

The Monocyte/HDL Cholesterol Ratio in Obstructive Sleep Apnea Syndrome

Obstrüktif Uyku Apne Sendromunda Monosit/HDL Kolesterol Oranı

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Abstract

Objective: Obstructive Sleep Apnea syndrome (OSAS) is the most common condition among sleep-related respiratory disorders. The etiology is not clear. However, systemic and local inflammation in the respiratory tract of the patients has been acknowledged. Monocytes and macrophages play the critical role in the inflammation process. These cells participate in the release of the proinflammatory cytokines in inflammation sites. High-density lipoprotein (HDL) cholesterol is a molecule with an anti-inflammatory effect. Monocyte/HDL cholesterol ratio (MHR) is an inflammation marker being used recently. In our study, we aimed to compare inflammation marker levels between patients diagnosed with OSAS with subsequent polysomnography and the non-OSAS group, determine the relationship between the severity of OSAS and MHR and, investigate the utility of the MHR for diagnosing OSAS.

Materials and Methods: The data from the patients' files who had polysomnography due to OSAS symptoms in our unit between July 2017 and December 2017 have been retrospectively analyzed, and polysomnography results were recorded. Demographic data and the results of biochemistry and complete blood count panels of patients with OSAS and who were not also were recorded.

Results: Out of 147 patients who underwent polysomnography in the period identified, 104 were diagnosed with OSAS. Monocyte count and MHR values were significantly high ($p<0.0001$ in both) and HDL levels were significantly low ($p=0.03$) in OSAS group. There was also a moderately significant positive correlation between apnea-hypopnea index (AHI) and MHR ($p<0.0001$, $r=0.411$).

Conclusion: MHR may be a useful tool for diagnosing OSAS. Because of the positive correlation between MHR and AHI which represents the severity of the disease, MHR may be used for the classification of OSAS.

Öz

Amaç: Obstrüktif Uyku Apne sendromu (OUAS) uyku ile ilişkili solunum bozuklukları içerisinde en sık görülen hastalıktır. OUAS'nin etiyolojisi kesin olarak bilinmemekle birlikte hastalarda sistemik ve havayolunda lokal enflamasyon varlığı gösterilmiştir. Monosit ve makrofajlar enflamasyonda rol alan önemli hücrelerdir. Enflamasyon bölgesinde proenflamatuvar sitokinlerin salınmasında görev alırlar. Yüksek dansiteli lipoprotein (YDL) kolesterolü anti-enflamatuvar etkisi olan bir moleküldür. Monosit/YDL kolesterol oranı (MYO) yakın zamanda kullanılmaya başlanan bir enflamasyon belirteçidir. Çalışmamızda ünitemizde polisomnografi ile OUAS tanısı alanların ve

almayanların enflamasyon düzeyini karşılaştırmayı, OUAS şiddeti ile MYO arasındaki ilişkiyi belirlemeyi ve MYO'nun OUAS tanısı için kullanılabilirliğini araştırmayı amaçladık.

Gereç ve Yöntemler: Ünitimizde Temmuz 2017 - Aralık 2017 tarihleri arasında OUAS kliniği ile polisomnografi yapılmış tüm olguların dosyaları retrospektif olarak incelendi ve polisomnografi sonuçları kaydedildi. OUAS tanısı alan ve almayanların demografik verileri ile biyokimyasal ve hemogram parametreleri kaydedildi

Bulgular: Belirlenen dönem içerisinde polisomnografik inceleme yapılan 147 hastadan 104'ü OUAS tanısı aldı. OUAS grubunda monosit sayısı anlamlı olarak yüksek ($p<0,0001$), YDL kolesterol düzeyi ise anlamlı şekilde düşük ($p=0,03$) ve MYO değeri anlamlı olarak yüksek bulundu ($p<0,0001$). OUAS hastalarda apne-hipopne indeksi (AHI) ve MYO arasında pozitif ve istatistiksel açıdan anlamlı orta derecede kuvvetli bir korelasyon tespit edildi ($p<0,0001$, $r=0,411$).

Sonuç: MYO, OUAS hastalarının tanısında kullanılabilecek bir parametre olabilir. OUAS ağırlığını gösteren AHI ile pozitif korelasyon göstermesi

Introduction

Obstructive Sleep Apnea syndrome (OSAS) is a syndrome characterized by a repeated full or partial airflow interruption in the airways during sleep (1). Prevalence rates vary from population to population and according to the parameters used to define OSAS (2-5). In a study of patients with the complaint of diurnal sleepiness, OSAS diagnosis rates were found to be 4% in males and 2% in females aged 30-60 years (6). Previous studies have determined high rates of systemic inflammation markers in OSAS patients in addition to airway inflammation and the majority of these inflammation markers have been determined to be related to the presence of OSAS and related to the severity of OSAS (7-10). Monocytes and macrophages are the most important types of cells that induce proinflammatory cytokine expression in the inflammation region (11). High-density lipoprotein (HDL) cholesterol is known to have antioxidant and anti-inflammatory effects. The monocyte/HDL-cholesterol ratio (MHR) has recently become a widely used marker of inflammation. A correlation has been established between MHR and several diseases. There are few studies in literature that have investigated the relationship between MHR and OSAS. In our study, we aimed to compare inflammation marker levels between patients diagnosed with OSAS based on polysomnography and the control group, determine the relationship between the severity of OSAS and MHR and, investigate the utility of the MHR for diagnosing OSAS.

Materials and Methods

This is a cross-sectional case control study and the study protocol was approved by Local Ethics Committee of Karabük University Training and Research Hospital (2018- 1/28). The data from the

patients' files who had polysomnography due to OSAS symptoms in our university between July 2017 and December 2017 have been retrospectively analyzed. Patients who had acute or chronic infections, renal (glomerular filtration rate <90 mL/min/1.73 m²), hepatic, autoimmune and oncological diseases were excluded from the study. The parameters such as sex, age, height, weight, smoking habits, comorbidities, the results of polisomnografia (PSG) and biochemistry and complete blood count panels were recorded. The patients who had an Apnea-Hypopnea index (AHI) ≥ 5 according to PSG were categorized as OSAS and the patients who had AHI < 5 were classified as a control group. In OSAS group the severity of the disease was considered as mild with 5-15, moderate with 16-30 and severe with >30 points according to AHI (12). MHR was calculated as the division of the monocyte count by HDL level.

Statistical Analysis

Analyses of the study data were made using SPSS Statistics 22.0 software (IBM Corp., NY, USA). Mean \pm standard deviation, median (25-75th percentiles) or n (%) were used for descriptive statistics. Conformity of the data to normal distribution was assessed with the Shapiro-Wilk test. The chi-square test was used for comparisons of the categorical data. Variables with normal distribution were compared with the Student's t-test and for variables not showing normal distribution, the Mann-Whitney U test was used. The Kruskal-Wallis test was used to compare MHR between control and OSAS subgroups. Post-hoc analysis was done as pairwise comparisons. Spearman's correlation was used for relationship between AHI and MHR. Receiver operating characteristic (ROC) curve analysis was applied to determine the cutoff value for MHR use in OSAS diagnosis. A two-tailed p value of $p<0.05$ was accepted as statistically significant.

Results

The data of 147 patients who had PSG between July and December 2017 was accessed. According to the AHI, the patients were separated into 2 groups as those determined with OSAS ($n=104$) with $AHI \geq 5$, and those without OSAS ($n=43$) with $AHI < 5$. In OSAS group; 50% of patients ($n=52$) had mild OSAS, 20.2% ($n=21$) had moderate OSAS and 29.8% had ($n=31$) heavy OSAS. The baseline characteristics of OSAS and control groups are shown in Table 1. The absolute monocyte count was found to be statistically significantly higher in the OSAS group than in the

Variable	OSAS	Control	p
Age (years)	51.1±12.1	47.4±11.4	0.080
Female	82 (78.8%)	26 (60.5%)	0.378
Male	22 (21.2%)	17 (39.5%)	
DM (+)	25 (24%)	12 (27.9%)	0.678
HT (+)	43 (41.3%)	18 (41.9%)	1.000
CAD (+)	7 (6.7%)	4 (9.3%)	0.731
OPD (+)	3 (2.9%)	2 (4.7%)	0.630
Smoking (+)	38 (36.5%)	12 (27.9%)	0.345

OSAS: Obstructive Sleep Apnea syndrome, DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, OPD: Obstructive pulmonary disease

control group ($p < 0.001$), and the HDL-cholesterol level was statistically significantly lower ($p = 0.03$). The other laboratory parameters were found to be similar in both groups ($p > 0.05$) (Table 2). The MHR value of the OSAS group was found to be statistically significantly high compared to that of the control group (11.64 vs 7.83, $p < 0.001$). The MHR values of the OSAS and control groups are shown in Figure 1. In the ROC analysis, the area under the curve was found to be 0.822 ($p < 0.001$). The cutoff value of MHR was determined to be 10.12 in the diagnosis of OSAS with sensitivity of 67.3% and specificity of 81.4% (Figure 2).

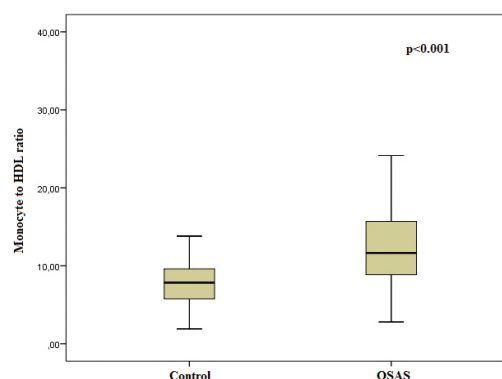


Figure 1. Monocyte to HDL ratio (median) of the OSAS and control groups

HDL: High-density lipoprotein, OSAS: Obstructive Sleep Apnea syndrome

Variable	OSAS	Control	p
Leukocyte ($10^3/\mu\text{L}$)	7610±1870	6370±1530	<0.001
Neutrophil ($10^3/\mu\text{L}$)	4080±1270	3290±960	<0.001
Lymphocyte ($10^3/\mu\text{L}$)	2730±790	2510±710	0.113
Monocyte ($10^3/\mu\text{L}$)	471.8 (397-607)	328.9 (282-392)	<0.001
Hb (gr/dL)	14.8 (13.7-15.8)	13.3 (12.4-15)	0.567
Thrombocyte ($10^3/\mu\text{L}$)	249 (210-285)	237 (204-278)	0.531
Glucose (mg/dL)	87 (79-99)	82 (75-105)	0.439
Urea (mg/dL)	31 (27-37)	32 (27-38)	0.951
Creatinin (mg/dL)	0.86±0.1	0.77±0.2	0.09
Total-cholesterol (mg/dL)	193.68±40.7	195.33±30.7	0.812
HDL-cholesterol (mg/dL)	39.5 (34-47)	42.8 (38-54)	0.037
Height (m)	1.70 (1.63-1.75)	1.64 (1.58-1.70)	0.001
Weight (kg)	90.5 (80-103)	90 (83-98)	0.422
BMI (kg/m^2)	32.4 (28.1-35.4)	33.9 (28.3-37.7)	0.255

OSAS: Obstructive Sleep Apnea syndrome, Hb: Hemoglobin, HDL: High-density lipoprotein, BMI: Body mass index

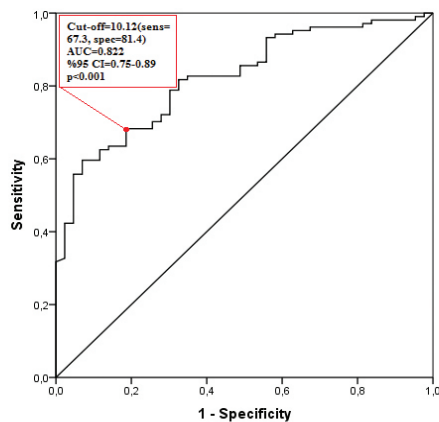


Figure 2. ROC curve of monocyte to HDL ratio for diagnosis OSAS

ROC: Receiver Operating Characteristic, HDL: High-density lipoprotein, OSAS: Obstructive Sleep Apnea syndrome

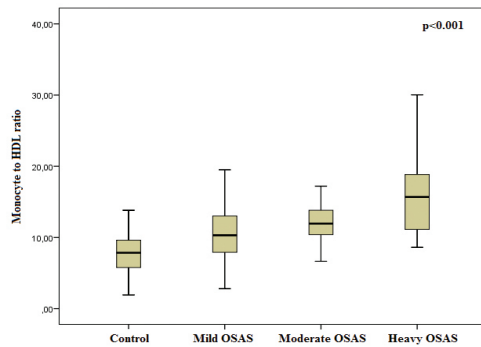


Figure 3. Monocyte to HDL ratio values of the control and OSAS subgroups (MHR was significantly different between control and all OSAS subgroups $p < 0.001$ and was significantly different between mild and heavy OSAS $p < 0.001$)

HDL: High-density lipoprotein, OSAS: Obstructive Sleep Apnea syndrome, MHR: Monocyte/HDL cholesterol ratio

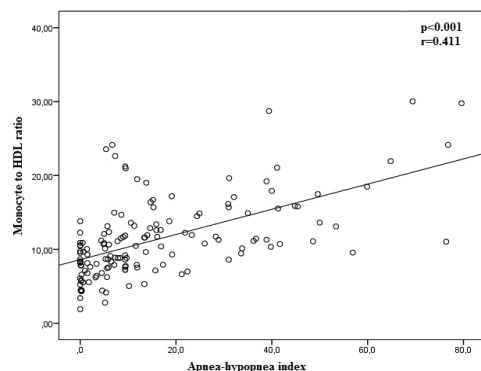


Figure 4. Correlation plot between apnea-hypopnea index and monocyte to HDL ratio

HDL: High-density lipoprotein

There was statistically significant difference between OSAS subgroups and control group regarding MHR ($p < 0.001$). The MHR values of the OSAS and control groups are shown in Figure 3. The evaluations of patients with OSAS showed a statistically significant, moderately strong correlation between AHI and MHR ($p < 0.001$, $r = 0.411$). The correlations between AHI and MHR are shown in Figure 4.

Discussion

As MHR is an inexpensive and readily available parameter, it has become more widely used in recent years, and has been related to several clinical conditions (13-16). The relationship between OSAS and MHR was first investigated by Atan et al. (17) in 2007, and it was determined that MHR could be a predictive marker in OSAS diagnosis. In the present study, the value of MHR of the patients with OSAS was determined to be statistically significantly higher than that of the control group. In this respect, the data of the current study are consistent with the results of the study by Atan et al. (17). In a recent multicentre study by Inonu Koseoglu et al. (18), the relationship of MHR and cardiovascular disease was investigated in OSAS patients and it was determined that MHR, as a systemic inflammation marker, could predict cardiovascular disease in OSAS patients. In the same study, a relationship was found between MHR and OSAS severity. The results of the current study demonstrated that as the severity of OSAS increases, MHR increases. Furthermore, a moderately strong positive correlation was determined between AHI and MHR. Our results were similar to the findings of the Inonu Koseoglu et al. (18) study. With an increase in the number of monocytes, which play an active role in inflammation, the MHR increases, and a decrease in HDL-cholesterol can also lead to an increase in MHR. In a study by Tamaki et al. (19), the monocyte count in OSAS patients was determined to be increased compared to the control group. In the current study, the monocyte count of the OSAS group was found to be statistically significantly higher than that of the control group. In a study evaluating the metabolic effects of OSAS in elderly patients, Zhuo et al. (20) showed that HDL-cholesterol was lower in the OSAS group than in the control group. In the current study, the HDL-cholesterol level was determined to be low in the OSAS group. These results of the current study were similar to those of Zhuo et al. (20). Moreover,

the MHR calculated with the absolute monocyte count and HDL-cholesterol values was found to be statistically significantly high in the OSAS group of the current study compared to the control group.

Conclusion

Along with the limitations of the smallness of the sample size and the retrospective design of the study, the rarity of studies regarding the importance of MHR in OSAS patients in the literature increases the significance of our research. MHR may be a useful tool in patients with clinically compatible with OSAS. Because positive correlation was detected between MHR and AHI suggesting that this parameter may be used for evaluations of the disease severity. More prospective and comprehensive studies are needed in order to understand whether MHR can be used in the classification of OSAS in the future.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Karabük University Training and Research Hospital non-Interventional Clinical Research Ethics Committee (2018- 1/28).

Informed Consent: It was not taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.A., O.Y., Design: M.A., O.Y., Data Collection or Processing: M.A., Analysis or Interpretation: M.A., O.Y., Literature Search: M.A., O.Y., Writing: M.A., O.Y.

Conflict of interest: The authors declare that they have no conflict of interest.

Financial Disclosure: The authors declare that they have no financial interests.

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