International Journal of Research in Medical Sciences
Raveesha A et al. Int J Res Med Sci. 2020 Nov;8(11):3983-3987
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20204890

Original Research Article

Relation between monocyte/high density lipoprotein ratio in acute ischemic stroke severity

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Received: 29 August 2020
Revised: 27 September 2020
Accepted: 03 October 2020

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ABSTRACT

Introduction: Stroke is a common neurological condition, with a high incidence of mortality and morbidity, especially in the elderly population. Inflammation and lipid abnormalities have been proposed for the pathophysiology development and progression of atherosclerosis. Monocyte count to High density lipoprotein (HDL) ratio (MHR) is proposed as a novel predictor of prognosis in cardiovascular diseases. In this study, we aim to investigate the relationship of MHR with stroke severity in acute ischemic stroke patients.
Methods: A total of 64 patients with acute ischemic stroke were inpatients of RLJH were included in the study. Patients were divided into 2 groups according to the National institute of health stroke (NIHS) score (group 1; national institute of health stroke scale (NIHSS) <16, group 2; NIHSS ≥16). MHR is the ratio obtained by dividing the monocyte count with HDL from a peripheral blood sample. Then the association between MHR and NIHSS score at the time of admission is evaluated.
Results: Accordingly, the results obtained revealed MHR was significantly lower in group 1 patients who have lower NIHSS score than group 2 patients who have higher NIHSS.
Conclusion: This study suggests that MHR is associated with stroke severity on admission in patients with acute ischemic stroke.

Keywords: Acute ischemic stroke, Monocyte, High density lipoprotein, MHR, NIH stroke scale

INTRODUCTION

Stroke is the common neurological condition, with a high incidence of mortality and morbidity, especially in the elderly population.[1] Atherosclerosis and cardio embolic stroke are the most common cause of acute ischemic stroke. It has been found dyslipidemia and inflammation in pathophysiology of atherosclerosis development. Inflammation and lipid abnormalities are involved in pathophysiology of atherosclerosis development.[2,3] Various studies have evaluated the high sensitivity C-reactive protein (hsCRP), fibrinogen, erythrocyte sedimentation rate, leukocyte count, fibrinogen, etc. as serum inflammatory parameters. Similarly monocyte is found to involve in atherosclerotic plaque formation by interacting with platelets and endothelial cells resulting in aggravation of inflammatory pathway, pro-thrombotic pathways and those plays main role in formation of atherosclerotic plaque at the vascular level.[4] High-density lipoprotein (HDL) protects the endothelium against the destructive effects of Low density lipoprotein (LDL). It is found that HDL by inhibiting oxidation of LDL to HDL protects endothelial from destructive effects of oxidized LDL, by inhibiting oxidation of LDL.[5] In this way, it is thought that HDL has anti-inflammatory effects. Also HDL cholesterol inhibits monocyte activities and interrupts the transformation of monocytes to macrophages, which decreases inflammation.[6] As a

consequence, combining measurements of HDL cholesterol and monocyte counts as the Monocyte to HDL ratio (MHR) might represent the basic inflammatory process. Recent reports have demonstrated that the increased MHR, which is obtained by dividing the monocyte count by the HDL value, may be a novel predictor of prognosis in cardiovascular diseases.[7,8] This provides a scope for the use of inflammatory markers in predicting the severity and prognosis of acute ischemic stroke. In this study, we aim to investigate the relationship of MHR with stroke severity in acute ischemic stroke patients.

METHODS

Study setting

A study was conducted in the Department of General Medicine at Sri DevarajUrs medical college, Kolar, Karnataka.

Study design

This was an observational study.

Sample size

The study included 64 subjects.

Sample size calculation

Sample size was estimated by using the prevalence of acute ischemic stroke 0.33% using the formula.

$$Sample\ size = (Z1{-}\propto \div 2)^2 p(1-p) \div d^2$$

Here $Z_{1-\alpha \div 2}$ =Is standard normal variate (at 5% type I error (p<0.005) it is 1.96 and at 1% type I error (p<0.01) it is 2.58). As in majority of studies p values are considered significant below 0.05 hence 1.96 is used in formula.

p=expected proportion in population based on previous studies or pilot studies.

d=absolute error or precision, has to be decided by researcher.

p=0.33 or 0.0033

q=99.67 or 0.99.67

d=2% or 0.02

Using the above values at 95% Confidence level a sample size of 32 subjects with opacity will be included in the study.

Considering 10% nonresponse a sample size of 32+3.2≈36subjects minimum sample size. We had taken 64 subjects.

Method of collecting data

Patients who fulfil the inclusion and exclusion criteria were included in our study.

Inclusion criteria

The inclusion criteria was as follows: acute Ischemic Stroke presenting within 24 hours of the onset of symptoms and age >18 years.

Exclusion criteria

The exclusion criteria was as follows: systematic acute/chronic inflammatory/autoimmune or infectious diseases, chronic connective tissue diseases, hematological disorders, cancer, severe liver, kidney or heart failure, acute coronary syndrome within the past three months, prior acute myocardial infarction, a history of major surgery or trauma, and chronic alcohol abuse.

Each patient underwent through clinical examination and was screened for routine hematological and biochemical parameters. On presentation severity of stroke was assessed using National institute of health (NIH) stroke scale. National institute of health stroke scale (NIHSS) contain 11 elements which are related to a specific function. Patients were divided into 2 groups according to the NIHS score (group 1, NIHSS <16 and group 2, >16).

MHR is the ratio derived by dividing the monocyte count with HDL from a peripheral blood sample. Then we evaluated the association between MHR and NIHSS score at the time of admission.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using Statistical package for social sciences (SPSS) 22 version software.

Categorical data was represented in the form of frequencies and proportions. Chi-square test or Fischer's exact test (for 2×2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. p<0.05 (probability that the result is true) was considered as statistically significant after assuming all the rules of statistical tests.

Microsoft excel, SPSS version 22 (IBM SPSS Statistics, Somers New York, United States of America) was used to analyze data.

RESULTS

In our study we had 64 subjects who were further divided into group 1 and group 2 based on NIHS score at admission. Group 1 (NIHSS <16) consists of 43 subjects and group 2 (NIHSS >16) consists of 21 subjects.

Table 1: Comparison of demographic and risk factors of the subjects between two groups.

Demographic characteristics	Group 1 (NIHSS <16) n=43	Group 2 (NIHSS ≥16) n=21	P value
Age (in years)	61.34±12.17	66.07±12.58	0.147
Gender (F/M)	20/23	5/16	0.105
Hypertension	25 (58.1%)	9 (42.8%)	0.294
Diabetes mellitus	25 (58.1%)	11 (52.38%)	0.790
COPD	3 (6.9%)	1 (4.7%)	0.731
Smoker	14 (32.5%)	12 (57.1%)	0.103
Alcoholic	5 (11.6%)	4 (19.04%)	0.763

Mean age in group 1 was 61.34±12.17 years and mean age in group 2 was 66.07±12.58 years.

In group 1 out of 43 subjects 20 subjects were female and 23 remaining were male. In group 2 out of 21 subjects 5 subjects were female and 16 remaining were male. There was no statistically significant difference found between the two groups with respect to age and gender.

Among group 1 population, 58.1% had hypertension, 58.1% had diabetes mellitus, 32.5% were smokers and 11.6% were alcoholic. Among group 2 population 42.8% had hypertension, 52.38% had diabetes mellitus, 57.1% were smokers in group 2 and 19.04% were alcoholic in group 2. There was no statistically significant difference found between the two groups with respect to hypertension, diabetes mellitus, Chronic obstructive pulmonary disease (COPD), smoking and alcohol.

When the two groups were compared in terms of laboratory parameters, there was no statistically significant difference between the two groups in terms of systolic blood pressure, diastolic blood pressure, platelets, blood urea, creatinine, hemoglobin, LDL and total cholesterol levels.

Table 2: Comparison of various parameters between two groups.

Parameters	Group 1 (NIHSS <16)		Group 2 (NIHSS ≥16)		P value
	Mean	SD	Mean	SD	
SBP (mmHg)	147	29	144	24	0.736
DBP (mmHg)	87	13	86	9	0.662
HB (g/dl)	13.2349	2.2155	13.8286	2.5275	0.340
Monocyte (10^9/l)	0.4558	0.0496	0.5748	0.0242	<0.001
Platelets	262.8	100.0	281.0	78.3	0.466
Blood urea	31	10	30	11	0.680
Serum creatinine (mg/dl)	0.7884	0.2855	0.8095	0.2427	0.772
Serum cholesterol	9.94	2.33	10.59	2.53	0.315
TG (mmol/l)	7.464	2.87	8.07	3.23	0.449
HDL (mmol/l)	2.502	0.308	1.7680	0.093	<0.001
LDL (mmol/l)	110	37	118	41	0.444
MHR	1.1289	0.088	1.016	0.072	<0.001

Table 3: Comparison of monocyte count, HDL levels and MHR value based on mortality.

Parameters	Survivors		Non-survivors		P value
	Mean	SD	Mean	SD	
Monocyte (10^9/l)	0.4713	0.0623	0.5656	0.0413	<0.001
HDL (mmol/l)	2.399	0.386	1.848	0.2859	<0.001
MHR	1.110	0.093	1.037	0.0953	0.014

On the other hand, there were statistically significant differences between the two groups in terms of monocyte and HDL levels.

Mean MHR in group 1 was 1.12±0.088 and Mean MHR in group 2 was 1.016±0.072.

There difference between the two groups with respect to monocyte to MHR was statistically significant with p<0.001.

Among 64 subjects whom we had included in our study 43 (67.18%) subjects were survived and remaining 21 (32.82%) subjects had a death.

Mean monocyte count was 0.471 (10^9/l) among survivors which was slightly lower than mean monocyte count 0.56 (10^9/l) among non-survivors. This difference in mean monocyte count between survivors and non survivors was statistically significant.

Mean HDL level was 2.39 (mmol/l) among survived which was slightly higher and statistically significant when compared with the mean HDL level among non survivors which was 1.84 (mmol/l).

Mean MHR value was 1.110 among survivors which was slightly higher than mean MHR value 1.037 among non survivors. The mean difference between survivors and non survivors with respect to MHR was statistically significant.

DISCUSSION

Only few studies have been done to demonstrate association between MHR and cardiovascular disease mortality. A study done by Kanbay et al. showed that increased MHR value is associated with worsening cardiovascular events in chronic kidney failure patients.[9] Karatas et al demonstrated that high levels of MHR is independent risk factor for cardio vascular risk after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction.[10] In a study done by Ozturk et al patients were divided into 2 groups according to the NIHS score (group 1; NIHSS <16, group 2; NIHSS ≥6).[11] Similarly in our study we had 64 subjects who were further divided into group 1 and group 2 based on NIHS score at admission. Group 1 (NIHSS <16) consists of 43 subjects and group 2 (NIHSS >16) consists of 21 subjects.

In our study there was no statistically significant difference found between the two groups with respect to age, gender, hypertension, diabetes mellitus, COPD, smoking and alcohol which was similar to the study done by Ozturk et al.[11]

In our study mean MHR in group 1 was 1.12±0.088 and mean MHR in group 2 was 1.016±0.072. There was significant difference between the two groups in terms of MHR which was similar to the studies done by Ozturk11et al and Alagoz et al which showed statistically difference between the two groups in terms of MHR.[12]

In our study HDL level and MHR value of the survivors were slightly higher, while the monocyte count was slightly lower compared to the non survivors. In contrast to our study a study done AsliBolayir et al classified ischemic stroke patients into two groups according to the 30-day mortality.[13] The comparison of the two groups in terms of monocyte count, HDL level and MHR value demonstrated that monocyte count and MHR value of the non survivors were statistically higher, while the HDL level was statistically lower compared to the survivor group. Liu et al observed high value of MHR was associated with risks of poor outcomes within 3 months after AIS.[14]

Our study was only a hospital-based study, limited by its small sample size and observational study design. But our study findings are an important step in this area where literature is scarce considering its usefulness in assessing the severity of ischemic stroke. Longer follow-up and large study group could increase the validation of MHR as a new marker.

CONCLUSION

We suggest that patients with moderate to severe, severe stroke will have higher monocyte counts, lower HDL levels. This study suggests that MHR is associated with stroke severity on admission in patients with acute ischemic stroke.

ACKNOWLEDGEMENTS

Authors would like to acknowledge all the subjects participated in the study. Everyone who contributed in the completion of the study including the technical staff.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Raveesha A, Meghashri V, Vishwanath R, Prabhakar K. Relation between monocyte/high density lipoprotein ratio in acute ischemic stroke severity. Int J Res Med Sci 2020;8:3983-7.