke has caused a significant load on the healthcare system. Ischemic stroke is the leading cause of mortality and disability among low-income people. Therefore, it is highly desirable to detect ischemic stroke at the onset so that primary defence is the keystone of management.

Atherosclerosis, particularly intracranial atherosclerosis, plays a crucial role in the progression of ischemic stroke. Pathophysiological studies have identified intracranial plaques that can lead to interarterial embolism, hemodynamic depression, in situ thromboembolism, and focal branch occlusion, thereby contributing to the development of ischemia.[1, 2]

However, these imaging techniques are expensive, time-consuming, require specialized settings, and are primarily used as supplementary data in clinical and research studies. Therefore, there is a need for a new marker for early diagnosis and prevention of ischemic stroke. Inflammation, oxidative stress, platelet activation, endothelial dysfunction, and lipid abnormalities have been proposed as key components in the pathophysiology of atherosclerosis growth and progression.[7, 8]

Monocytes and T lymphocytes play an essential role in stroke pathogenesis by increasing the production of inflammatory cytokines, promoting infiltration and lipid core formation, and exacerbating brain damage. On the other hand, high-density lipoprotein cholesterol (HDL-C) protects endothelial cells from inflammation to oxidative stress by regulating monocyte activation and the proliferation of

monocyte progenitor cells. It also suppresses macrophage migration and low-density lipoprotein (LDL) molecule oxidation. [10]

Based on the pathogenesis of atherosclerosis, HDL-C levels have antioxidant and anti-inflammatory properties as lipid parameters. They can mitigate the adverse effects of LDL-C on endothelial cells, limiting atherosclerosis. Conversely, monocytes are a hematological marker that increases during inflammation. Thus, based on literature findings, while HDL-C levels decline, monocyte levels increase in atherosclerosis, which in turn is expected to elevate the monocyte to HDL-C ratio (MHR) value. Building upon these observations, the MHR has emerged as a preferred model for assessing the prognosis of cardiovascular events and evaluating atherosclerosis. [9]

The National Institutes of Health Stroke Scale (NIHSS) is a well-standardized and widely used tool for assessing stroke severity, predicting patient outcomes and prognosis, and monitoring treatment efficacy. However, the use of MHR in acute ischemic stroke (AIS) and its correlation with NIHSS is relatively unexplored.

Therefore, the aim of this study was to evaluate the MHR in AIS patients and its correlation with the NIHSS for predicting stroke severity. By comparing the MHR value with the NIHSS score, we can determine whether there is a correlation between the two. This study sought to assess the ratio of MHR in AIS and its correlation with NIHSS to predict the severity of AIS.

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2. Material and Methods

This hospital – based, prospective, observational study.

Inclusion Criteria

The patients included in this study were individuals diagnosed with AIS.

Exclusion Criteria

Patients with hemorrhagic stroke, venous sinus thrombosis, autoimmune disease, hepatic or renal disease, connective tissue disorders, moribund condition, seizure disorders, mental or physical illness, and refusal to participate in the study were excluded. The clinical examination, and computed tomography or magnetic resonance imaging of the brain were applied to diagnose acute stroke. The stroke severity was determined using the National Institute of Health Stroke Scale (NIHSS) among all patients at admission and release. Stroke severity was categorized as minor strokes (1–4), moderate strokes (5–15), moderate to severe strokes (16–20), and severe strokes (21–42). An in-house, fully automated hematology analyzer performed the fasting lipid profile and complete blood count (CBC) test to measure the MHR. Therefore, we performed a CBC test in which the ratio of monocytes to HDL was obtained by dividing the absolute number of monocytes by HDL. This MHR ratio was further correlated to calculated reference values from a control group (same age and sex) and NIHSS severity scores (at admission and discharge).

Statistical Analysis

Continuous variables were presented as mean \pm standard deviation (SD), while categorical variables were expressed as frequencies and percentages. Independent t-tests compared parameters between cases and controls. A significance level of $p < 0.05$ indicated statistical significance.

3. Results

Of 100 patients, 55 males and 45 females were matched with a control group containing 57 males and 43 females. Most patients with AIS were between 50 and 69 years (73%), and their age had a mean of 62.26 ± 9.12 years. The average HDL ratio of male cases was 39.3 mg/dL, and that of female cases was 47.2 mg/dL. The mean duration of onset of symptoms is 38 hours (1.5 days), with a range of presentation from 8 to 140 hours (5.8 days).

	Total no. of patients	Admission (mean \pm SD)		
		Monocyte (per mm ³)	HDL level (mg/dl)	MHR
Improves	77	582 + 79	43.14 + 4.89	13.66 + 2.44
Deteriorated	8	686.25 + 103.09	37.75 + 3.57	18.48 + 4.02
Static	15	584.66 + 75.20	42.2 + 5.08	14.12 + 3.07

4. Discussion

Our study involved AIS patients (100) and the same number of age- and sex-matched controls. In our study, the largest cases (73%) were in the 50–69-year-old group. In this study, the mean age of cases was 61.04 ± 8.65 years.

We have not taken the patients presented in the window period. The mean discharge period was 6.3 days, showing a negative correlation with MHR. Right hemiparesis with or without cranial nerve involvement was the very common focal neurological deficit, accounting for 49% of the cases when compared to 45% of the cases with left hemiparesis with or without cranial nerve involvement. Approximately 6% of cases showed features of posterior circulation stroke, such as dizziness and incoordination. The stroke severity in patients of different groups based on NIHSS score showed the maximum was in NIHSS score group 5–15 (moderate stroke).

A total of 71 patients had NIHSS scores between 5 and 15, and 61 patients had NIHSS scores between 5 and 15 at discharge. We found a moderately strong and statistically significant correlation between monocyte counts at admission and NIHSS scores. As NIHSS scores decreased, HDL levels decreased proportionally. The correlation between his HDL level on admission and his NIHSS score was negative, moderately strong, and statistically significant.

Monocyte to HDL-C ratio (MHR) was calculated in patients with different NIHSS scores. It was lowest in NIHSS score groups 14, that is, 11.02 ± 1.15 , increased to 13.66 ± 2.10 in NIHSS groups 5–15, and MHR in NIHSS scores 16–20 was 16.60 ± 2.47 , and the ratio was highest in NIHSS groups 21–42, 22.04 ± 1.14 . At admission, a statistically significant correlation was found between MHR and NIHSS scores.

Among 100 patients, 77 improved, eight worsened, and 15 were static, according to the clinical status of the various NIHSS score groups assessed at discharge. Most patients who improved were shown to have much lower mean heart rates than those who deteriorated.

Pearson Correlation Coefficient	0.7415
t- value	5.203
p- value	0.0001
n	100

NIHSS Score	No. of patients	MHR
1- 4	11	11.02 ± 1.15
5- 15	71	13.66 ± 2.10
16- 20	14	16.60 ± 2.47
21- 42	4	22.04 ± 1.14

In our study, 23% of stroke patients had a history of ischemic heart disease (IHD). Furthermore, monocytes, known as indicators of chronic inflammation, primarily interact with platelets and endothelial cells, exacerbating inflammatory and prothrombotic processes. They actively contribute to the formation, progression, and rupture of atherosclerotic plaques. Conversely, HDL-C protects endothelial cells from inflammation to oxidative stress by

regulating monocyte activation and proliferation. It also inhibits macrophage migration and LDL molecule oxidation. Considering the pathogenesis of atherosclerosis, HDL-C levels possess antioxidant and anti-inflammatory properties, which help mitigate the detrimental effects of LDL-C on endothelial cells and limit atherosclerosis. Simultaneously, monocytes serve as hematological markers that increase during inflammatory conditions.

Monocyte to HDL-C Ratio (MHR) and Clinical Outcome In our study, among 100 patients, 77 showed improvement, eight worsened, and 15 remained static. At admission, the MHR in 77 patients who improved was 13.662.44. Eight deteriorated patients had an MHR value of 18.484.02. This suggested that the MHR value at admission was low for those who improved and high for those who deteriorated. As a result of this data, it is possible to conclude that admission MHR values predict severity and prognosis in stroke patients. Limitations of our study include small sample size, single-center patient inclusion, lack of long-term follow-up to assess MHR as a predictor of prognostic outcomes in AIS.

5. Conclusion

The MHR is a simple, inexpensive, and readily available method that may help predict disease severity and functional outcomes in AIS patients. There is a proven linear correlation between this ratio and NIHSS scores. Moreover, this ratio can be calculated even in limited-resource health setups. However, further investigations are necessary to validate our results. Our study strongly supports the routine calculation of this ratio and its potential contribution to risk stratification in AIS patients.

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