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Monocyte count to high density lipoprotein cholesterol ratio in subjects with overweight and obesity

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Abstract

Monocyte count to high-density lipoprotein cholesterol (HDL-C) ratio (MHR) is a novel index that may be a prognostic marker in disorders associated with atherosclerosis and systemic inflammation. There is insufficient data about the role of MHR in increased body weight. We aimed to investigate the relationship of MHR with insulin resistance and other metabolic components in subjects with obesity and overweight. Non-diabetic and normotensive adults who did not use any drugs were included. The study population was allocated into three groups according to body mass index (BMI) as control, overweight, and obesity. The clinical and demographical data were compared between groups and a correlation analysis of MHR with metabolic parameters was performed. A total of 255 subjects (103 men) with obesity (n=107, mean age 40±11 years), overweight (n=99, mean age 39±11 years) and healthy controls (n=49, mean age 36±12 years) were included. MHR values were significantly higher in the obesity (MHR=11.80±5.50; p=0.003) and overweight (MHR =10.70±5.60; p=0.033) groups compared to the controls (MHR=9.10±3.70; 1.39±0.77). MHR was significantly correlated to BMI (r =0.235, p <0.001), waist circumference (r=0.253, p <0.001), homeostasis model assessment of insulin resistance (r=0.187, p=0.003), triglyceride (r=0.294, p<0.001), systolic (r=0.142, p=0.023) and diastolic blood pressure (r=0.149, p=0.017). MHR cutoff for predicting metabolic syndrome (MetS) was 11.0 and the AUC value was 0.707 [(sensitivity: 67%; specificity: 65%), (p<0.001)]. MHR appears to be a practical measure that is significantly associated with obesity and the components of MetS. Future prospective studies are warranted to determine the prognostic role of MHR in the cardiometabolic outcomes of people with obesity.

Keywords: Monocyte count to high-density lipoprotein cholesterol ratio, insulin resistance, obesity, overweight, metabolic syndrome

Introduction

Obesity is a chronic metabolic disease with growing global prevalence which causes and causing so many clinical problems including type 2 diabetes mellitus (T2DM), hypertension (HT), non-alcoholic fatty liver disease (NAFLD), obstructive sleep apnea syndrome (OSAS), and coronary artery disease (CAD) [1,2]. Many different predisposing factors such as genetic causes, imbalances of energy exchange in the organism, sedentary life, smoking, and alcohol use pave the way for the development process of obesity [3]. The main result of obesity playing role in the basic pathogenesis of obesity related chronic diseases is systemic insulin resistance. In addition, the chronic inflammatory process that occurs as a result of insulin resistance establishes the relationship between obesity and systemic atherosclerosis [4,5].

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Monocyte count to high-density lipoprotein cholesterol (HDL-C) ratio (MHR) is a novel index that appears to be related with atherosclerosis and chronic inflammation [6,7]. Elevated MHR values has been reported in obesity-related diseases, such as metabolic syndrome (MetS), NAFLD or polycystic ovary syndrome (PCOS) [8-10]. Considering these data, we hypothesized that MHR might be an important parameter in the obesity process and associated with insulin resistance [11].

As far as we know, there is not enough data about the role of MHR in overweight subjects or in patietns with obesity. The aim of this study is to investigate the relationship of MHR with metabolic parameters such as body mass index (BMI), waist circumference (WC) and insulin resistance in subjects with overweight and obesity.

Materials and Methods

We retrospectively analyzed our patient files between 2020-2021 and categorized all adult patients according to their BMI. Ethics committee approval of this study was obtained from the local ethics committee of Balikesir University Medical School (approval

number: 2021-237) and this study was performed according to the Helsinki Declaration.

Study design and population

In this study, non-diabetic and normotensive adult subjects who did not use any drugs were included. Two hundred and fifty-five subjects were allocated as normal, overweight or obesity according to BMI measures. Subjects with the following conditions or diseases were excluded: acute or chronic inflammatory diseases, active infection, presence of T2DM, HT, malignancy, pregnancy, chronic drug use (anti-inflammatory agents, antidiabetic, antihypertensive, antilipidemic drugs, etc.).

Definition of Metabolic Disorders

All subjects were classified into three groups [obesity group (BMI ≥30kg/m²), overweight group (BMI=25-29.99kg/m²) and control group (BMI=18.5–24.99kg/m²)] with respect to their BMI [12]. T2DM was classified by internationally accepted criteria [fasting plasma glucose (FPG) ≥126mg/dl, oral glucose tolerance test 2-hour PG ≥200mg/dl, glycosylated hemoglobin ≥6.5% or taking antidiabetic medication] [13]. According to blood pressure (BP) measurement, values above 140/90mmHg were classified as HT [14].

According to the NCEP ATP III, a patient with three or more of the criteria for metabolic disorder listed here was defined as MetS: [15] (1) Central obesity: WC≥102cm in male and≥88cm in female; (2) high BP: ≥130/85mmHg or treatment of previously diagnosed HT; (3) HDL-C <40mg/dL in male and <50mg/dL in female; (4) hypertriglyceridemia: triglyceride (TG) level≥150mg/dL; (5) FPG ≥100mg/dL or treatment of previously diagnosed T2DM.

Clinical and laboratory data

The patient file archive was reviewed retrospectively, and the clinical and laboratory parameters of the subjects were recorded on the computer data system. BMI values were calculated with the formula of [weight (kg)/ height² (m²)]. WC was measured from the line located at the mid-point between the lowest rib and anterior superior iliac crest. BP was measured three times in the seated position (Omron brand M2 sphygmomanometer) and the mean value was registered.

Bioelectrical impedance method was used for complete blood count and subgroup analyses [Beckman coulter LH 780 hematology analyzer (Beckman Coulter, Inc., USA)]. FPG, total cholesterol (TC), TG, HDL-C, creatinine, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were measured by the enzymatic colorimetric method [Beckman coulter AU 680 chemistry analyzer (Beckman Coulter, Inc., USA)]. Low-density lipoprotein cholesterol (LDL-C) was evaluated by Friedewald formula [LDL-C=TC-(HDL-C+TG/5)] [16]. The serum basal insulin level was measured by chemiluminescence method [Immunoassay UniCel DXI800 (Beckman Coulter, Inc., USA)]. Assessment of insulin resistance was done using by modified homeostasis model assessment of insulin resistance [HOMA-IR =fasting plasma insulin (μU/ml)×FPG (mg/dl)/405] method [17].

Statistical analysis

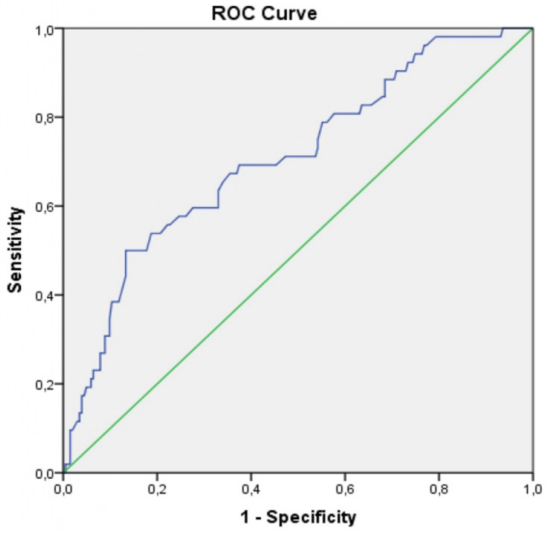
The data obtained in this study were recorded on a computer database and analyzed using Statistical Package for Social Science 22.0 package program (SPSS, Inc., Chicago, IL, USA). The variables were assessed for normality using the Shapiro-Wilk test. It was determined that variables did not meet the normality hypothesis and the Mann-Whitney U test is used for univariate analysis. The correlation analyzes were done by combining all of the individuals and using the Spearman-Rho method. Categorical variables were expressed as number (%) and continuous variables were expressed as mean±standard deviation. The p-value of <0.05 was considered statistically significant. The effective MHR cutoff point to predict MetS was calculated by receiver operating characteristic (ROC) curve analysis.

Results

A total of 255 subjects (103men) with obesity (n=107, mean age 40±11 years), overweight (n=99, mean age 39±11 years) and healthy control subjects (n=49, mean age 36±12 years) were included.

In the comparison between the groups, BMI and WC were higher in both obesity [(BMI=34.22±3.60; p=0.001), (WC=107.20±14.10; p=0.001)] and overweight [(BMI =27.45±1.39; p=0.001), (WC =95.60±7.70; p=0.001)] subjects compared to the control group (BMI =22.25±1.90; WC=81.10±9.00). On the other hand, MHR and HOMA-IR values were significantly higher in obesity [(MHR =11.80±5.50; p=0.003), (HOMA-IR=3.65±4.36; p=0.001)] and overweight [(MHR =10.70±5.60; p=0.033), (HOMA-IR=2.29± 1.86; p=0.001)] subjects compared to the controls [(MHR=9.10± 3.70; 1.39±0.77), (HOMA-IR =1.39±0.77)] (Table 1).

In the whole group analysis, groups with and without MetS were compared. The group of subjects with MetS [(n=52), (MHR =13.7±5.7)] had significantly higher MHR than the group of subjects without MetS [(n=203), (MHR=10.1±5.0)] (p=0.001). In the ROC curve analysis performed to predict MetS, the cutoff value of MHR was 11.0 and the AUC value was 0.707 [(sensitivity: 67%; specificity: 65%), (p<0.001)] (Figure 1).



	AUC (95%)	Cut off	p	Sensitivity (%)	Specificity (%)
MHR	0.707 (0.627-0.788)	11.0	< 0.001	67	65

Figure 1. ROC curve analysis to determine the cutoff value of the MHR for predicting MetS

Table 1. Comparison of demographic characteristics and laboratory data in subjects with obesity, overweight and control groups

	Obesity group (n =107)	Overweight group (n=99)	Control group (n =49)	p1* (Obesity - Overweight)	p2* (Obesity - Control)	p3* (Overweight - Control)
Age (year)	40±11	39±11	36±12	0.299	0.038	0.163
BMI (kg/m²)	34.22±3.60	27.45±1.39	22.25±1.90	0.001	0.001	0.001
WC (cm)	107.20±14.10	95.60±7.70	81.10±9.00	0.001	0.001	0.001
SBP (mmHg)	125.90±17.20	119.9±13.0	108.0±13.1	0.005	0.001	0.001
DBP (mmHg)	81.50±10.30	77.20±10.20	69.10±9.40	0.001	0.001	0.001
MONO (×103/µL)	0.55±0.19	0.54±0.25	0.49±0.17	0.540	0.157	0.339
Glucose (mg/dL)	100.00±17.00	99.00±31.00	93.00±8.00	0.332	0.006	0.038
Insulin (mIU/L)	13.63±12.29	9.36±7.32	6.03±3.21	0.001	0.001	0.001
HOMA-IR (%)	3.65±4.36	2.29±1.86	1.39±0.77	0.001	0.001	0.001
Creatinine (mg/dL)	0.88±0.13	0.92±0.16	0.85±0.14	0.067	0.268	0.015
ALT (IU/L)	26.00±19.00	26.00±20.00	16.00±7.00	0.395	0.001	0.001
AST (IU/L)	21.00±9.00	21.00±10.00	19.00±6.00	0.488	0.071	0.228
TC (mg/dL)	200.00±43.00	201.00±36.00	189.00±34.00	0.612	0.155	0.051
LDL-C (mg/dL)	120.80±37.80	123.50±29.60	110.30±29.30	0.323	0.105	0.011
HDL-C (mg/dL)	49.90±13.00	52.00±11.00	57.30±12.20	0.098	0.001	0.008
TG (mg/dL)	156.20±95.60	130.60±75.10	106.30±106.90	0.009	0.001	0.001
MHR	11.80±5.50	10.70±5.60	9.10±3.70	0.199	0.003	0.033

Values are expressed as mean ±Standard Deviation (SD) and are statistically significant (p/0.05). BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; WBC: white blood cell; Hb: hemoglobin; PLT: platelet; NEU: neutrophil; MONO: monocyte; HOMA-IR: homeostasis model assessment of insulin resistance; ALT: aminotransaminase; AST: aspartate aminotransferase; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TG: triglyceride; MHR: monocyte count to high density lipoprotein ratio.

In correlation analysis of the study population (n=255), there were significant positive correlations between the MHR and BMI, WC, HOMA-IR, TG, systolic BP (SBP) and diastolic BP (DBP) [(r=0.235, p<0.001), (r=0.253, p<0.001), (r=0.187, p=0.003), (r=0.294, p<0.001), (r=0.142, p=0.023), (r=0.149, p=0.017), respectively] (Figure 2).

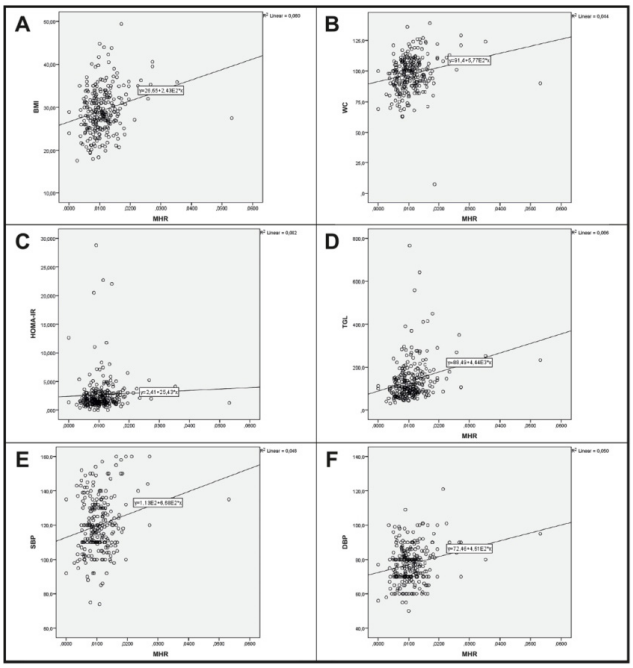


Figure 2. Correlation of MHR with insulin resistance and other metabolic components

Discussion

MHR, which is associated with different inflammatory diseases in the current literature, is a novel index that has been studied recently [18-20]. Not surprisingly, the increase in the serum levels of monocyte count in inflammatory pathologies is one of the main factors that play a role in the evaluation of this index [6]. However, the relationship of low HDL-C levels with both atherosclerosis and systemic inflammation is an entity [21,22]. MHR is related with various inflammatory pathologies such as PCOS, multiple sclerosis, and psoriasis [10,23,24]. It is also associated with atherosclerotic diseases such as ischemic stroke, ischemic optic neuropathy and CAD [25,26]. Furthermore, few clinical trials have reported that relationship between MHR and obesity-related diseases such as OSAS, MetS, and NAFLD [8,9,27]. On the other hand, no study examining the relationship of MHR with metabolic parameters in overweight subjects and people with obesity has been found in the current literature. To the best of our knowledge, this was the first study to show relationship of MHR with metabolic components in non-diabetic and non-hypertensive subjects with overweight and obesity. Our findings revealed that the MHR values of the overweight and obesity subjects are significantly higher than healthy controls. In addition, we found that MHR is significantly associated with BMI, WC, BP and insulin resistance in this clinically relevant condition.

In literature, there is scarce data regarding the role of MHR in subjects with MetS. In their retrospective study, Battaglia et al. analyzed a population of 771 subjects and found that MHR index is significantly associated to BMI and WC in subjects with

MetS. At the same time, it has been determined that gender, BMI and hyperglycemia were the most important variables that had an effect on MHR [11]. In another study by Vahit et al., MHR value was higher in MetS patients (n=371) than healthy controls (n=392) [9]. Furthermore, Uslu et al. investigated the relationship of MHR with MetS and also MetS severity in 147 patients and 134 healthy controls. MHR values of the patients were significantly higher when compared to controls. In addition, MHR showed a significant and positive association with the severity of MetS. They also described MHR cut off value of 9.36 as predictive of MetS [28]. Because of the strict inclusion criteria in the present study, only 52 subjects were identified as having MetS according to the NCEP III. As expected, when compared to healthy controls, we found that patients with MetS had higher BMI, WC, SBP, DBP, glucose, insulin, HOMA-IR and TG levels and lower HDL-C levels than the subjects without MetS. On the other hand, MHR values were significantly higher in subjects with MetS compared to the subjects without MetS. Moreover, we found that MHR is significantly and positively correlated with the levels of BMI, WC, BP, insulin resistance, and TG levels and negatively correlated with HDL-C levels. All these findings suggest that MHR is significantly associated with MetS and its components, and it might be an important index for the evaluation of MetS in clinical practice.

There is limited data in the literature regarding the relationship of MHR with HT [29,30]. In the present study, MHR was found to be significantly and positively associated with SBP and DBP in normotensive subjects. It is well known that essential HT is strongly related to insulin resistance and subclinical inflammation. Based on this information, we suggest that MHR can be considered a marker in the evaluation of HT. In addition, the possible association of MHR with the complications of HT (retinopathy, nephropathy, eg.) and the role of the effect of various anti-hypertensive medications on MHR levels remain to be elucidated.

We think that the main limitation of our study is the cross-sectional nature of the project, which does not allow an analysis of the longitudinal changes of MHR and also the effect of therapy (weight loss). Secondly, our study represents the experience of a single center and therefore cannot be generalized to the entire population. Lastly, the assessment of insulin resistance was made with the HOMA IR index, but it could not be done with euglycemic hyperinsulinemic clamp method, which is the gold standard method. On the other hand, the strength of the present study is the exclusion of confounding factors such as DM, HT, CAD and chronic use of medications etc. in investigating the relationship of MHR with obesity. Because this index can be affected by these diseases and medications frequently used in these metabolic confounders.

Conclusion

In conclusion, MHR which can be easily evaluated in clinical practice is significantly associated with obesity indices and with the components of MetS in overweight and obesity subjects. Considering this data, we suggest that the possible role of MHR in predicting the outcomes of metabolic disorders and also their cardiovascular consequences should be investigated in larger prospective studies.

Conflict of interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical approval

Ethics committee approval of this study was obtained from the local ethics committee of Balikesir University Medical School (approval number: 2021-237) and this study was performed according to the Helsinki Declaration.

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