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Comparison of Familial Mediterranean Fever patients by triglyceride/high-density lipoprotein ratio

Ailesel Akdeniz Ateşi hastalarının trigliserid/yüksek dansiteli lipoprotein oranına göre karşılaştırılması

Ahmet AKTAŞ[1], Mustafa Asım GEDİKLİ[1], Ali ŞAHİN[1]

[1]Sivas Cumhuriyet University, Faculty of Medicine, Department of Internal Medicine, Department of Internal Diseases, 58140, Sivas-Turkey

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Abstract

Aim: In this study, we aimed to show whether there is a relationship between FMF disease and cardiovascular risk by comparing Triglyceride/HDL-Cholesterol ratios between FMF patients and the control group.

Materials and Methods: A total of 300 patients, including 150 Familial Mediterranean Fever (FMF) patients and 150 control groups aged 18-65, were included in our study. Triglyceride/HDL-Cholesterol ratios of the patients were compared.

Results: Triglyceride/HDL-Cholesterol ratio was statistically significantly higher in the FMF group than the control group (p=0.026).

Conclusion: In FMF patients, the Triglyceride/HDL-Cholesterol ratio can be used as an inexpensive, reproducible predictor in showing a cardiac risk.

Keywords: FMF; Triglyceride/HDL-Cholesterol ratio; cardiac risk.

Öz

Amaç: Bu çalışmada, Ailevi Akdeniz Ateşi (AAA) hastaları ve kontrol grubu arasında Trigliserit/HDL-Kolesterol oranlarını karşılaştırarak, AAA hastalığı ile kardiyovasküler risk arasında bir ilişki olup olmadığını göstermeyi amaçladık.

Gereç ve Yöntem: Çalışmamıza 150 Ailevi Akdeniz Ateşi (AAA) hastası ve 18-65 yaş arası 150 kontrol grubu olmak üzere toplam 300 hasta dahil edildi. Hastaların trigliserid/HDL-Kolesterol oranları karşılaştırıldı.

Bulgular: Trigliserid / HDL-Kolesterol oranı, kontrol grubuna göre AAA grubunda istatistiksel olarak anlamlı yüksek bulundu (p = 0,026).

Sonuç: AAA hastalarında Trigliserid/HDL-Kolesterol oranı, kardiyak riski göstermede ucuz, tekrarlanabilir bir prediktör olarak kullanılabilir.

Anahtar Kelimeler: AAA, Trigliserid/HDL-Kolesterol oranı, kardiyak risk.

Yazışma Adresi/Address for Correspondence: Ahmet AKTAŞ, Sivas Cumhuriyet University, Faculty of Medicine, Department of Internal Medicine, Department of Internal Diseases, 58140, Sivas-Turkey, E-mail: ahmetaktas0142@hotmail.com

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Introduction

Familial Mediterranean Fever (FMF); is a disease accompanied by painful, non-infectious inflammatory attacks of serous membranes and fever, characterized by the development of amyloidosis over time. It passes with autosomal recessive inheritance and is frequently seen, especially in Mediterranean countries. FMF disease is a common health problem in our country. Early diagnosis of FMF is essential in terms of treating the disease and preventing possible complications.[1]

Pain attacks and pronounced fever characterize FMF. Fever and serositis attack repeating the clinical picture of FMF disease. Although the frequency of attacks varies from patient to patient, patients may not show any symptoms between attacks. Patients can spend an extended period without attacks. Generally, the first attack occurs in almost all patients before the age of 20. Although the clinical findings are very different in the attacks, the most common attack type, fever, abdominal pain, and joint findings are attacks.[2]

The presence of amyloidosis is the main feature that determines the prognosis of FMF disease. This protein, called serum amyloid A (SAA), is produced by the liver and is thought to be the cleavage product of an acute phase reactant that occurs during malignancy, tissue damage, infection, FMF attack, and other inflammatory events.[3]

There is a mutation in the Mediterranean Fever (MEFV) gene in FMF patients located on the short arm of chromosome16. The MEFV gene is responsible for the production of pyrin. Inflammation, apoptosis, and cytokine regulation develop as a result of pyrin production. The MEFV mutation causes pyrin dysfunction, thereby inhibiting the pro-regulatory function against pro-inflammatory cytokine release and neutrophil activation. TNF-a and IL-1b, one of the cytokines formed as a result of the MEFV mutation, cause inflammation in FMF patients.[4]

It is known that an increase in systemic inflammation is an independent risk factor for Coronary Artery Disease (CAD). Previous studies reported that patients with FMF applied with acute coronary syndrome during an attack. It has been shown that patients with FMF have a higher rate of developing ischemic heart disease than healthy individuals with similar risk factors.[5]

Deaths due to coronary heart disease are the most common cause of death all over the world. LDL cholesterol is a modifiable risk factor for deaths from coronary artery disease.[6, 7] The relationship between high LDL levels and increased mortality has been shown in many studies. Unlike high LDL cholesterol, HDL cholesterol is a factor that reduces cardiovascular deaths.[8] However, the results of studies related to the triglyceride level with cardiovascular mortality are not exact. A study conducted in 2009 with 544 women who underwent angiography showed that the Triglyceride/HDL-C ratio was associated with cardiovascular events and mortality.[9] In another study published in 2017, cholesterol levels such as LDL, HDL-C, and triglycerides were variable, so using the ratio triglyceride/HDL-C ratio was superior to other values showing mortality.[10]

The triglyceride/HDL-Cholesterol ratio is a useful marker in the evaluation of insulin resistance and early CVD. In some studies, it is considered ideal that the TG-HDLC ratio is less than 0.87. Triglyceride/HDL-Cholesterol ratio above 1.74 is a very high risk for coronary artery disease.[11]

In this study, we aimed to demonstrate the availability of the cheap and easily accessible Triglyceride/HDL-Cholesterol ratio in the relationship between FMF disease and cardiac risk by comparing the rates of Triglyceride/HDL-Cholesterol among FMF patients and healthy individuals.

Materials and Methods

The type of the study

Our study was conducted as a single-center, retrospective, and archive scan.

The population and the sample of the study

The files of FMF patients admitted to the hospital were examined, and lipid values and laboratory values of 150 patients out of 260

FMF patients admitted to the hospital were found.

The patients included in the control group did not have any accompanying diseases, they consisted entirely of healthy volunteers.

Patients with previous coronary artery disease, pregnancy, obesity, malignancy, and lipid-lowering therapy, patients who had an FMF attack for the past two weeks, patients with an active infection, and who received antibiotic therapy, thyroid function tests were abnormal, and those diagnosed with heart failure were excluded from the study.

General assessment and measurements

An entire medical history and physical examination were performed and recorded in every one of the cases contemplated. The body weight, waist circumference and body height measured, and body mass index (BMI) was calculated utilizing the following formula: BMI=weight (kg)/height (m^2).

Laboratory measurements

Blood samples were obtained from the antecubital vein after the first admission and following a 12hour fasting. Biochemical analyses were performed with an Architect Ci 8200 (Abbott Laboratories, Lake Bluff, IL, USA), Full blood counts were performed with an XN-1000 Automated Hematology Analyzer (Sysmex, Tokyo, Japan), and biochemical analyses were performed with an Architect Ci8200 (Abbott Laboratories, Lake Bluff, IL, USA). Fasting blood glucose, creatinine, albumin, total protein, blood urea nitrogen, total cholesterol, low-density lipoprotein, very low- density lipoprotein, high-density lipoprotein, and triglycerides were measured during the biochemical analysis.

Data collection

We made a file scan of 150 FMF patients and 150 healthy individuals aged 18-65 who applied to University Faculty of Medicine Hospital Internal Medicine and Rheumatology Outpatient Clinics between January 1, 2019, and January 1, 2020, compared their triglyceride/HDL-Cholesterol ratios in terms of cardiac risk.

Statistical analysis

Statistical Package for Social Sciences (SPSS), version 22.0 (SPSS Inc. Chicago, USA) computer package program was used to analyze the research data. In the descriptive statistics section, categorical variables are presented as numbers, percentages, and continuous variables are presented with mean±standard deviation. The consistency of continuous variables to normal distribution was evaluated using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). If the data of continuous variables show normal distribution due to the normality analysis, the Independent Sample t-test was used for comparative analysis between two groups. Mann-Whitney U test was used if it did not show normal distribution. Pearson's correlation analysis is used to show the relationship between WBC, sedimentation, CRP levels, and Triglyceride/HDL cholesterol ratio. In this study, the statistical significance level was accepted as $p < 0.05$.

Ethics committee approval

Before the study, our university ethics committee approval was obtained with the decision dated 08.07.2020 and numbered 2020-07/26. It was conducted by the principles of the Declaration of Helsinki.

Results

A total of 300 patients, 200 women, and 100 men, were included in our study. The average age of the FMF group was 35.6. Ninety-nine of the FMF group were women (66%), and fifty-one were men (34%). One hundred one of the control groups were female (67%), forty-nine were male (33%), and the average age was 35.9. There was no difference in height, weight, body mass index, fasting blood glucose, blood urea nitrogen and creatinine values of both groups (Table 1).

The average triglyceride/HDL-Cholesterol ratio of patients with FMF was 1.6262±1.1934, while those without FMF were 1.3054±1.2895. According to these parameters, the claim that those with FMF had a higher Triglyceride/HDL-Cholesterol ratio was found statistically significant (p=0.026) (Table 2).

WBC mean was 8666±1306, sedimentation means was 25.29±2.2, mean CRP was 33.32±6.5 in patients with FMF. In the control group, the WBC mean was 6835±1436, sedimentation means was 8.1±4.3, CRP mean was 6.76±2.4. A positive, statistically significant, but weak relationship was found between the triglyceride/HDL-Cholesterol ratio and sediments and WBC (Table 3).

Table 1. Comparison of demographic and laboratory values of FMF patients and control group

	FMF	Control	*p*
Age	35.6±12.3	35.9±11.9	0.63
Gender			
Female	99(66%)	101(67%)	0.62
Male	51(34%)	49(33%)	0.56
Height, m	1,66±0,08	1,63±0,07	0.114
Weight, kg	86±12	86±15	0.996
BMI, kg/m2	28,9±5,0	29,0±3,7	0.312
Fasting blood glucose(mg/dl)	90±5	91±4	0.256
Creatinin (mg/dl)	0,79±0,15	0,76±0,12	0.178

Table 2. Comparison of FMG and Control Group Triglyceride / HDL Ratios

	FMF	Control	*p*
Trigliserid/HDL Ratio	1.6262±1.19339	1.3054±1.28951	0.026

Table 3. Comparison of WBC, CRP, Sedimentation levels

	FMF	Control	*p*
White Blood Cell (WBC)	8666±1306	6835±1436	0.001
CRP	33.32±6.5	6.76±2.4	0.022
Sedimentation	25.29±2.2	8.1±4.3	0.025

Discussion

FMF is an autosomal recessive autoinflammatory disease characterized by inflammation of the serous membranes such as the peritoneum, pleura, and pericardium, accompanied by fever and arthritis. Studies in previous FMF patients have reported increased endothelial dysfunction and intima-media thickness. Studies have also shown an increased cardiac risk in amyloidosis-associated FMF for reasons such as inflammation markers and increased asymmetric dimethylarginine.[12]

The serum triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio, known as the atherogenic plasma index, is one of the main risk factors for CVD and metabolic syndrome. In studies conducted, a high TG/HDL C ratio has been associated with endothelial dysfunction.[13]

The atherogenic link between low HDL and high triglycerides is essential. High levels of triglyceride-rich VLDL create small-dense LDL during lipolysis and lipid exchange. This molecule plays an essential role in its relationship with oxidized-LDL in atherogenesis. These circulating accumulative LDL molecules form fast-catabolized small-dense HDL. The atherogenic ring is complemented in this way.[14] While the triglyceride level alone was a vital risk factor in the Copenhagen Male Study, its stratification according to HDL level provided risk prediction with increased accuracy. In subsequent studies, the TG/HDL ratio is a significant parameter showing cardiovascular disease's risk and prognosis.[15] On the other hand, studies in non-diabetic groups have shown that the TG/HDL ratio is an indicator of insulin resistance and a cardiovascular risk factor.[16] It has also been shown to be useful in evaluating dietary therapy's effectiveness in metabolic syndrome.[17]

In previous studies, the triglyceride/HDL cholesterol ratio was defined as > 1.7 high. It has been reported that those with a low risk of cardiovascular disease have a lower Triglyceride/HDL-Cholesterol ratio than those with a high risk of cardiovascular disease. This relationship between triglyceride/HDL-Cholesterol ratio and cardiac risk is statistically matched after gender, age, BMI, resting systolic blood pressure, resting heart rate, smoking, antihypertensive therapy used, fasting glucose, LDL cholesterol level, alcohol

consumption, and physical activity levels. It is meaningful. According to the results of previous studies, a strong relationship has been reported between cardiovascular disease and triglyceride-HDL cholesterol ratio even after matching glucose level and other confounding factors.[18, 19]

Our study found the triglyceride/HDL cholesterol ratio in the FMF group at a statistically higher rate than the healthy population (p=0.026). We found WBC, Sedimentation, and CRP levels higher in FMF patients than in the healthy control group. We found a positive, statistically significant, but weak relationship between Triglyceride/HDL-Cholesterol ratio due to increased inflammation and WBC.

Conclusion

Cardiovascular mortality has increased and increased coronary artery disease prevalence due to increased inflammation and cytokines in FMF patients. The high Triglyceride HDL-Cholesterol ratio in FMF patients compared to the control group may be a marker that can be used to evaluate atherosclerosis and coronary artery disease diagnosis as an inexpensive, easily applicable, and reproducible method. More extensive studies are needed to use the Triglyceride/HDL-Cholesterol ratio as an atherogenicity index in FMF patients and standardize a cut-off value in related FMF patients.

Ethics Committee Approval

Before the study, our university ethics committee approval was obtained with the decision dated 08.07.2020 and numbered 2020-07/26. It was conducted by the principles of the Declaration of Helsinki.

Informed Consent

From all patients included in the study an informed consent form was obtained.

Author Contributions

A.A set up the main idea and hypothesis of the study. A.A and A.S. developed the theory and edited the material method section. M.A.G evaluated the data in the results section. The discussion part of the article was written by A.A and A.S, M.A.G reviewed and made the necessary corrections and approved. In addition, all authors discussed the entire study and approved its final version.

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Conflict of Interest

The authors declared no conflict of interest.

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Our article has not been submitted anywhere.

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