



Study of Correlation of Monocyte to HDL ratio with Carotid Artery Intima Media Thickness (CIMT) in Acute Ischemic Stroke patients

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Abstract

Introduction: Stroke is considered as one of the leading causes of death and disability across the world. Studies have shown that Large-artery atherosclerosis accounts for almost one-fifth of all ischemic stroke incidence which can be measured as carotid artery intima media thickness using doppler scan. Monocytes are recruited in Acute Ischemic Stroke, which promotes the damage of blood-brain barrier by releasing inflammatory mediators. It plays a critical role in almost all stages of progression and destabilization of the plaque. HDL cholesterol has anti-inflammatory, antithrombotic, antioxidant effects and anti-atherogenic effects. HDL levels decline while monocyte levels increase in case of atherosclerosis, thus the monocyte to HDL ratio is expected to increase.

Aim & Objective: To correlate monocyte to HDL ratio with the carotid artery intima-media thickness in acute ischemic stroke patients

Methods: It is a hospital based cross-sectional study. The sample size was calculated to be 64. Patients admitted within the first 7 days of symptoms and diagnosed as acute ischemic stroke based on CT or MRI findings, were enrolled into this study from both genders. Monocyte to HDL ratio was calculated and Carotid artery intima media thickness using carotid vessel doppler scan was measured.

Result: In correlation analysis, Monocyte-HDL ratio showed a significant positive correlation with both CIMT ($r=0.44$, $p\text{-value} < 0.001$) and NIHSS ($r=0.265$, $p\text{-value}=0.034$). Logistical regression was done for predicting carotid artery intima media thickness from Monocyte-HDL ratio and it was found to be statistically significant with an odds ratio of 1.131 and $p\text{-value}$ of 0.005

Conclusion: MHR (monocyte to HDL Ratio) can be used as a simple cost effective screening tool for assessing the severity of carotid artery intima media thickness in Acute ischemic stroke patients.

Keywords: Monocyte to HDL Ratio, Intima Media thickness, Carotid Artery, Ischemic Stroke

Introduction

Stroke is considered as one of the leading causes of death and disability across the world, consisting of two major types, haemorrhagic and ischemic¹. Even though haemorrhagic stroke has higher mortality risk than ischemic one, ischemic stroke is ten-times more frequent². Regarding to the mechanism of injury,

ischemic stroke have been classified into subtypes. Large-artery atherosclerosis, cardiogenic embolism, small vessel occlusive disease, stroke of other determined etiology and stroke of undetermined etiology are considered³. Large-artery atherosclerosis

is relevant to our study, accounts for almost one-fifth of all ischemic stroke incidence⁴.

Inflammatory process plays a pivotal role in development and destabilization of atherosclerosis and cerebrovascular diseases⁵. Monocytes were recruited to the ischemic area in the early stages of inflammatory response when Acute Ischemic Stroke occurs, which promoted the damage of blood-brain barrier by releasing inflammatory mediators. Furthermore, it plays a critical role in almost all stages of progression and destabilization of the plaque^{5,6}.

Monocyte is a hallmark of chronic inflammation and interact primarily with platelets and endothelial cells resulting in aggravation of inflammatory, pro-thrombotic pathways and are known to play an active role in the formation, progression and rupture of an atherosclerotic plaque at the vascular level. Conversely, the high-density lipoprotein-cholesterol (HDL-C) protect endothelial cells from inflammation and oxidative stress through controlling monocyte activation and proliferation of monocyte progenitor cells, as well as suppressing the migration of macrophages and oxidation of low-density lipoprotein (LDL) molecules. HDL cholesterol has anti-inflammatory, antithrombotic, and antioxidant effects. HDL cholesterol is classically known to have anti-atherogenic effects. HDL is appraised to be a protective molecule against cardiovascular and cerebrovascular disorders.

HDL levels decline while monocyte levels increase in cases of atherosclerosis, thus, the Monocyte to HDL ratio is expected to increase. Increased monocyte count to HDL ratio (MHR) has emerged as a novel prognostic marker in inflammatory process and associated with atherosclerosis and vascular stenosis^{7,8}. Many studies have shown that Monocyte to HDL ratio can be a significant and independent predictor of poor functional outcome in patients with CVA. In this study, we aimed to determine whether Monocyte to HDL Ratio can be used as a predictor to know the severity of Carotid artery Intimal thickening in acute ischemic stroke patients.

Aims And Objectives

- To correlate monocyte to HDL ratio with the carotid artery intima-media thickness in acute ischemic stroke patients
- To correlate monocyte to HDL ratio with the severity of Acute ischemic stroke based on the NIHSS score.

Materials And Methods

Study Area and design This study was conducted at Sri Manakula Vinayagar medical college and hospital from September 2022 to October 2023 for a period of 12 months. The study design employed was a cross sectional study.

Sample Size The sample size was calculated to be 64 by using Open Epi software, Version 3 with 72% Sensitivity, 64% Confidence Interval, 11% Precision based on a study done on similar ground by Abus S et al, the study was titled: Monocyte to HDL ratio in the Prediction of Carotid Artery Intima-media Thickness¹³.

Inclusion criteria Any patient diagnosed as Acute ischemic stroke within first 7 days of symptoms will be enrolled into this study from both genders. An ischemic stroke was described as patient with symptoms suggestive of stroke along with a documented ischemic lesion on computed tomography (CT) or magnetic resonance image (MRI) of the Brain, even if the symptoms were temporary.

Exclusion criteria

1. Atrial fibrillation, Infective endocarditis, Mechanical prosthetic valve, severe mitral stenosis.
2. Acute/chronic inflammatory/autoimmune or infectious diseases.
3. Taking immunosuppressants, Immunosuppressive diseases.
4. Haematological disorders
5. Antihyperlipidemic treatment history

Sampling Procedure

Any patient admitted under General Medicine Department who were diagnosed as Acute ischemic stroke within first 7 days of symptoms along with a documented ischemic lesion on computed tomography (CT) or magnetic resonance image (MRI) of the Brain, after fulfilling inclusion criteria and screening for the Exclusion Criteria based on Complete Blood count, Echocardiography and standard questionnaire were included in the study. An informed and written consent was obtained from all study participants/ patient attendees prior to the start of the study. Demographic data, history, clinical examination and details of investigations done will be recorded in the study proforma.

After admission, 3 ml of venous blood was drawn from the patient by a trained nurse after informed and written consent . Complete blood count including monocyte count and lipid profile were obtained from the blood sample collected . Monocyte to HDL ratio was calculated . Carotid artery intima- media thickness (CIMT) was estimated by Carotid vessel Doppler scan.

CIMT measurements were performed manually using a high-resolution B-mode tomographic ultrasound system with a linear 10 MHz transducer. Precision of the CIMT measurement is 0.01 mm. The sonographers measured CIMT on the far-wall of the right and left common carotid arteries, 1.5 cm proximal to the bifurcation. The transducer was manipulated so that the lumen diameter was maximized in the longitudinal plane. The first and second lines represent the lumen-intimal interface and the collage-contained upper layer of tunica adventitia, respectively. The mean value of the right and left common carotid IMT was used for analysis

Monocyte to HDL ratio (MHR) was correlated with Carotid Artery Intima-media Thickness .Based on the previous study¹³ conducted on similar background , the ROC curve analysis showed the cut-off value of

≥ 13.4 for MHR with a sensitivity of 72% and a specificity of 60.7% in identifying clinically significant carotid artery stenosis. Based on this subjects were divided into two groups according to carotid IMT: those with carotid IMT >0.9 mm (increased) and those with carotid IMT ≤ 0.9 mm (normal). The Monocyte to HDL ratio were corelated with carotid artery intima media thickness in both the groups .NIHSS (National Institute Of Health Stroke Scale) were also assessed on arrival of the patient to the hospital. Monocyte to HDL ratios were also corelated with the severity of acute ischemic stroke based on NIHSS score.

Data was entered in EpiInfo software and analysed using SPSS software Version 17.0. The categorical data is expressed in terms of rates, ratios, and percentages and the continuous data will be expressed in terms of mean \pm standard deviation. Continuous data was compared using independent sample t-test.

Results :

Fig-1: 62 %(n=40) of the patients had normal carotid artery intima media thickness, 38%(n=24) had increased thickness .

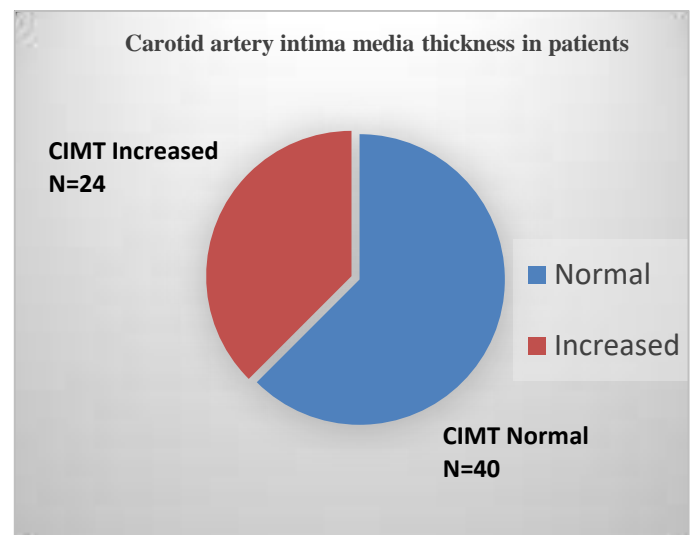


Table no.1: Patient characteristics among both the group

S. No	Parameter	CIMT Normal N=40	CIMT increased N=24
1	Age	56.38 ± 12.96 (mean + SD)	61.88 ± 10.70 (mean + SD)
2	Sex	Male – 62.5 % Female – 37.5 %	Male – 75 % Female – 25 %
3	Risk factors	Nil – 72.5% Smoking – 15% Alcohol – 5 % Both – 7.5%	Nil – 37.5 % Smoking – 25% Alcohol – 8.3% Both – 29.2%
4	Comorbidities	Nil – 12.5% Systemic hypertension – 65% Type 2 diabetes mellitus – 12.5% Both – 10%	Nil – 8.3% Systemic hypertension – 50% Type 2 diabetes mellitus – 12.5% Both – 29.2%
5	Treatment taken for comorbidities	Yes – 60 % No – 40 %	Yes – 54.2 % No – 45.8 %
6	Monocyte	512.09 ± 227.62 (mean + SD)	709.53 ± 186.335 (mean + SD)
7	HDL	39.75 ± 8.60 (mean + SD)	35.04 ± 6.53 (mean + SD)

Fig-2 :Monocyte comparison among both the groups. It was found that monocytes were increased in the “CIMT increased” group with a mean value of 709.53 ± 186.335 (mean ± SD), compared with “CIMT normal” group with a mean value of 512.09 ± 227.62(mean±SD).

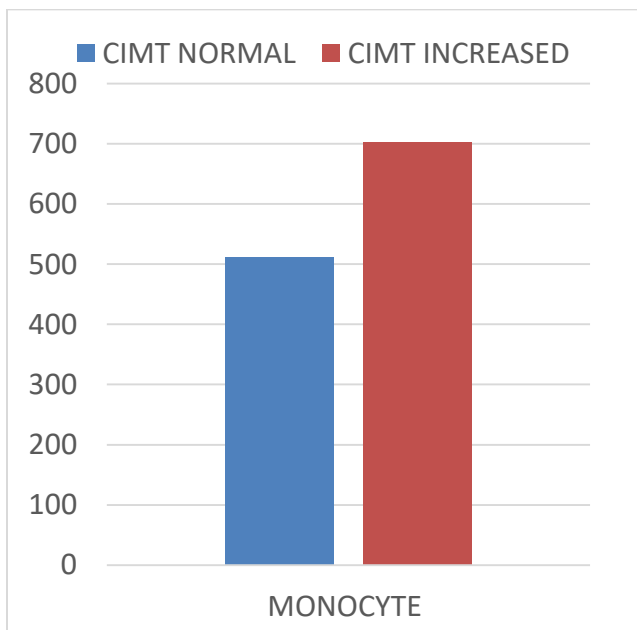


Fig-2 :Monocyte comparison among both the groups. It was found that monocytes were increased in the “CIMT increased” group with a mean value of 709.53 ± 186.335 (mean ± SD), compared with “CIMT normal” group with a mean value of 512.09 ± 227.62 (mean ± SD) .

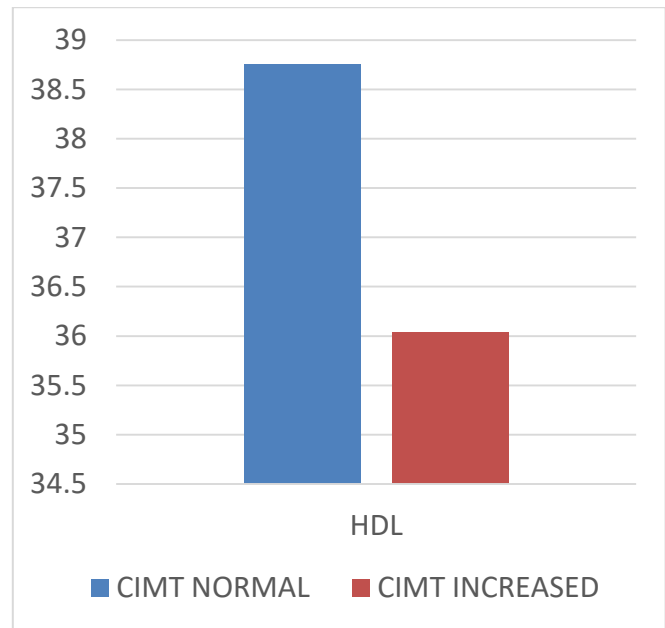


Fig -3: Monocyte to HDL ratio in “CIMT increased” group. 91.7%(n=22) had elevated monocyte to HDL Ratio , whereas 8.3% (n=2) had decreased monocyte to HDL Ratio.

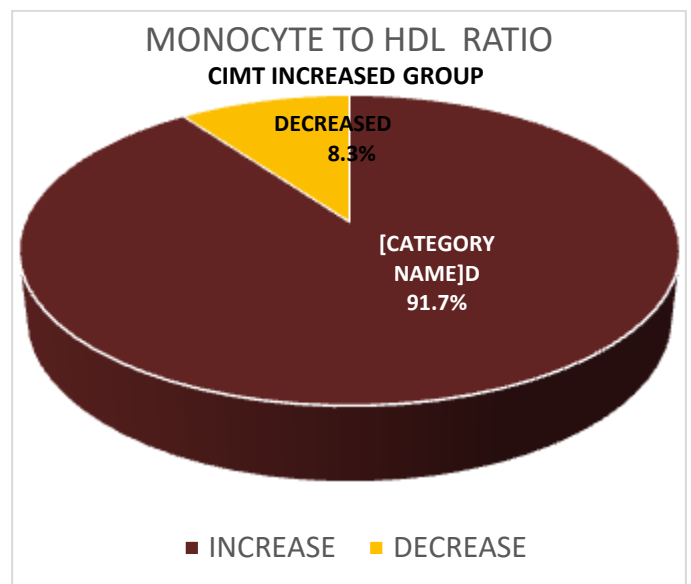


Fig -4 : Monocyte to HDL ratio in “**CIMT normal**” group. 65%(n=26) had decreased monocyte to HDL Ratio , where as 35% (n=14) had increased monocyte to HDL Ratio.

Fig-6 : NIHSS score among “**CIMT Normal Group**”. 30% had minor stroke , 65 % had moderate stroke and only 5 % had moderate to severe stroke .

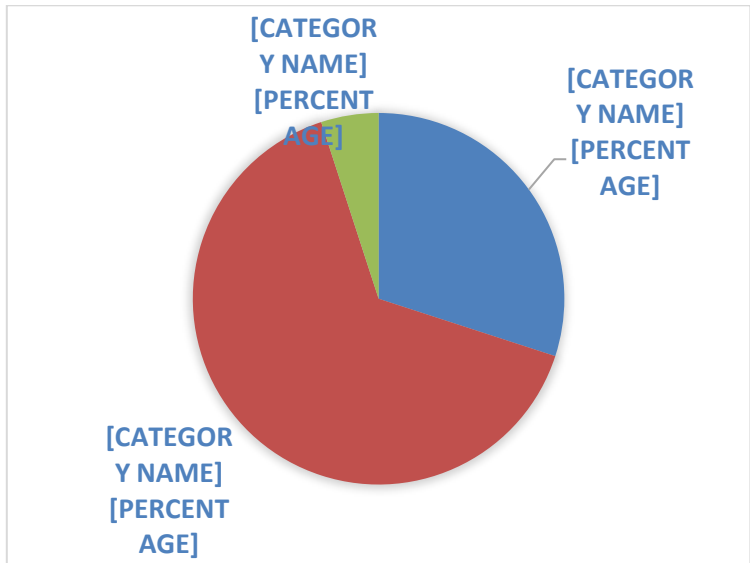
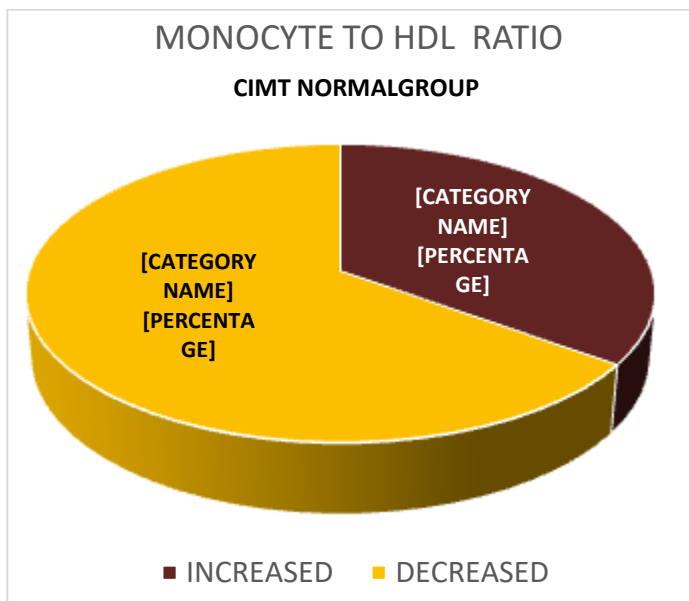
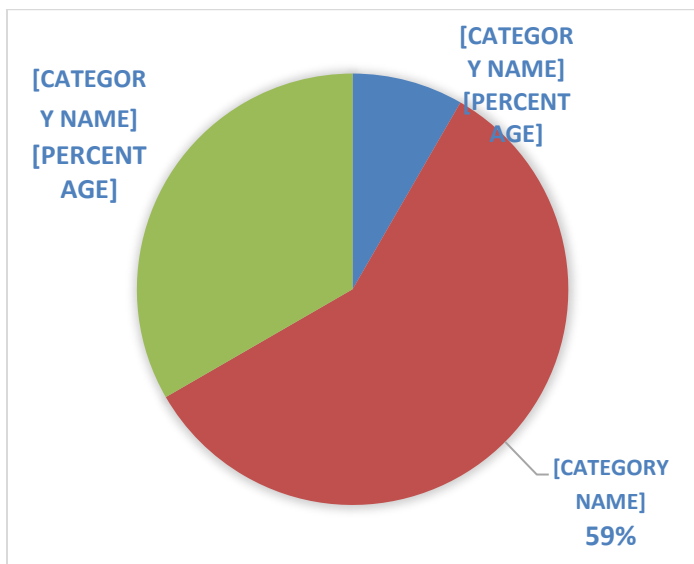


Fig-5 : NIHSS score among “**CIMT Increased**” Group. 59% had moderate stroke , 33 % had moderate to severe stroke whereas 8 % had minor stroke

Table no.2 : Correlation analysis representing association of MHR with CIMT and NIHSS. In correlation analysis, Monocyte-HDL ratio showed a significant positive correlation with both CIMT (r=0.44, p-value=<0.001) and NIHSS (r=0.265, p-value=0.034).



S. No	Variables	Correlation coefficient (r)	P value
1	CIMT	0.44	<0.001
2	NIHSS	0.265	0.034

Table no. 3: Logistic regression analysis for predicting CIMT from MHR . Logistical regression was done for predicting carotid artery intima media thickness from Monocyte-HDL ratio and it was found to be statistically significant with an odds ratio of 1.131 and p- value of 0.005

S. No	Variable	Odds ratio	95% CI		P value
1	MHR	1.131	1.039	1.232	0.005

DISCUSSION

In this study, it was found that monocytes were increased in the “CIMT increased” group, compared with “CIMT normal” group and HDL levels were decreased in the “CIMT increased” group, compared with “CIMT normal”. Results of the present study demonstrate that MHR is significantly higher in subjects with increased carotid IMT. Our findings demonstrate that MHR value is significantly correlated with carotid CIMT and that an MHR value of >13.4 was predictive for increased carotid IMT (≥ 0.9 mm).

Abuş et al, conducted a study in Malatya, Turkey in 2021 titled Monocyte to HDL Ratio in The Prediction of Carotid Artery Intima-Media Thickness , which showed the inflammation marker Monocyte to HDL Ratio can be used as a simple and cost- effective marker to predict increased carotid Intima-Media Thickness which is accepted as the indicator of subclinical atherosclerosis¹³

Monocytes change into macrophages within the arterial intima and express scavenger receptors, thus converting into foamy macrophages, which play a critical role in the occurrence and development of atherosclerosis. Beyond their activity inside the arterial wall, several immune stimulatory agents and

cytokines presenting in blood circulation affect the circulating monocytes and, therefore, contribute to the pathogenesis . In this briefly explained the complex process, inflammatory activity is likely responsible for plaque instability which may promote plaque rupture, fissuring, or erosion.

High-density lipoprotein, which has been acknowledged as an anti-atherosclerotic lipoprotein under normal physiological conditions, neutralizes the atherosclerotic role of the monocytes. Also, HDL provides various anti-atherosclerotic properties, independent from the monocyte-blocking functions. The atherosclerotic functions of the monocytes and monocyte-blocking properties possessed by HDL have led to the suggestion that MHR could be a valuable indicator of atherosclerosis. Additionally, increased carotid IMT is currently accepted as an indicator of endothelial dysfunction and early atherosclerosis; therefore, the correlation between MHR values and increased carotid IMT is very likely an indication of the presence of subclinical atherosclerosis.

CONCLUSION

The Monocyte-to-HDL ratio is significantly correlated with carotid IMT values. MHR appears as an independent predictor of increased carotid IMT. Since MHR(monocyte to HDL Ratio) can be easily acquired in a cost effective manner, it can serve as a convenient clinical tool for risk stratification in a resource limited setting and guide preventive and treatment strategies for clinicians in routine clinical care.

REFERENCE

1. Katan M, Luft A. Global Burden of Stroke. *Seminars in Neurology*. 2018;38(02):208-211.
2. Andersen K, Olsen T, Dehlendorff C, Kammersgaard L. Hemorrhagic and Ischemic Strokes Compared. *Stroke*. 2009;40(6):2068-2072.

3. Adams H, Bendixen B, Kappelle L, Biller J, Love B, Gordon D et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke*. 1993;24(1):35-41.
4. White H, Boden-Albala B, Wang C, Elkind M, Rundek T, Wright C et al. Ischemic Stroke Subtype Incidence Among Whites, Blacks, and Hispanics. *Circulation*. 2005;111(10):1327-1331.
5. Geovanini G, Libby P. Atherosclerosis and inflammation: overview and updates. *Clinical Science*. 2018;132(12):1243-1252.
6. Ganjali S, Gotto A, Ruscica M, Atkin S, Butler A, Banach M et al. Monocyte-to-HDL-cholesterol ratio as a prognostic marker in cardiovascular diseases. *Journal of Cellular Physiology*. 2018;233(12):9237-9246.
7. Canpolat U, Çetin E, Cetin S, Aydin S, Akboga M, Yayla C et al. Association of Monocyte-to-HDL Cholesterol Ratio with Slow Coronary Flow is Linked to Systemic Inflammation. *Clinical and Applied Thrombosis/Hemostasis*. 2015;22(5):476-482.
8. Ancuta P, Wang J, Gabuzda D. CD16+ monocytes produce IL-6, CCL2, and matrix metalloproteinase-9 upon interaction with CX3CL1-expressing endothelial cells. *Journal of Leukocyte Biology*. 2006;80(5):1156-1164.
9. Yurtdaş M, Yaylali Y, Özdemir M. The role of monocyte to HDL ratio in predicting clinically significant carotid stenosis in patients with asymptomatic carotid artery disease. 2022.
10. Eren F, Yildogan A, Ongun G, Ozdemir G, Ozturk S. Monocyte/High Density Lipoprotein Ratio in Patients with Symptomatic Carotid Artery Stenosis and Its Relationship with Stenosis Degree. *Medical Bulletin of Haseki*. 2022;60(1):13-19.
11. Chen J, Li C, Liu Z, Shen Y, Ding F, Shu X et al. The Role of Monocyte to High-Density Lipoprotein Cholesterol Ratio in Prediction of Carotid Intima-Media Thickness in Patients With Type 2 Diabetes. *Frontiers in Endocrinology*. 2019;10.
12. Zuo B, Zhu S, Meng X, Zhao D, Zhang J. Monocyte/lymphocyte ratio is associated with carotid stenosis in ischemic stroke: A retrospective analysis. *Brain and Behavior*. 2019;9(10).
13. Abus S, Akturk E. Monocyte to HDL Ratio in The Prediction of Carotid Artery Intima-Media Thickness. *Medical Records*. 2021.