Monocyte High Density Lipoprotein Cholesterol Ratio as a New Prognostic Factor for Mesenteric Embolism

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ABSTRACT

Objective: To determine the effectiveness of the ratio of monocyte count to high density lipoprotein cholesterol in predicting in-hospital mortality.

Study Design: Descriptive study.

Place and Duration of Study: Intensive Care Unite, Adana Numune Research and Training Hospital, Turkey, from January 2018 to December 2019.

Methodology: Patients admitted to the intensive care unit with the diagnosis of mesenteric embolism were included in the study. Monocyte count and high-density lipoprotein cholesterol (HDL) values were determined. Monocyte HDL Ratio (MHR) values of the patients were calculated. SPSS 26 package programme was used to investigate the effectiveness of MHR in predicting mortality.

Results: The mean age of the 81 patients was 69.9 ±10.6 years. In the group with mortality, the number of monocytes and MHR were significantly higher than the group without mortality ($p<0.05$). In the mortality group, HDL value was significantly lower ($p<0.05$) than the non-mortality group. Sensitivity of the MHR cutoff value of 19 was 81.8%, positive predictive value was 96.4%, specificity value was 97.9%, negative predictive value was 88.7%.

Conclusion: For patients diagnosed with acute mesenteric embolism, the use of predictors in terms of mortality estimation is very important for the faster implementation of treatment modalities. MHR value can be used as a strong predictor.

Key Words: Mesenteric embolism, Monocyte, HDL cholesterol, MHR, Mortality.

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INTRODUCTION

Acute mesenteric embolism is a disease with a high mortality rate that can cause acute abdominal pain. Despite recent developments in diagnosis and treatment methods, the mortality rate of this disease is approximately 40–70%.¹ Serum markers have been investigated as easy-to-apply methods of assisting in early diagnosis of acute mesenteric embolism. However, the role of serum markers in the diagnosis of this disease is quite limited.

Previous studies have shown that an increase in the number of monocytes and a decrease in HDL levels may be associated with inflammation and oxidative stress.²⁻⁵ Many studies have used MHR to determine whether inflammation and atherosclerosis contribute to the etiopathogenesis of cardiovascular and cerebrovascular diseases.⁶⁻¹¹

The results of these studies emphasised that MHR is an independent predictor in relation to inflammation caused by vascular injury.

Although many studies have examined the relationship between MHR and inflammatory processes, no research has examined the relationship between mesenteric embolism and MHR to the best of authors' knowledge.

The aim of the present study was to determine whether MHR is effective in predicting the in-hospital mortality of patients diagnosed with mesenteric embolism.

METHODOLOGY

Patients hospitalised in the intensive care unit of Adana Numune Research and Training Hospital, Turkey with diagnoses of mesenteric embolism from January 2018 to December 2019 were scanned from the medical information system. This process yielded the files of 90 patients diagnosed with mesenteric embolism, according to the international diagnostic code. The criteria for inclusion were age over 18 years, full data access, radiological diagnosis of mesenteric embolism in the superior and/or inferior mesenteric artery, not refusing treatment, having been admitted to the study centre, and presenting within first four hours of symptoms initiation.

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Table I: Evaluation of patients' demographic, hematological and biochemical parameters.

	Min-Max			Median	Mean $\pm$ SD./n-%		
Age	53	-	87	71	69.96	$\pm$	10.58
Gender: Male Female					39 42		48.1 51.9
Fever ($^{\circ}$ C)	36.2	-	37.2	36.5	36.50	$\pm$	0.27
Heart rate (pulse/minute)	64	-	150	91	93.8	$\pm$	16.2
SBP (mm-Hg)	80	-	162	120	118.90	$\pm$	17.26
DBP (mm-Hg)	50	-	99	70	69.09	$\pm$	9.59
Glucose (mg/dL)	56	-	248	136	143.02	$\pm$	43.73
Urea (mg/dL)	13.9	-	86.1	40.5	42.07	$\pm$	14.96
Creatinin (mg/dL)	0.31	-	1.64	0.99	1.00	$\pm$	0.35
ALT (U/L)	11	-	47	21	24.01	$\pm$	10.88
AST (U/L)	12	-	49	31	30.32	$\pm$	10.37
Sodium (mEq/L)	134	-	149	138	138.44	$\pm$	3.19
Potassium (mEq/L)	3.43	-	5.32	4.12	4.22	$\pm$	0.55
Calcium (mg/dL)	7.1	-	9.8	8.6	8.5	$\pm$	0.8
Albumine (g/L)	33.1	-	47.6	37.2	37.86	$\pm$	2.55
Hemoglobin (g/dL)	10.1	-	16.9	12.3	12.45	$\pm$	1.44
Hematocrite (%)	30.7	-	48.3	37.1	37.42	$\pm$	4.56
Platelets ($10^3/\mu$ L)	109	-	760	252	273.54	$\pm$	117.24
Monocyte ($/\mu$ L)	580	-	1254	812	836.85	$\pm$	174.25
HDL (mg/dL)	33	-	56	46	45.77	$\pm$	4.68
MHR	10.74	-	31.62	17.91	18.54	$\pm$	4.67
Surgery: No Yes					10 71		12.3 87.7
Discharge					48		59.3
Death					33		40.7

A total of 81 patients met these criteria and were included in the study. Patients who were under the age of 18 years, had missing data or whose data could not be accessed, left the hospital by refusing treatment, had non-occlusive mesenteric ischemia in radiological reporting, and patients who died before the diagnosis of mesenteric embolism were excluded. Patients' age, gender, abdominal computed tomography reports, whether they had an operation or not, hospitalisation times were recorded. The diagnosis of mesenteric embolism was made on the basis of reported findings on contrast enhanced computed tomography.

According to the guidelines of the European Society for Trauma and Emergency Surgery, medical treatments included fluid replacement with crystalloids, standard unfractionated heparin infusion, and broad-spectrum intravenous antibiotic therapy.¹² All participants were admitted to the intensive care unit. At follow-up, laparotomy was applied to patients who presented with evidence of peritonitis or developed later and perforation was detected in direct abdominal X-ray. Necrotic bowel

resection and embolectomy were performed in patients undergoing laparotomy. These patients were also given standard anticoagulant therapy.

Blood samples were taken at the time of admission to the emergency medicine department and within the first hours of symptom development. Hemogram and biochemical parameter measurements were taken on venous blood samples from the antecubital region at the time of application. WBC count, hemoglobin, hematocrit, and monocyte values were determined and recorded from the hemogram parameters. Glucose, urea, creatinine, aspartate aminotransferase (ALT), alanine aminotransferase (AST), sodium, potassium, calcium, albumin, and HDL cholesterol values were determined and recorded from the biochemistry parameters. The MHR of each sample was obtained by dividing the number of monocytes ($/\mu$ L) by the HDL cholesterol (mg/dL) level. Complete blood count measurements were taken using the Sysmex XN 10 (Automated Hematology Analyzer XN series, Sysmex Corporation, 1-5-1 Wakoinohama-Kaigandori Chuo-ku, Kobe 651-0073, Japan) automated measuring device.

Table II: Comparison of vital signs, hematological and biochemical parameters of groups.

	Discharge		Exitus		p-value
	Median (IQR) / Mean ± S.D		Median (IQR) / Mean ± S.D		
Age	69.0 / 60.0-80.8		72.0 / 63.-79.0		0.561 ^m
Gender:					
Male	27 (n)	56.3 (%)	12 (n)	36.3 (%)	0.078 ^{x²}
Female	21 (n)	43.8 (%)	21 (n)	63.7 (%)	
Fever (°C)	36.5/36.2-36.7		36.4/36.2-36.7		0.482 ^m
Heart rate (pulse/minute)	89.0/78.0-101.5		98.0/88.0-106.0		0.088 ^m
SBP (mm-Hg)	120/110.0-134.8		114.0/98.0-130.0		0.057 ^m
DBP (mm-Hg)	70.0/60.5-75.0		69.0/60.0-76.0		0.533 ^m
Glucose (mg/dL)	138.5/108.0-172.8		128.0/109.5-185.5		0.382 ^m
Urea (mg/dL)	40.8±15.6		44.0±14.0		0.348 ^t
Creatinin (mg/dL)	0.8/0.7-1.3		1.2/0.8-1.4		0.119 ^m
ALT (U/L)	18.0/15.0-26.0		24.0/17.0-42.0		0.050 ^m
AST (U/L)	25.5/21.3-38.0		36.0/23.0-42.0		0.068 ^m
Sodium (mEq/L)	137/136.0-140.0		139.0/136.0-144.0		0.108 ^m
Potassium (mEq/L)	4.0/3.8-4.5		4.1/3.6-5.0		0.495 ^m
Calcium (mg/dL)	8.7/7.8-9.3		8.5/7.8-9.2		0.510 ^m
Albumine (g/L)	38.0/35.8-39.7		36.9/36.2-38.8		0.322 ^m
Hemoglobin (g/dL)	12.3/11.1-14.0		12.3/11.8-13.0		0.855 ^m
Hematocrite (%)	37.4±5.3		37.5±3.3		0.875 ^t
Platelets (10³/µl)	252.0/220.0-305.5		258.0/179.5-349.0		0.571 ^m
Monocyte (/µl)	717.5/642.8-795.3		1005.0/893.5-1093.5		<0.001 ^m
HDL (mg/dL)	48.0/45.0-49.8		43.0/39.5-47.5		<0.001 ^m
MHR	15.2/14.0-17.1		22.6/20.2-25.1		<0.001 ^m
Surgery:					
No	4 (n)	8.3 (%)	6 (n)	18.2 (%)	0.302 ^{x²}
Yes	44 (n)	91.7 (%)	27 (n)	81.8 (%)	

Table III: Logistic regression analysis for monocyte, HDL and MHR.

	Univariate model					Multivariate model				
	OR	95% CI			p-value	OR	95% CI			p-value
Monocyte	1.018	1.010	-	1.026	<0.001					
HDL	0.834	0.743	-	0.937	0.002					
MHR	2.792	1.663	-	4.690	<0.001	2.792	1.663	-	4.690	<0.001

Biochemical parameters were measured using the Beucher Coulter AU5800 (Beckman Coulter GmbH Europark Fichtenhain B 13 47807 Krefeld, Germany) automatic measuring device.

qualitative data. A ROC analysis and logistic regression were used to determine the effect levels. SPSS 26.0 was used for statistical analysis.

Mean, standard deviation, median, minimum, maximum, frequency, and percentage values were used as descriptive statistics. The distribution of variables was checked using a Shapiro-Wilk test. An independent samples t-test and a Mann-Whitney U-test were used to compare the quantitative data, and a Chi-square Fisher's exact test was used to compare the

RESULTS

Of the 81 patients included in the present study, 48.1% (n = 39) were males and 51.9% (n = 42) were females. The mean age of the patients was 69.9 $\pm$ 10.6 years. The mean and standard deviation values of the vital signs and hematological

and biochemical parameters are shown in Table I. The age and gender distributions of the patients with and without mortality did not differ significantly ($p > 0.05$).

Table IV: The area under the curve for monocyte, HDL and MHR.

	Area under curve	% 95 CI		p-value
Monocyte	0.939	0.890	- 0.987	<0.001
HDL	0.271	0.149	- 0.393	<0.001
MHR	0.965	0.930	- 1.000	<0.001

Figure 1: MHR distribution of groups.

Figure 2: ROC analysis for MHR.

Further, these groups did not differ significantly ($p > 0.05$) in terms of mortality, fever, heart rate, systolic or diastolic blood pressure, glucose, urea, creatinine, ALT, AST, sodium, potassium, calcium, albumin, hemoglobin, hematocrit, or platelet values. However, the numbers of monocytes and MHRs were significantly higher in the group with mortality than in the group without mortality ($p < 0.05$). On the other hand, HDL values were significantly lower in the mortality group than in the non-mortality group ($p < 0.05$; Figure 1, Table II).

Significant efficacy ($p < 0.05$) of the monocyte, HDL, and MHR values was observed in the univariate model. Significant independent efficacy ($p < 0.05$) of the MHR was observed in the multivariate regression model (Table III). Significant efficacy ($p < 0.001$) of the monocyte value [0.939(0.890 - 0.987)], the HDL value [0.271 (0.149 - 0.393)], and the MHR value [0.965 (0.930 - 1.00)] was observed in the prediction of mortality (Table IV, Figure 2). The sensitivity of the MHR cutoff value of 19 was 81.8%, the positive predictive value was 96.4%, the specificity value was 97.9%, and the negative predictive value was 88.7%.

DISCUSSION

The main findings of this study were that patients diagnosed with mesenteric embolism had significantly higher monocyte counts, lower HDL cholesterol levels, and higher MHR. To the best of authors' knowledge, these findings are the first study in the literature to show an increase in MHR in patients with mesenteric. Increasing of monocyte counts and decreasing of HDL cholesterol levels were another important findings of this study.

The most important causes of high mortality in acute mesenteric embolism include difficulties and delays in diagnosis before necrosis occurs in the intestinal tissue. Therefore, the recognition of this disease without evidence of necrosis or peritoneal inflammation in the intestine is one of the important factors affecting mortality.¹³⁻¹⁵ Biochemical and hematological markers can be applied simply, which are inexpensive, and provide rapid results. However, data regarding the use of these markers to predict mortality in cases of mesenteric embolism are limited. To the best of authors' knowledge, no previous study has investigated the effectiveness of MHR in predicting mortality in cases of mesenteric embolism, which are considered to result from a thromboembolic cause. Therefore, this study appears to be the first in the literature to reveal that MHR as an independent marker of mortality in patients diagnosed with mesenteric embolism.

In the present study, monocyte counts were significantly higher in the mortality group than in the non-mortality group. Monocytes play an important role in the progression of atherosclerosis as an immune-mediated process by binding to

adhesion molecules expressed on the damaged vascular endothelium.^{9,16,17} The role of monocytes in atherosclerosis is not limited to macrophage function in the arterial wall. Further, immune-stimulating agents can affect growth factors, oxidised lipids, platelet-induced activation products, and many soluble factors associated with atherosclerosis, such as eicosanoids. As a result, monocytes play a role in the pathogenesis of vascular diseases and in complications that can occur through the inflammatory process.¹⁸ The data obtained in the present study revealed that an increased monocyte count is an important parameter in mortality prediction.

HDL consists of subgroups of different diameters, densities, and lipid and protein compositions. Several of the biological activities of HDL result from its heterogeneous structure. Aside from reverse cholesterol transport, HDL has demonstrated antioxidant, anti-inflammatory, antiapoptotic, anti-thrombotic, and antiatherosclerotic effects.^{9,19,20} HDL prevents monocyte flow into the arterial wall with reduced F-actin, thereby reducing the expression of CD11b on monocytes and endothelial adhesion molecules and preventing monocytes from adhering to the endothelium.²¹ These processes protect endothelial cells from inflammation and oxidative stress.^{2,4} Reduction of HDL cholesterol in the blood would reverse these processes and eliminate this shield of protection against inflammation and oxidative processes. In the present study, HDL was shown to be significantly low in patients with mesenteric embolism resulting in death. Therefore, a decrease in HDL cholesterol levels may serve as an effective marker for mortality prediction, as it would render monocytes insufficient to neutralize pro-inflammatory and pro-oxidant effects.

In the present study, the cutoff value of MHR was above 19, its sensitivity was 81.5%, its specificity was 97.9%, its positive predictive value was 96.4%, and its negative predictive value was 88.7%. This study is the first to demonstrate, through multivariate analysis, that MHR is a very strong independent predictor of mortality in patients diagnosed with mesenteric embolism. High monocyte counts and low HDL cholesterol levels have been associated with inflammation and oxidative stress,²⁻⁵ and MHR has been highlighted as a new prognosis marker for some cardiovascular diseases.⁶⁻⁸ The literature has also emphasised that the MHR has an independent predictive role in revealing the relationships between cardiovascular diseases (e.g., ST elevation myocardial infarction, saphenous vein graft disease, and primary hypertension resulting in asymptomatic organ damage), carotid artery intima thickness, the left ventricular mass index, urinary protein and albumin levels, and metabolic syndrome.^{10,11,22,23} However, no previous study has revealed the relationship between the MHR and mortality in cases of mesenteric embolism.

There are some limitations in this study. One of them is the retrospective design of the study, and also the number of

patients included in the study. In this study, the number of patients was limited to 81. Prospective studies involving more patients may provide more meaningful information.

CONCLUSION

The mortality rate of acute mesenteric embolism is affected by early diagnosis and early revascularisation treatments. The use of predictors for the prediction of mortality is very important for these patients in order to apply treatment modalities faster. MHR value can be used as a strong predictor. The cutoff values obtained may contribute to the literature, and to large-scale studies in which multi-centred, prospective patients will be analysed.

ETHICAL APPROVAL:

The study was approved by Ethics Committee of Non-Interventional Clinical Researches of Adana City Research and Training Hospital (Decision No.65 and Decision Date 18.12.2019).

PATIENTS' CONSENT:

The data was collected retrospectively from Hospital Automation System and Archives, after obtaining necessary permission from the management.

CONFLICT OF INTEREST:

Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

BSA, AK: Made substantial contributions to the conception or design, acquisition, analysis, or interpretation of data for the work, drafted the work and revised it critically for important intellectual content; approved the final version to be published; agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Planned and designed the work; analysed, or interpreted data for the work; drafted the work or revised it critically for important intellectual content. Drafted the work and revised it critically for important intellectual content.

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