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Original Research Article

THE ROLE OF MONOCYTE COUNT TO HIGH-DENSITY LIPOPROTEIN CHOLESTEROL RATIO IN PREDICTING THE SEVERITY OF ACUTE ISCHEMIC STROKE AND ITS CORRELATION WITH THE NIHSS

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ABSTRACT

Background: Stroke is defined as the development of a focal neurological deficit secondary to the obstruction of the blood flow to the brain, and stroke is the fifth leading cause of disability and the fourth leading cause of mortality in India. Increasing the monocyte count with a decrease in the high-density lipoprotein cholesterol level enhances atherosclerosis formation and activates thrombocyte activation with an increased release of inflammatory mediators. The National Institute of Health Stroke Scale was found to be a standardised instrument used to determine the severity of the stroke. **Aim:** To assess the role of the Monocyte HDL Ratio (MHR) in acute ischemic stroke patients and to find its correlation with the National Institute of Health Stroke Scale (NIHSS) to predict the severity of the condition. **Materials and Methods:** This prospective observational study was conducted in a tertiary care centre in Trichy, Tamil Nadu, India. The test was conducted between November 2023 and April 2024 for 6months. Patients with the diagnosis of acute ischemic stroke were included in the study. After the initial assessment, the severity of the stroke was determined by the NIHSS scale followed by monocyte to HDL-C ratio (MHR) obtained from the patient's complete blood count and lipid profile at the time of admission. **Result:** A total of 100 patients with controls participated in this study. The maximum number of patients we found to be more than 60 years old (55%) and were males (58%). Hypertension (60%) and hypercholesterolemia (46%) are the most common risk factors encountered in the study. Right hemiparesis was noted in half of the patients (50%). The study showed a significant positive correlation between the NIHSS score and the MHR value (p-<0.001). MHR values were greater among patients who deteriorated (18 + 0.94) than those who improved (12.4 $\pm$ 0.99). **Conclusion:** Acute ischemic stroke is the leading cause of morbidity and mortality in recent times. The monocyte to HDL-C ratio was found to be a simple, faster and cost-effective prognostic marker in determining the severity and outcome of the patient.

INTRODUCTION

Stroke is one of the upcoming health problems in today's world. Due to the increase in Western culture, stress, urbanisation, and poor eating habits have further increased the incidence of stroke in recent times.[1] A stroke is also referred to as an acute cerebrovascular accident, and it is a medical emergency. It is characterised by the compromise in cerebral perfusion or vasculature, which leads to the development of localised neurological impairment.[2] The American Heart Association or the American Stroke Association defines a stroke as an acute episode of neurological impairment lasting for more than 24 hours. Stroke has been mainly divided into two types, namely ischemic stroke and hemorrhagic stroke.[3] And approximately 85% of the strokes were found to be ischemic in nature. The ischemic stroke was further divided into embolic, thrombotic and lacunar strokes.[2]

Hypertension, diabetes mellitus, smoking, alcoholism, obesity, and arterial fibrillation were found to be the most common risk factors for stroke.[4] The incidence of stroke was found to be

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around 800,000 people annually, and it is the fifth leading cause of death in the United States of America.[5] Stroke is also one of the leading causes of disability. In India, stroke ranks as the fifth most common cause of disability and the fourth most common cause of death. India has a high and rising stroke prevalence, with an estimated 119–145 cases per 100,000 people each year.[6] Over 1.25 million new stroke incidents were reported in India in 2021, 51% rise from 1990. The treatment of stroke also significantly affects the economy of the individual and the country. Stroke accounts for 0.66% of the world's GDP, and the cost will rise to one trillion USD by the end of 2030.[7]

In the pathogenesis of atherosclerosis, inflammation, oxidative stress, activation of platelets, and endothelial dysfunctions play an essential role in atherosclerosis growth and progression. The monocytes lead to the production of reactive oxygen species, and they further differentiate into foamy macrophages, which release various pro-inflammatory cytokines that drive the circulating monocytes to the lesion sites, causing vulnerable Atherosclerotic plaques, which in turn cause thrombosis and poor clinical outcome.[8,9] It is also involved in lipid core formation and further exacerbates brain damage. On the other hand, high-density lipoprotein cholesterol (HDL-C) is a type of lipoprotein which helps in the clearance of cholesterol from the bloodstream, and it is referred to as “good cholesterol”. The HDL-C is associated with a lower risk of heart disease and stroke. HDL-C protects the endothelial cells from various reactions, such as inflammation secondary to the oxidative stress produced during the activation of the monocytes and the proliferation of the monocyte progenitor cells.[10] The HDL-C also suppress the migration of the macrophages and the oxidation of the low-density lipoprotein molecule. Based on this, the HDL-C was found to have antioxidant, anti-inflammatory and anti-inflammatory properties, and it prevents the adverse effect of the LDL-C on the endothelial cells and decreases atherosclerosis formation.[11] During the process of atherosclerosis, there is a decline in the level of HDL-C with the increase in the monocyte count, further elevating the monocyte to the high-density lipoprotein cholesterol ratio (MHR).

Monocyte to the high-density lipoprotein cholesterol ratio (MHR). The monocyte-to-HDL-C ratio (MHR) is a unique composite predictor indicating the equilibrium between the monocytes inflammatory and oxidative stress and HDL-C levels. The prognostic capacity of MHR for clinical outcomes may surpass that of independent monocyte count and HDL-C levels.[12] The previous studies had shown that the MHR values were found to be independently correlated with the increase in the risk of disability and death of the patient with intracerebral haemorrhage.[13] The National Institute of Health Stroke Scale (NIHSS) was a standardised and widely accepted tool to evaluate stroke severity and help to predict the disease's outcome. There is not much data which correlates the MHR in acute ischemic stroke and its correlation with the NIHSS.[14]

So, this study was done to assess the role of the MHR in acute ischemic stroke patients and to find its correlation with the National Institute of Health Stroke Scale (NIHSS) to predict the severity of the condition

MATERIALS AND METHODS

Study design

This hospital-based prospective observational study was conducted in the Department of General Medicine at Trichy SRM Medical College Hospital and Research Centre, Irungalur, Trichy, India. The study was conducted between November 2023 and April 2024 for 6months.

Inclusion Criteria

All the patients who presented to the hospital during the study period with acute ischemic stroke were included in the study with ages more than 18 years of both sexes. The diagnosis of acute ischemic stroke was made based on the temporal profile of the clinical syndrome, CT scan and MRI brain.

Exclusion Criteria

The patients with hemorrhagic stroke, deep vein thrombosis, malignancy, connective tissue, hepatic disease, liver disease, seizure disorder, stroke mimics, autoimmune disorder and those who were not willing to participate in the study were excluded from the study.

Data collection

After obtaining approval from the Institute Ethics committee, informed and written consent were obtained from the patients and the patient's attendees in case of the unconscious attender. All acute ischemic stroke patients who had symptoms within 7 days were included in the study. All the patients were subjected to proper history taking following general and neurological examinations. Then, the severity of the stroke was determined by the NIHSS scale on day 1and the 5th day of the admission. The stroke's severity was categorised as mild stroke (1-4), moderate stroke (5-15), moderate to severe stroke (16-20), and severe stroke (21-42).

After that, all the patients were subjected to the complete blood count, and this was done using the fully automated five-part haematology analyser at our central laboratory to find the monocyte level followed by the fasting lipid profile of the patient in the fully automated biochemistry analyser. Then, the MHR was calculated based on the values.

Statistical Analysis

Continuous variables were repressed as mean and standard deviation, while the categorical variable was expressed in frequency and percentage. All the data were entered in Microsoft Excel, and analysis was performed with the IBM SPSS Statistics for Windows, Version 25.0 (released 2017, IBM Corp., Armonk, NY). The unpaired t-test was used to find

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the significant difference between the values, and the Pearson correlation was done to determine the correlation between the MHR and the NIHSS.

Ethical approval

The study protocol received approval from the Internal Human Ethics Committee of Trichy SRM Medical College Hospital and Research Centre, Irungalur, Trichy, India., under reference number 1136/ TSRMMCH&RC/ME-1/2023-IEC No:163

RESULTS

A total of 100 patients with the diagnosis of acute ischemic stroke participated in the study, with a similar number of patients in the control group. The study's most common age group affected by stroke was more than 60 years, accounting for 55%, followed by 40 to 60years, accounting for 30%. More than half of the patients (59%) were found to be males, and the females contributed to 42% of the total study population; about 60% of the patients with acute ischemic stroke were from urban areas, as in Table 1.

Table 1: Socio-demographic details of the patient

Variable	Control group		Study s group	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Age (in years)				
18-40	12	12	15	15
40-60	35	35	30	30
>60	53	53	55	55
Gender				
Male	55	55	58	58
Female	45	45	42	42
Residence				
Urban	56	56	60	60
Rural	44	44	40	40

On exploring the risk factors of the patients, hypertension was noted in 60% of the patients in the study group, followed by hypercholesterolemia in 46% and diabetes in 42%. Smoking and alcohol were noted in 33% and 30% of the acute stroke patients who participated in the study, as in Table 2.

Table 2: Distribution of risk factors between the groups

Risk factors	Control group		Study group	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Hypertension	55	55	60	60
Diabetes	35	35	42	42
Hypercholesterolemia	42	42	46	46
Smoking	30	30	33	33
Alcoholism	24	24	30	30

Based on the type of stroke, right hemiparesis with or without cranial nerve involvement was found to be the most common type of stroke encountered among the patients in the busy, accounting for 50%, followed by 40% and left hemiparesis and about 10% o the patient had posterior circulation stroke, as in Table 3.

Table 3: Distribution of the patients based on the type of stroke

Type of stroke	Frequency (n)	Percentage (%)
Right hemiparesis	50	50
Left hemiparesis	40	40
Posterior circulation stroke	10	10

The study found that the average monocyte count was 546 + 23.99 in the study group compared to 312.5 + 36.52 in the control group, with a significant difference. Also, the HDL-C was significantly lower in the study group, 40.5 + 4.37, compared to 53.21 + 2.85 in the control group. MHR was significantly higher in the study group, 13.7 + 2.19, compared to 5.9 + 1.01 in the control group, as in Table 4.

Table 4: Comparison of various parameters between the groups

Parameters	Control		Study		T value	p-value
	Mean	SD	Mean	SD		
Absolute Monocyte count	312.5	36.52	546	23.99	53.44	<0.001
HDL	53.21	2.85	40.5	4.37	24.28	<0.001
MHR	5.9	1.01	13.7	2.19	32.21	<0.001

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In finding the correlation between the MHR and NIHSS scores, the study found a significant positive correlation between the two(p-<0.001). The study showed an increase in the NIHSS score, which is associated with the MHR value increases, as shown in Table 5 and Figure 1.

Table 5: Comparison of NIHSS with MHR score

NIHSS Score	No of patients	MHR	t-value	p-value
1-4	17	11.3 + 0.76	0.950	<0.001
5-15	62	13.2 + 1.08		
16-20	17	16.7 + 0.78		
21-42	4	19.1 + 0.64		

Among the 100 patients who participated in the study, about 67 patients had improved with a mean MHR value of 12.4 + 0.99, 21 patients were found to be static with a mean MHR value of 15.3 + 0.79, and 12 patients deteriorated with a mean MGR value of 18 + 0.94, as in Table 6.

Table 6: Various parameters concerning the outcome of the patient

Status of patient	Total no of patients	Admission (mean ± SD)		
		Monocyte (mm3)	HDL (mg/dl)	MHR
Improved	67	523.2 ± 13.41	43 ± 2.49	12.4 ± 0.99
Deteriorated	12	590 ± 3.58	32.8 ± 1.46	18 ± 0.94
Static	21	565.1 ± 7.25	36.9 ± 1.54	15.3 ± 0.79

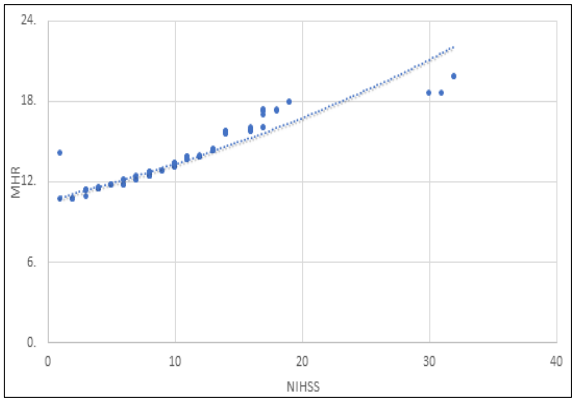

Figure 1: Correlation between MHR and NIHSS

The study also noted a significant positive correlation between the NIHSS score and the absolute monocyte count. A significant negative correlation has been observed between the NIHSS score and the HDL-C levels in the blood, as in Figure 2,3.

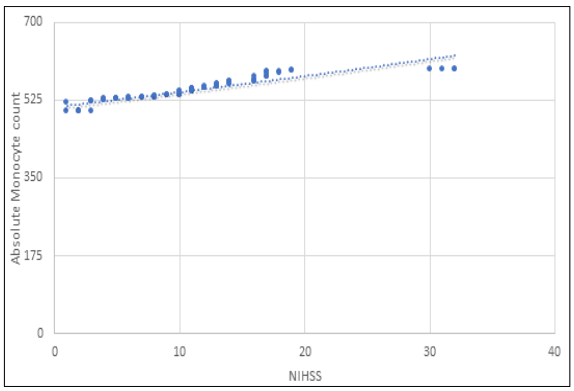

Figure 2: Correlation between the absolute monocyte count and the NIHSS score

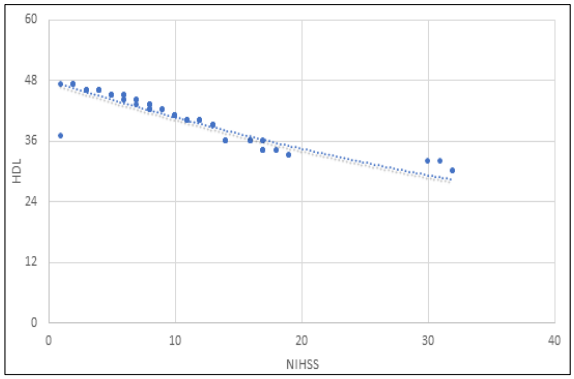

Figure 3: Correlation between the High-Density Lipoprotein and the NIHSS score

DISCUSSION

Stroke is one of the common neurological problems encountered in medical practice. The complications in stroke patients are due to the delay in bringing the patient to the hospital, the delay in initiating the treatment, or poor follow-up. Although many investigations were found to be available to diagnose the stroke, none of the investigations were found to be effective to assess the prognosis of the patient. A recent study showed that the monocyte to HDL-C ratio comprising basic haematological and biochemical parameters was found to be helpful in the evaluation of the severity of the patient and also helped to assess the prognosis of the disease. Hence, we want to conduct the same study in our hospital located in southern part of Tamilnadu to evaluate the efficacy of the MHR in detecting the severity and the prognosis of stroke patients.

And in our study, about 55% of the patients were more than 60 years of age. Studies have shown that age is a significant risk factor for the causation of stroke.[15] The risk for acute ischemic stroke was found to increase with the increase in the age of the patients, and the studies had shown the risk of stroke was found to double after 45 years of age—the study by Howard G. et al,[16] Showed that about 23% of

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strokes in the United States of America were found to occur after 85 years of age. In our study, about 58% of the acute stroke patients were found to be males, and 60% were from the urban area. Similar to our study, the study by Ojha PT et al,[17] Males were found to be more commonly affected by stroke (53%). Whereas the study the study by Caso V et al.[18] It showed that stroke was found to be more commonly seen among female patients than male patients, and stroke encountered by female patients had a poor prognosis for disease when compared to male patients. The study by Kalita J et al,[19] The prevalence of stroke was found to be more commonly noted in the urban areas and contributed to 3.26% compared to the rural area, which accounts for 1.21%.

In our study, hypertension (60%), followed by hypercholesterolemia (46%), was found to be the most common risk factor for stroke, and diabetes contributed to 42% of the patients in the study. The study by Cipolla, MJ et al,[20] showed that the risk factors were a more critical factor for stroke, and the incidence and prognosis of the disease were directly related to the patient's risk factor. The study also found that hypertension is the most common risk factor for stroke. The study by Wajngarten M et al,[21] also supports this finding, as hypertension is the most common risk factor. Our study showed that right hemiparesis was the most common type of stroke, accounting for 50%, followed by left hemiparesis. Similar to our study, the study by Sharma D et al,[12] also showed that right-sided hemiparesis was found to be the most common type of stroke(49%0 followed by 45% of the patients who had left-sided hemiparesis.

In our study, the absolute monocyte count in the patients and controls was found to be 546 + 23.99 and 312.5 + 36.52, respectively, and the HDL-C in the cases and controls was also found to be 40.5 + 4.37 and 53.21 + 2.85 respectively. Similar to Our study, the study by Sharma D et al,[12] showed a higher level of absolute monocyte count (590) in the case group when compared to the control group 9394) and also the study by Jefferies E et al,[22] It also showed that the HDL-C was lower in the stroke patients compared to the control group. And the higher HDL in the control group was because of the antioxidant, anti-inflammatory, and antithrombotic effects. The metaanalysis by Qie R et al,[23] A 1 mmol/L increase in the HDL-C level decreased the risk of stroke by 18%.

The MHR was calculated by dividing the absolute monocyte count by the HDL-C levels. Our study also found that MHR was significantly higher in the study group, 13.7 + 2.19, compared to 5.9 + 1.01 in the control group and showed a significant and positive correlation with the NIHSS score. In the study by Bolayir A. et al,[24] the MHR value was significantly higher with the acute ischemic stroke patients 13.58 compared to the control groups 9.46. The study by Sharma D et al,[25] also showed a significant and positive correlation between the NIHSS and the MHR value. The study by Liu H et al,[26] also found that a higher MHR level was independently associated with the patient's poor outcome at 3 months.

Our study showed that the MHR value in the improved patients was lower (12.4 + 0.99) compared to the deteriorated patients (18 + 0.94). From this, it was clear that the MHR value at the time of the admission helped to assess the prognosis of the disease and also helped to determine the severity of the disease. The study by Liu H et al,[26] also reported that the MHR value was found to help predict the prognosis of patients with atherosclerosis and ischemic stroke. And the study by Sharma D et al,[25] also supports our study's finding.

Limitation

The major limitation of our study was the smaller sample size, which was conducted in a single centre.

CONCLUSION

Stroke is an emergency health condition which needs proper treatment and rehabilitation to decrease the morbidity and mortality of the patient. The MHR is an easy, fast, inexpensive, and easily available test used to determine the severity of the disease which can be done even at the peripheral level hospital with the minimum facility. Our study showed a significant positive correlation between the MHR and the NIHSS score. Hence, MHR maybe used as an adjuvant prognostic marker to determine the severity of the stroke.

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