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Original Article

Can the Monocyte/HDL Ratio be used as A Marker to Predict Fatty Liver and Its Stages?

[1]Ece Yiğit, [2]İlknur Sayar
[1]Istanbul Medipol University, Faculty of Medicine, Department of Internal Medicine, Istanbul, Turkey
[2]Memorial Ataşehir Hospital, Department of Gynecology and Obstetrics, Istanbul, Turkey

Corresponding author: İlknur Sayar, Ataşehir Memorial Hospital, Istanbul, Turkey
E-mail: sayar_ilknur@hotmail.com
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ABSTRACT

Background: Our study aims to determine whether the monocyte/HDL ratio is a marker that can be used to predict the presence and stage of non-alcoholic fatty liver.

Material and Method: Patients aged 18-65 years without known chronic diseases and medication use who applied to our hospital for a check-up were included in the study. Patients were divided into 4 groups based on ultrasonography findings: those without hepatosteatosis, those with stage 1, stage 2, and stage 3 hepatosteatosis. Groups were compared in terms of fasting glucose, insulin resistance, lipid profile, liver function tests, monocyte/HDL ratios.

Results: Fasting glucose, insulin resistance, total cholesterol, LDL cholesterol, triglycerides, alanine aminotransferase, monocytes, and monocyte/HDL ratio were significantly higher in the group with hepatosteatosis than in the group without hepatosteatosis, and this increase was directly proportional to the stage. HDL was significantly lower in the hepatosteatosis group than in the group without hepatosteatosis, and HDL decreased further as the stage of hepatosteatosis increased. No difference was found between the groups in terms of aspartate aminotransferase. Multivariate regression analyses revealed that hepatosteatosis was independently associated with alanine aminotransferase, insulin resistance, and monocyte/HDL ratio.

Conclusion: Monocyte/HDL ratio can be considered a simple, easily accessible, and inexpensive marker to predict the presence and stages of hepatosteatosis.

Keywords: Hepatosteatosis, inflammation, insulin resistance, monocyte/HDL ratio, non-alcoholic fatty liver disease

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a condition marked by abnormal fat accumulation in the liver that is unrelated to alcohol consumption (1). Fat accumulation in hepatocytes can cause inflammation and hepatocyte damage, and if it progresses further, it can cause fibrosis, cirrhosis, and even hepatocellular carcinoma (2). NAFLD affects more than a quarter of the adult population worldwide, and its prevalence is expected to rise to 56% in the next decade (3). NAFLD is closely linked to sedentary lifestyle, high-calorie diet, and obesity, as well as insulin resistance, type 2 diabetes mellitus, and metabolic syndrome, and is thus the most common liver disease seen in developed countries (4). The fact that it is very common and has serious life-threatening consequences makes NAFLD important. Most patients with hepatosteatosis (HS) are asymptomatic. Patients are usually detected incidentally with elevated liver function tests and ultrasonography findings. Hepatic transaminases are normal in two-thirds of patients but increased in one-third of patients, typically dominated by alanine aminotransferase (ALT). On ultrasonography, hepatomegaly and increased liver echogenicity are in favor of the presence of HS (5). Although biopsy is the definitive diagnostic method, it is performed in selected cases considering the cost and risk. Chronic low-grade inflammation has been identified as an essential component of NAFLD pathophysiology, implying that markers of chronic inflammation may predict the presence and stage of NAFLD (6). C-reactive protein (CRP), tumor necrosis factor- α (TNF-α), interleukin (IL)-1, IL-6, IL-8, and monocyte chemoattractant protein 1 (MKP-1) are chronic inflammation markers that have been linked to NAFLD (7,8). In recent years, monocyte/

HDL ratio (MHR) has come to the forefront as a new marker of systemic inflammation (9). Monocytes are natural inflammatory cells responsible for the increase in proinflammatory cytokines (10). HDL is a cholesterol subtype with antioxidant and anti-inflammatory effects (11). Considering the proinflammatory properties of monocytes and the anti-inflammatory properties of HDL, it was thought that the MHR may be a noninvasive, easily accessible, and low-cost marker that can be used to predict the presence and stage of an inflammatory disease such as NAFLD. This study aims to determine the association of MHR with the presence and stages of HS.

MATERIAL AND METHODS

Our study is a retrospective study in which we included patients aged 18-65 years who had a check-up at Istanbul Medipol University Hospital between January 2020 and January 2023. Demographic data of patients including age, sex and comorbidities, laboratory parameters including fasting blood glucose, insulin resistance, lipid profile (total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides), liver enzymes (ALT and aspartate aminotransferase (AST)) and complete blood count, abdominal ultrasonography (USG) findings indicating HS status were obtained and recorded on our patient management information system. Patients were divided into four groups based on USG findings: those without HS, those with stage 1 HS, those with stage 2 HS, and those with stage 3 HS and compared in terms of demographic data and laboratory parameters. Monocyte counts from the patients' complete blood counts were divided by HDL cholesterol, and MHR were calculated to determine whether this parameter differed in the group with HS compared to the group without HS, as well as whether it differed between the stages in the group with HS, and whether it was a marker that could be used to predict the presence and stages of HS.

Studying Laboratory Parameters

Blood samples were obtained after 12 hours of fasting. Whole blood counts were analyzed by Sysmex XN-1000 (USA) device. Fasting blood glucose, total cholesterol, LDL, HDL, triglycerides, ALT, AST were analyzed by Roche Hitachi Cobas C501 (Switzerland), fasting insulin levels were analyzed by Roche Hitachi Cobas e601 (Switzerland), HOMA-IR was calculated as follows: fasting insulin (mIU/ml) x fasting blood glucose (mg/dl) / 405. The presence of one or more of total cholesterol > 200, LDL > 130, triglycerides > 150, HDL < 40 for men and HDL < 50 for women was considered dyslipidemia. Fasting blood glucose ≥126 was considered diabetes mellitus and HOMA-IR > 2.4 was considered insulin resistance. The normal range of ALT is 0-33 U/L in women, 0-41 U/L in men, and the normal range of AST is 0-32 U/L in women and 0-40 U/L in men. Values above these were considered as liver enzyme elevation. Monocyte normal range is 0.16-0.90 10*3/µL. Values above this were accepted as monocytosis. Results above these values were considered elevated liver enzymes. Normal values for monocytes; results above this were considered monocytosis.

Diagnosis of Hepatosteatosis Based on USG Findings

Ultrasound imaging was performed on all patients by a single radiologist with the abdominal probe of the GE logiq 9 pro ultrasound device in B mode.

The severity of echogenicity was graded (12,13);

Grade 1: Mild diffuse echogenicity increase

Grade 2: Moderate increase in echogenicity

Grade 3: Portal vein wall with increased echogenicity; inability to visualize the diaphragm and posterior part of the liver

Inclusion Criteria

Male and female patients between the ages of 18-65 who did not have a diagnosed chronic disease and did not regularly use medication/food supplement were included in our study.

Exclusion Criteria

Patients under 18 and over 65 years old, patients with hypertension, hyperlipidemia, diabetes mellitus, malignancy, anemia, thyroid dysfunction, renal dysfunction, chronic liver disease coronary artery disease, heart failure, acute/chronic inflammatory disease, acute/chronic infection, patients using alcohol (female > 20 g/day - male > 30 g/day), antibiotics, oral antidiabetic, antihypertensive, statin, fenofibrate and/or any drug/food supplement for the treatment of obesity, patients with HbsAg+ / Anti HCV+ and smokers were not included in our study.

STATISTICAL ANALYSIS

All analyses were performed on IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). For the normality check, histogram and Q-Q plots were used. Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables. Normally distributed continuous variables were analyzed with the independent samples t test or one way analysis of variance (ANOVA) depending on count of groups. Non-normally distributed continuous variables were analyzed with the Mann Whitney U test or Kruskal Wallis test depending on count of groups. Categorical variables were analyzed with the chi-square tests. Pairwise comparisons were adjusted by the Bonferroni correction method. Prediction performance of the monocyte to HDL ratio was assessed by using Receiver Operating Characteristic (ROC) curve analysis. Optimal cut-off points were determined by using Youden

index. Logistic regression analyses were performed to determine significant factors independently associated with the hepatic steatosis. Variables were analyzed with the univariable regression analysis and statistically significant variables were included into the multivariable analysis. Pearson or Spearman correlation coefficients were calculated to evaluate relationships between continuous variables. Two-tailed p-values of less than 0.05 were considered statistically significant.

RESULTS

We included 106 patients with HS and 85 healthy controls into our study. Age was significantly higher in the patients than in the controls (p<0.001). We found no significant difference between groups in terms of sex. Fifty eight (54.72%) patients had grade 1, 28 (26.42%) patients had grade 2 and 20 (18.87%) patients had grade 3 HS.

ALT (p<0.001), elevated liver function test percentage (p<0.001), fasting blood glucose (p<0.001), impaired fasting glucose percentage (p<0.001), HOMA-IR (p<0.001), insulin resistance percentage (p<0.001), total cholesterol (p<0.001), triglyceride (p<0.001), LDL (p<0.001), dyslipidemia percentage (p<0.001), monocyte count (p<0.001) and MHR (p<0.001) was significantly higher in the hepatic steatosis group than in the control group. HDL (p<0.001) was significantly lower in the HS group than in the control group. There were no significant difference between groups in terms of AST (Table 1).

MHR had 81.13% sensitivity, 72.94% specificity, 77.49% accuracy, 78.90% positive predictive value and 75.60% negative predictive value to predict hepatic steatosis for the cut-off point of 12.4 (values higher than this indicate hepatic steatosis). Area under ROC curve was 0.823 (95% CI: 0.763 - 0.882, p<0.001).

Multivariable logistic regression analysis had revealed that elevated liver function tests, insulin resistance and high MHR (>12.4) were independently associated with the hepatic steatosis. Individuals with elevated liver function tests had 3.195-fold higher risk to had hepatic steatosis than other individuals had (OR: 3.195, 95% CI: 1.291 - 7.909, p=0.012). Individuals with insulin resistance had 8.498-fold higher risk to had HS than other individuals had (OR: 8.498, 95% CI: 3.435 - 21.021, p<0.001). Individuals with high MHR (>12.4) had 9.973-fold higher risk to had HS than other

Table 1. Summary of variables with regard to hepatic steatosis

	Hepatic steatosis		
	No (n=85)	Yes (n=106)	p
Age	45 (39 - 57)	55 (46 - 62)	<0.001
Sex			
Male	43 (50.59%)	51 (48.11%)	0.734
Female	42 (49.41%)	55 (51.89%)	
Hepatic steatosis grade			
Grade 1	-	58 (54.72%)	-
Grade 2	-	28 (26.42%)	
Grade 3	-	20 (18.87%)	
ALT	26.81 ± 7.06	36.46 ± 15.63	<0.001
AST	25.40 ± 6.31	27.13 ± 10.03	0.147
Elevated liver function test	29 (34.12%)	67 (63.21%)	<0.001
Fasting blood glucose	91.27 ± 12.88	102.75 ± 13.01	<0.001
Impaired fasting glucose	22 (25.88%)	62 (58.49%)	<0.001
HOMA-IR	1.8 (1.6 - 2.2)	3.35 (2.2 - 5.6)	<0.001
Insulin resistance	11 (12.94%)	69 (65.09%)	<0.001
Total cholesterol	154.91 ± 29.19	189.26 ± 40.71	<0.001
Triglyceride	107 (64 - 136)	154.5 (110 - 189)	<0.001
LDL	94 (84 - 107)	112.5 (96 - 136)	<0.001
HDL	51.25 ± 13.11	43.46 ± 9.62	<0.001
Dyslipidemia	47 (55.29%)	85 (80.19%)	<0.001
Monocyte	496.59 ± 186.42	768.68 ± 267.20	<0.001
Monocyte to HDL ratio	10.24 ± 4.67	18.80 ± 8.70	<0.001

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables.

individuals had (OR: 9.973, 95% CI: 4.187 - 23.757, p<0.001) (Table 2).

Age was significantly higher in the grade 1, grade 2 and grade 3 than in the grade 0 (p<0.001). We found no significant differences between grades in terms of sex. ALT was significantly higher in the grade 2 than in the grade 0, also was significantly higher in the grade 3 than in the other grades (p<0.001). Elevated liver function tests percentage was significantly higher in the grade 2 than in the grade 0, also was significantly higher in the grade 3 than in the grade 0 and grade 1 (p<0.001). Fasting blood glucose was significantly higher in the grade 1, grade 2 and grade 3 than in the grade 0, also was significantly higher in the grade 3 than in the grade 1 (p<0.001). Impaired fasting glucose percentage was significantly higher in the grade 2 and grade 3 than in the grade 0 (p<0.001). HOMA-IR was significantly higher in the grade 1, grade 2 and grade 3 than in the grade 0, also was significantly higher in the grade 2 and grade 3 than in the grade 1 (p<0.001). Insulin resistance percentage was significantly higher in the grade 1, grade 2 and grade 3 than in the grade 0, also was significantly higher in the grade 2 and grade 3 than in the grade 1 (p<0.001). Total cholesterol was significantly higher in the grade 1, grade 2 and grade 3 than in the grade 0, also was significantly higher in the grade 2 and grade 3 than in the grade 1 (p<0.001). Triglyceride was significantly higher in the grade 2 and grade 3 than in the grade 0 and grade 1 (p<0.001). LDL was significantly higher in the grade 1 and grade 2 than in the grade 0, also was significantly higher in the grade 3 than in the other grades (p<0.001). HDL was significantly lower in the grade 2 and grade 3 than in the grade 0, also was significantly lower in the grade 3 than in the grade 1 (p<0.001). Dyslipidemia percentage was significantly higher in the grade 2 and grade 3 than in the grade 0, also was significantly higher in the grade 3 than in the grade 1 (p<0.001). Monocyte count was significantly higher in the grade 1, grade 2 and grade 3 than in the grade 0, also was significantly higher in the grade 3 than in the grade 1 (p<0.001). MHR was significantly higher in the grade 1, grade 2 and grade 3 than in the grade 0, also was significantly higher in the grade 2 and grade 3 than in the grade 1 (p<0.001) (Figure 1). There were no significant difference between grades in terms of AST (Table 3).

MHR had 81.25% sensitivity, 80.42% specificity, 80.63% accuracy, 58.21% positive predictive value and 92.70% negative predictive value to predict grade 2&3 HS for the cut-off point of 16.1 (values higher than this indicate grade 2 or grade 3 hepatic steatosis). Area under ROC curve was 0.821 (95% CI: 0.744 - 0.899, p<0.001) (Figure 2).

Multivariable logistic regression analysis had revealed that elevated liver function tests, insulin resistance and high MHR (>16.1) were independently associated with the grade 2&3 hepatic steatosis. Individuals with elevated liver function tests had 5.015-fold higher risk to had grade 2&3 HS than other individuals had (OR: 5.015, 95% CI: 1.498 - 16.792, p=0.009). Individuals with insulin resistance had 25.112-fold higher risk to had grade 2&3 HS than other individuals had (OR: 25.112, 95% CI: 6.404 - 98.475, p<0.001). Individuals with high MHR (>16.1) had 8.905-fold higher risk to had grade 2&3 HS than other individuals had (OR: 8.905, 95% CI: 2.863 - 27.694, p<0.001) (Table 4).

MHR was positively correlated with age (r=0.248, p=0.001), ALT (r=0.312, p<0.001), fasting blood glucose (r=0.297, p<0.001), HOMA-IR (r=0.436, p<0.001), total cholesterol (r=0.388, p<0.001), triglyceride (r=0.328, p<0.001) and LDL (r=0.413, p<0.001). We found no correlation between MHR and AST (Table 5).

DISCUSSION

Our study, in which we evaluated whether the MHR is a marker that can be used to predict the presence and stages of HS, found that the MHR was much higher in patients with HS compared to those without HS and this elevation increased in direct proportion to the stage.

Various markers are used in the diagnosis of inflammatory

Table 2. Odds ratios for hepatic steatosis, logistic regression analysis results

	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.066 (1.035 - 1.098)	<0.001	1.040 (0.998 - 1.084)	0.060
Sex, Female	1.104 (0.624 - 1.954)	0.734		
Elevated liver function test	3.317 (1.825 - 6.029)	<0.001	3.195 (1.291 - 7.909)	0.012
Impaired fasting glucose	4.035 (2.170 - 7.504)	<0.001	1.666 (0.694 - 4.000)	0.254
Insulin resistance	12.545 (5.933 - 26.526)	<0.001	8.498 (3.435 - 21.021)	<0.001
Dyslipidemia	3.273 (1.724 - 6.213)	<0.001	0.998 (0.412 - 2.418)	0.996
Monocyte to HDL ratio, >12.4	11.591 (5.858 - 22.936)	<0.001	9.973 (4.187 - 23.757)	<0.001
Nagelkerke R^2	-		0.594	

OR: Odds ratio, CI: Confidence interval

Table 3. Summary of variables with regard to hepatic steatosis grade

	Hepatic steatosis grade				
	Grade 0 (n=85)	**Grade 1 (n=58)**	**Grade 2 (n=28)**	**Grade 3 (n=20)**	**p**
Age	45 (39 - 57)	55 (46 - 62) *	52.5 (46 - 62) *	58 (48 - 63) *	<0.001
Sex					
Male	43 (50.59%)	27 (46.55%)	12 (42.86%)	12 (60.00%)	0.657
Female	42 (49.41%)	31 (53.45%)	16 (57.14%)	8 (40.00%)	
ALT	26.81 ± 7.06	30.16 ± 12.97	36.43 ± 9.03 *	54.80 ± 15.94 *#§	<0.001
AST	25.40 ± 6.31	26.97 ± 11.49	27.79 ± 7.42	26.70 ± 8.97	0.424
Elevated liver function test	29 (34.12%)	28 (48.28%)	20 (71.43%) *	19 (95.00%) *#	<0.001
Fasting blood glucose	91.27 ± 12.88	98.84 ± 12.84 *	104.68 ± 10.37 *	111.40 ± 12.57 *#	<0.001
Impaired fasting glucose	22 (25.88%)	27 (46.55%)	20 (71.43%) *	15 (75.00%) *	<0.001
HOMA-IR	1.8 (1.6 - 2.2)	2.35 (1.8 - 3.2) *	5.0 (3.95 - 7.2) *#	8.65 (4.1 - 10.2) *#	<0.001
Insulin resistance	11 (12.94%)	24 (41.38%) *	26 (92.86%) *#	19 (95.00%) *#	<0.001
Total cholesterol	154.91 ± 29.19	176.60 ± 25.50 *	199.39 ± 40.40 *#	211.80 ± 60.96 *#	<0.001
Triglyceride	107 (64 - 136)	131.5 (79 - 158)	167 (120 - 203) *#	215 (178.5 - 262) *#	<0.001
LDL	94 (84 - 107)	104 (95 - 120) *	117.5 (96.5 - 145) *	155.5 (139 - 166) *#§	<0.001
HDL	51.25 ± 13.11	46.98 ± 9.55	40.71 ± 8.15 *	37.10 ± 7.17 *#	<0.001
Dyslipidemia	47 (55.29%)	39 (67.24%)	26 (92.86%) *	20 (100.00%) *#	<0.001
Monocyte	496.59 ± 186.42	710.00 ± 229.72 *	810.36 ± 326.05 *	880.50 ± 242.76 *#	<0.001
Monocyte to HDL ratio	10.24 ± 4.67	15.72 ± 6.00 *	20.75 ± 9.38 *#	25.02 ± 10.46 *#	<0.001

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables. *: Significant difference from Grade 0, #: significant difference from Grade 1, §: Significant difference from Grade 2

diseases and the evaluation of treatment response, but the majority of these markers are not used in daily practice due to high costs and difficulty in access. Therefore, simple, easily accessible, and low-cost markers are required for the detection of the presence and severity of inflammation (14). Monocyte/HDL ratio is one of the new markers being tested for this purpose.

Monocytes, which account for approximately 3-8% of leukocytes in peripheral blood, play an important role in the regulation of inflammatory processes. HDL inhibits the transmigration of monocytes and the expression of endothelial adhesion molecules. This prevents macrophages from transferring lipid loads to the arterial wall (11). Recent research has also shown that HDL regulates the proliferation of monocyte progenitor cells (15). All of these findings indicate that monocytes have pro-inflammatory effects, and HDL cholesterol acts as a factor that reverses this process. Given the anti-inflammatory effects of monocytes and HDL, the ratio of these two values to each other has emerged as a good indicator of inflammation.

The effectiveness of the MHR in predicting the diagnosis and prognosis of many diseases with inflammation in their etiology has been studied since the idea that it

Table 4. Odds ratios for grade 2&3 hepatic steatosis, logistic regression analysis results

	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.045 (1.011 - 1.081)	0.010	0.985 (0.930 - 1.044)	0.613
Sex, Female	0.959 (0.499 - 1.844)	0.900		
Elevated liver function test	6.538 (2.943 - 14.527)	<0.001	5.015 (1.498 - 16.792)	0.009
Impaired fasting glucose	5.165 (2.503 - 10.656)	<0.001	2.538 (0.783 - 8.229)	0.121
Insulin resistance	46.286 (13.538 - 158.243)	<0.001	25.112 (6.404 - 98.475)	<0.001
Dyslipidemia	15.244 (3.559 - 65.297)	<0.001	5.524 (0.950 - 32.113)	0.057
Monocyte to HDL ratio, >16.1	17.798 (7.728 - 40.988)	<0.001	8.905 (2.863 - 27.694)	<0.001
Nagelkerke R^2	-		0.710	

OR: Odds ratio, CI: Confidence interval

may be a marker of inflammation and oxidative stress emerged. There is even evidence that it may indicate low-grade systemic inflammation in the absence of overt disease manifestation. For example, obesity causes low-grade chronic systemic inflammation. In a recent study conducted in Turkey, the status of the MHR in obese and non-obese individuals was investigated, and it was discovered that MHR was higher in obese individuals, and this increase was directly proportional to the degree of obesity (16). These studies led to the conclusion that MHR is a marker that can reflect even the pre-inflammatory state and correlates with the severity of inflammation.

Table 5. Correlations between monocyte to HDL ratio and other variables

	Monocyte to HDL ratio	
	r	p
Age, years	0.248	0.001
ALT	0.312	<0.001
AST	0.062	0.394
Fasting blood glucose, mg/dl	0.297	<0.001
HOMA-IR	0.436	<0.001
Total cholesterol, mg/dl	0.388	<0.001
Triglyceride, mg/dl	0.328	<0.001
LDL, mg/dl	0.413	<0.001

r: Correlation coefficient

Our study showed that MHR was much higher in the group with HS than in the group without HS. Furthermore, as the HS stage increased, the MHR also increased. The reason for this is that inflammation becomes more severe as fat accumulation increases in hepatocytes (17).

Since NAFLD is so common and has such serious consequences, it must be diagnosed early and closely monitored. Due to the mechanisms involved in pathogenesis, it is important to remember that NAFLD is linked not only to liver-related mortality but also to cardiovascular mortality (18). The MHR is also used to predict the prognosis of cardiovascular disease (19,20). According to the World Health Organization's 2020 report, 30 million people aged 30 to 69 die each year as a result of non-communicable diseases. The most common cause of noncommunicable diseases is metabolic abnormalities. HS is common in societies with obesity, hyperlipidemia, insulin resistance, type 2 Diabetes Mellitus, and metabolic syndrome (21). As a result, high-risk individuals with these diseases should be thoroughly examined for the presence of NAFLD. Similarly, the presence of these diseases must be investigated in a patient in whom HS is detected for any reason (22).

The prevalence of all these predisposing diseases, and thus the prevalence of NAFLD increases with age (23). Consistent with this data, our study showed that age was significantly higher in the group with HS compared to the group without HS. Hospital visits for these patients increase after diagnosis, and this situation causes a serious economic burden. There was no difference in the sex distribution between the HS and non-HS groups in our study. This was thought to be due to the similar prevalence of predisposing diseases in men and women. In the study of Yozgat et al. investigating the MHR in NAFLD, similar to our study, age was found to be higher in the group with HS, but no difference was observed in terms of sex distribution (10).

Insulin resistance is widely regarded as the primary cause of metabolic syndrome and NAFLD. The metabolic

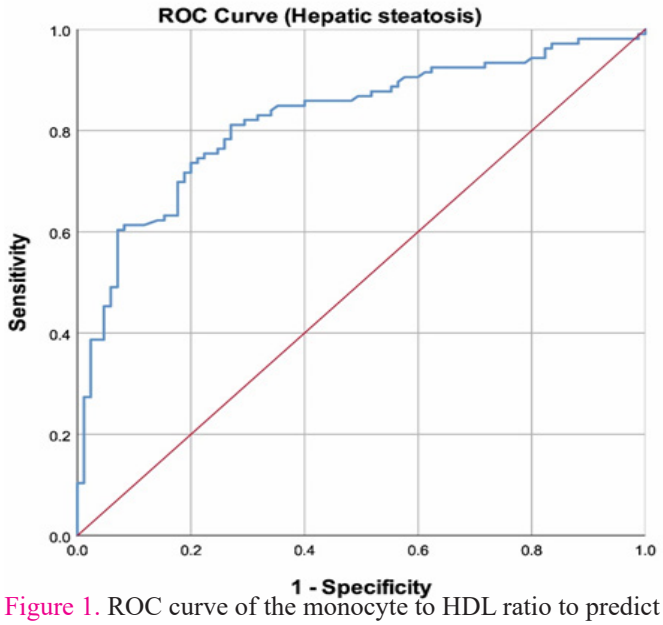

Figure 1. ROC curve of the monocyte to HDL ratio to predict hepatic steatosis

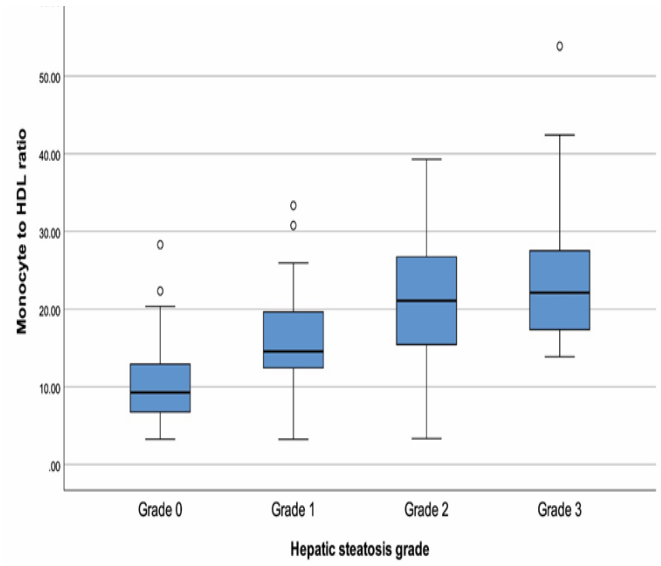

Figure 2. Box-plot of the monocyte to HDL ratio with regard to hepatic steatosis grade

syndrome is characterized by low HDL and increased triglycerides levels. Insulin resistance promotes lipolysis in adipose tissue, which results in the release of free fatty acids and their storage in the liver, and thus the development of HS. Dyslipidemia has a direct impact on the onset and progression of HS (24). Non-HDL cholesterol is a value that indicates the total level of harmful fats in the blood and can be calculated simply by subtracting HDL cholesterol from total cholesterol. IR causes a decrease in HDL cholesterol levels and an increase in NON-HDL cholesterol levels. In a study conducted in China in which 2717 individuals were followed up for an average of 1.6 years, a significant correlation was found between newly developing NAFLD and non-HDL/HDL cholesterol levels (25). In the presence of HS, trigliseride increase is also observed in addition to low HDL. In a recent study of 18061 patients, trigliseride /HDL ratio was found to be directly associated with NAFLD and this was also associated with insulin resistance (26).

AST and ALT are markers of hepatocellular damage. AST is found in the liver, heart muscle, skeletal muscle, kidneys, brain, pancreas, lungs, leukocytes, and erythrocytes. It is not as sensitive and specific for the liver as ALT. ALT is a liver-specific enzyme and ALT increase is more prominent than AST increase in laboratory findings reflecting HS (27).

However, in our study, fasting blood glucose, insulin resistance, total cholesterol, LDL, triglyceride, and ALT were significantly higher in the group with HS compared to those without HS and these values increased as the stage of HS increased and when correlation analysis was performed, MHR was positively correlated with these values. HDL was significantly lower in the group with HS compared to the group without HS and decreased as the stage of HS increased. There was no significant difference in terms of AST between the HS and non-HS groups.

Regression analyses show that the MHR is an important predictor of HS. Only ALT, insulin resistance, and the MHR are found to be independently associated with HS. A patient with increased ALT, the liver function test that best reflects HS, is 3.1 times more likely to have HS, and a patient with insulin resistance, the most important risk factor for HS, is 8.4 times more likely to have HS. The possibility of HS is 9.9 times higher in patients with an increased MHR. The study's findings indicate that, just as we investigate the presence of HS in a patient with increased ALT and insulin resistance, we need to be equally careful in a patient with a high MHR and risk factors for HS.

LIMITATIONS OF THE STUDY

Ours is a single-center study involving 191 patients. We don't have the patients' height, weight, or Body Mass Index parameters because the study was done retrospectively. Multicenter prospective studies with a larger number of patients that include these parameters are required. Furthermore, a recent infection may have affected the patients' monocyte values, but there is no information about this in the patient files. Another limitation is that the diagnosis of HS is made using USG. USG has the disadvantages of being a subjective evaluation, the difficulty of use in obese patients, and low sensitivity in histologic liposis below 30%.

CONCLUSION

MHR is closely associated with the presence and stages of NAFLD. It can be used as a marker to predict the presence and stages of HS in high-risk groups and may also be useful in evaluating the treatment response.

DECLARATIONS

Ethics Committee Approval: Approval of the the study was obtained from the Istanbul Medipol University Non-Invasive Clinical Research Ethics Committee for the study. (Date: 30.01.2023 / Number: E-10840098-772.02-739)

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Author contributions: The idea, method and planning of the study, data collection and statistical analysis were made by Ece Yiğit, the evaluation and interpretation of the findings, literature review and article drafting were made by İlknur Sayar. All authors read and approved the final manuscript.

Conflict of interest: None

Informed consent form: Since the study is a retrospective study based on the examination of patient files, informed consent form was not obtained.

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