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Monocyte/High-Density Lipoprotein Ratio: An Indicator of Oxidative Stress and Disease Severity in Lichen Planus Patients

Monosit/Yüksek Yoğunluklu Lipoprotein Oranı: Liken Planus Hastalarında Oksidatif Stres ve Hastalık Şiddetinin Bir Göstergesi

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ÖZET

Amaç: Liken planusun etyopatogenezi tam olarak bilinmemekle birlikte ilaçlar, enfeksiyonlar, otoimmün faktörler, genetik faktörler ve oksidatif stres mekanizmaları gibi çeşitli faktörlerle ilişkili olduğu fark edilmiştir. Oksidatif stres, kanser ve kronik inflamatuar hastalıklar gibi çeşitli hastalıkların patogenezinde rol oynar. Tam kan sayımı parametreleri, kronik inflamatuar süreçlerle ilişkili birçok hastalık için oksidatif stres tanısal biyobelirteçleri olarak kullanılabilir. Son dönemde yapılan klinik çalışmalarda monosit/yüksek yoğunluklu lipoprotein (HDL) oranının birçok kronik dermatozda oksidatif stresin bir belirteci olarak faydalı olabileceği gösterilmiştir. Ancak bildiğimiz kadarıyla liken planus vakalarında oksidatif stres ile monosit/HDL oranı arasındaki ilişki literatürde henüz çalışılmamıştır.

Gereçler ve Yöntem: Şubat 2018 ile Temmuz 2021 tarihleri arasında üçüncü basamak bir üniversite hastanesinin dermatoloji kliniğinde liken planus tanısıyla takip edilen olguların dosyaları retrospektif olarak incelendi. 99'u histopatolojik ve klinik olarak doğrulanmış liken planus olgusu ve 102 yaş ve cinsiyet uyumlu kontrol grubu dahil olmak üzere toplam 201 katılımcı vardı.

Bulgular: Monosit değerleri (p=0,16) ve HDL düzeyleri (p=0,26) her iki grup arasında istatistiksel olarak farklı bulunmazken, monosit/yüksek yoğunluklu lipoprotein (HDL) oranının liken planus grubunda kontrol grubuna göre istatistiksel olarak anlamlı derecede yüksek olduğu tespit edildi (p=0,04). Oral liken planus olgularında oral hastalık şiddet skoru ile ürik asit değerleri arasında korelasyon bulunmazken (p=0,11), oral hastalık şiddet skoru ile CRP (p=0,03) ve monosit/yüksek yoğunluklu lipoprotein (HDL) oranı (p=0,001) değerleri arasında korelasyon saptandı.

Sonuç: Çalışmada liken planus hastalarında monosit/yüksek yoğunluklu lipoprotein (HDL) düzeylerinin kontrol grubuna göre anlamlı derecede yüksek olduğunu bulduk. Yine monosit/yüksek yoğunluklu lipoprotein (HDL) oranını oral mukoza hastalığı şiddet skoru ile CRP'ye göre daha iyi korelasyon gösterdiğini tespit ettik. Monosit/yüksek yoğunluklu lipoprotein (HDL) oranının liken planuslu hastaların takibinde hastalık aktivitesini değerlendirmede potansiyel bir belirteç olabileceğini düşünüyoruz.

Anahtar Kelimeler: Liken planus, oral mukoza, monosit/yüksek yoğunluklu lipoprotein oranı

ABSTRACT

Aim: Although the etiopathogenesis of lichen planus is not clearly known, it has been noticed to be associated with various factors such as drugs, infections, autoimmune factors, genetic factors, and oxidative stress mechanisms. Oxidative stress is implicated in the pathogenesis of various diseases such as cancer and chronic inflammatory diseases. Complete blood count parameters can be utilized as oxidative stress diagnostic biomarkers for many diseases related to chronic inflammatory processes. In recent clinical studies, it has been shown that the monocyte/high-density lipoprotein (HDL) ratio (MHR) may be useful as a marker of oxidative stress in many chronic dermatoses. However, as far as we know, the relationship between oxidative stress and monocyte/HDL ratio in lichen planus cases has not been studied in the literature yet.

Materials and Methods: The files of cases who were followed up with lichen planus in the dermatology clinic of a tertiary university hospital between February 2018 and July 2021 were reviewed retrospectively. There were 201 participants in the analysis, including 99 histopathologically and clinically verified LP cases and 102 age and sex-matched controls.

Results: Monocyte values (p=0.16) and HDL levels (p=0.26) were not statistically different for both groups, but the MHR value (p=0.04) was detected to be statistically significantly higher in the lichen planus group than in the control group. In oral lichen planus cases, whilst the oral disease severity score and uric acid values were not correlated (p=0.11), the oral disease severity score was correlated with the CRP (p=0.03) and MHR (p=0.001) values.

Conclusions: In the study, we found that MHR levels were significantly higher in lichen planus patients compared to the control group. Again, we detected that MHR had a better correlation with oral mucosa disease severity score than CRP. We suggest that MHR may be a potential index to assess disease activity in follow-up patients with lichen planus.

Keywords: Lichen planus, oral mucosa, monocyte/high-density lipoprotein ratio

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INTRODUCTION

Lichen planus (LP) is an inflammatory dermatosis with characteristic histopathological and clinical properties. Lichen planus tends to affect the skin and oral mucosa but may involve the scalp, nails, anogenital, and esophagus regions. Although the etiopathogenesis of lichen planus is not clearly known, it has been noticed to be associated with various factors such as drugs, infections, hereditary factors, autoimmune factors, and oxidative stress mechanisms (1).

Oxidative stress is based on metabolic reactions using oxygen and indicates a disturbance in the equilibrium state of prooxidant / antioxidant reactions in alive organisms. Excessive oxidative stress can impair cellular proteins, lipids, or DNA by inhibiting the regular functions of cells. Therefore, oxidative stress is implicated in the pathogenesis of various diseases such as cancer and chronic inflammatory diseases (2). Additionally, there is much information on the role of oxidative stress in many chronic inflammatory dermatologic disorders such as acne vulgaris, psoriasis vulgaris, pemphigus vulgaris, and lichen planus (3). When the role of oxidative stress in LP, which is a chronic inflammatory disease, is investigated, it is observed that the relevant publications are mostly related to oral LP (4).

Complete blood count parameters can be utilized as oxidative stress diagnostic biomarkers for many diseases related to chronic inflammatory processes (2,3,4). In some studies, the use of some hematological parameters (eg. neutrophil) and biochemical parameters (eg. C - reactive protein, uric acid) as an indicator of oxidative stress in lichen planus has been investigated (5). In recent clinical studies, it has been shown that the monocyte/high-density lipoprotein (HDL) ratio may be useful as an indicator of oxidative stress in many chronic dermatoses (6,7,8,9). However, as far as we know, the relationship between oxidative stress and monocyte/HDL ratio (MHR) in lichen planus cases has not been studied in the literature yet. In our study, it was planned to evaluate the monocyte / HDL ratio in lichen planus cases in terms of its power to show oxidative stress and its intercourse with disease severity.

MATERIAL AND METHODS

The files of cases who were followed up with lichen planus in the dermatology clinic of a tertiary university hospital between February 2018 and July 2021 were reviewed retrospectively. Patients who were diagnosed with lichen planus histopathologically or clinically between these dates and were followed up regularly in our clinic with a lichen planus patient file were included in the study. The patients consisted of lichen ruber planus, oral lichen planus, lichen planus pigmentosus, lichen planopilaris, and hypertrophic lichen planus subtypes. Oral lichen planus; It was used only for cases with oral mucosal involvement and no cutaneous involvement. Patients with any systemic disorder (diabetes mellitus, hypertension, heart disease, hyperlipidemia, thyroid disease, etc.) or another cutaneous disease and those who received any systemic or topical treatment in the last three months were excluded. Cases that applied to the dermatology outpatient clinic for any reason and did not have a dermatological disease and did not meet the exclusion criteria were included in our study as the control group. The reason for these cases to apply to the dermatology clinic was to get a prescription for the moisturizers they use regularly or to consult about cosmetic defects that do not cause skin disease. There were 201 participants in the analysis, including 99 histopathologically and clinically verified LP cases and 102 age and sex-matched controls.

The involved sites and pain were determined in the clinical examination according to an oral mucosa disease severity system developed by Escudier et al. 106 points is the maximum score (min, 0 – max, 106) in the scoring system (10). It was recorded patients' age, gender, areas of involvement, disease duration, and disease severity scores at the time of diagnosis from the recorded information in the patients' files. Again, it was recorded the complete blood count parameters and biochemistry parameters (triglyceride, C-reactive protein (CRP), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and uric acid) requested at the time of diagnosis. In addition, the monocyte/HDL ratio was obtained and recorded.

Ethics committee confirmation

All the operations followed the Helsinki declaration and the local ethics committee confirmation was ensured for the study (Decision date and number: 2021/3423).

Statistical analysis

The associations between the numerical data were interpreted with Student's t-test for independent examples when normality assumptions were supplied and nonparametric equals of the same tests in cases where normality was not reached. The One-way ANOVA test was utilized for comparison between lichen subgroups. The chi-square test specified the associations between categorical factors. Pearson's correlation analysis was applied to the relationship between parameters. The p-value of smaller than 0.05 was taken as statistically significant.

RESULTS

A total of 201 participants, including 99 lichen cases and 102 control cases, were included in the study. 56 (56.6%) lichen planus patients were women. The mean age of the lichen cases was 51±14.3 (18-86) and the average disease period was 40.2±33.9 months. 57 (56%) of the participants in the control group were female, and the mean age of the control group was 50.7±13.2. There was no statistically significant distinction between the two groups in terms of age and sex. When the lichen planus group and control group data were compared, it was found that triglyceride (p=0.01), total cholesterol (p=0.02), and CRP values (p=0.05) in the lichen group were statistically significantly higher than the control group. Monocyte values (p=0.16) and HDL levels (p=0.26) were not statistically different for both groups, but the MHR value (p=0.04) was detected to be statistically significantly higher in the lichen planus group than in the control group. The histogram of MHR values of the lichen planus group and the control group is shown in Figure 1. The collation of the lichen planus group and control group

data was summarized in Table 1.

When the subgroups of lichen planus cases were evaluated according to their clinical types, it was found that the uric acid value (p=0.002) was statistically significantly different between the clinical groups, but the CRP (p=0.16) and MHR values (p=0.98) were not different. The ratios of lichen planus clinical types and the relationship between MHR, CRP, uric acid levels and clinical types are shown in Table 2.

In oral lichen planus cases, while the oral disease severity score and uric acid values were not correlated (p=0.11), the oral disease severity score was correlated with the CRP (p=0.03) and MHR (p=0.001) values. The correlation graph between oral mucosa disease severity score and MHR value is shown in Figure 2.

Table 1. Comparison of the lichen planus and control group

	Lichen planus group	Control group	p value
Age	51±14.3	50.7±13.2	0.86
Gender (female), n (%)	56 (56.6%)	57 (56%)	0.9
WBC (×10³/ml)	8.59±2.74	7.95±2.34	0.08
Neutrophil (×10³/ml)	5.78±4.8	4.84±1.35	0.07
Monocyte (×10³/ml)	0.52±0.32	0.46±0.3	0.16
HDL(mg/dl)	46.5±9.93	48.1±10	0.26
MHR	0.012±0.0085	0.099±0.006	0.04
LDL(mg/dl)	106.2±36.49	99.65±32.4	0.18
Total cholesterol (mg/dl)	187.25±12.7	173.35±42.1	0.02
Trigylceride (mg/dl)	161.54±85.1	133±71	0.01
Uric acid (mg/dL)	4.55±1.12	4.27±1.35	0.1
CRP (mg/L)	2.92±3.17	2.18±2.1	0.05

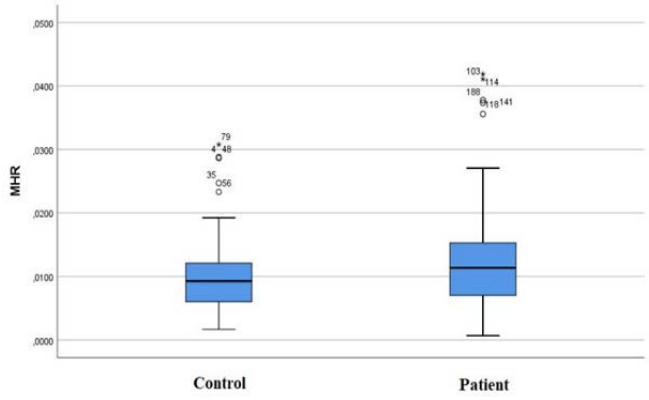

Figure 1. Monocyte/HDL cholesterol ratio (MHR) for the patients and controls

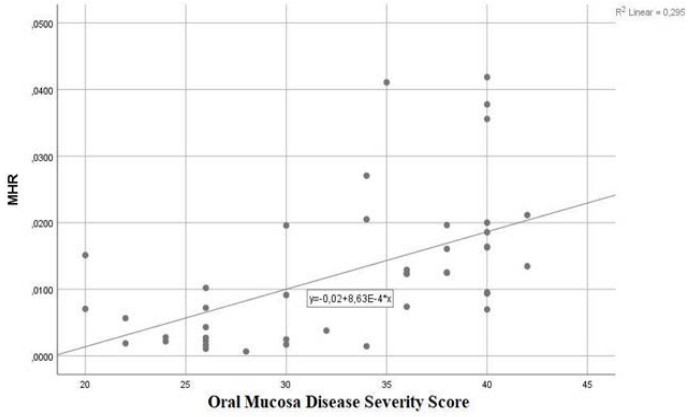

Figure 2. The correlation graph between oral mucosa disease severity score and MHR value

Table 2. Lichen planus clinical types and MHR, CRP, Uric acid levels

Clinical type	Number of patients, n (%)	MHR	p value	CRP (mg/L)	p value	Uric acid (mg/dL)	p value
Lichen ruber planus	51 (51.5%)	0.012±0.008	0.98	2.42±3.1	0.16	4.48±1.1	0.002
Oral lichen planus	29 (29.3%)	0.012±0.011		3.51±3.1		5.12±1.05	
Lichen planus pigmentosus	7 (7.1%)	0.011±0.003		5.17±4.6		4.13±1.04	
Lichen planopilaris	6 (6.1%)	0.01±0.003		2.9±2.76		4.1±0.4	
Hypertrophic lichen planus	6 (6.1%)	0.012±0.004		1.7±0.65		3.38±0.9	

DISCUSSION

In the study, we found that MHR levels were significantly higher in lichen planus cases compared to the control group. Again, we detected that MHR had a better correlation with oral mucosa disease severity score than CRP. We suggest that MHR may be a potential index to assess disease activity in follow-up patients with lichen planus. To the best of our knowledge, this is the first study in the literature to evaluate the relationship between lichen planus and MHR. The limitation of our research is its retrospective character.

In recent years, the relationship between metabolic syndrome and lichen planus has been clearly demonstrated (11). Again, the incidence of hyperlipidemia was detected to be higher in lichen planus cases than in the normal population (12,13). Although we did not examine all metabolic syndrome parameters in the study, triglyceride and total cholesterol values were detected to be statistically significantly higher in lichen planus patients compared to the control group, in line with the literature.

Lichen planus is a common mucocutaneous disease of unbeknown etiology, in which cytotoxic T lymphocytes cause chronic inflammation and trigger apoptosis of epithelial cells (1,2,14). The factors blamed for the etiology of lichen planus are oxidative stress and systemic inflammation, as in many diseases (2,14). The relationship between oxidative stress and systemic inflammation in the pathogenesis of many diseases, especially cancer and chronic inflammatory diseases, is well known (2,3,15). There are many studies in the literature investigating hemogram and biochemistry parameters as markers of oxidative stress and systemic inflammation. Neutrophils and monocytes are known as cost-effective and simple hemogram parameters that show systemic inflammation in many diseases (16). It can be considered as a systemic inflammation marker alone or with ratios such as neutrophil/lymphocyte, and monocyte / lymphocyte ratios (17,18). In our study, although neutrophil and monocyte counts were higher in the lichen planus group than in the control group, they were not statistically significant.

In recent studies, it has been argued that the increase in MHR value may increase more significantly than other inflammatory parameters in various chronic inflammatory diseases such as metabolic syndrome, diabetes mellitus, and coronary artery disease (19,20). It has also been argued that MHR value can be used as a systemic inflammation marker in many dermatological diseases such as acne (6,9,21), psoriasis (8), behçet's disease (22), and vitiligo (7). Önder et al. (21) argued that the increase in MHR in acne cases using isotretinoin may be more significant than other laboratory parameters in predicting systemic inflammation. In our study, although there was no significant difference in monocyte and HDL levels in lichen planus cases compared to the control group, a statistically significant difference was found in MHR levels. Again, among the systemic inflammation values (CRP, uric acid, MHR) we determined in our data, MHR values were found to be more significant than others between lichen planus and the control group.

In the literature, oral lichen planus has been found to be the type in which systemic inflammation and its consequences (such as metabolic syndrome, diabetes mellitus, hyperlipidemia) are observed the most among the sub-clinical types of lichen planus (1,11). In our study, the lichen planus subclinical types were compared in terms of inflammatory parameters, it was found that the MHR value was higher in the oral lichen planus group, but it was not significant. In terms of other systemic inflammatory markers (CRP, uric acid), it was seen that there was a statistically significant difference between subgroups only in uric acid values. It was determined that this statistical difference was due to the high uric acid value in the oral lichen planus group. Consistent with the literature, our study concluded that systemic inflammation may be more prominent in the oral lichen planus group.

In the literature, Demirbaş et al. (7) found a correlation between vitiligo severity and MHR. In our study, the correlation between disease severity score and systemic inflammatory markers (CRP, MHR, Uric acid) in oral lichen planus patients were examined, it was detected that CRP and MHR were positively correlated with oral mucosal disease severity score. Remarkably, the positive correlation of MHR with disease severity was found to be a stronger indicator than CRP.

CONCLUSION

In our study, MHR levels in lichen planus were significantly higher than in the control group. Again, it was observed that MHR had a better correlation with the oral mucosal disease severity score in lichen planus than CRP. We think that MHR may be a potential index to evaluate disease activity in the follow-up of patients with lichen planus. Additional studies with larger exemplary sizes are needed to strengthen the conclusions drawn in this study and the clinical significance of MHR.

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