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Evaluation of Serum Lipids and Castelli Risk Indexes of Cutaneous Lichen Planus Patients: A Retrospective Case–Control Study

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Abstract

Objective: Lichen planus (LP) is a cutaneous inflammatory disease, and accompanying dyslipidemia may be detected in LP patients. This study aimed to examine cardiovascular disease (CVD) markers and dyslipidemia in LP patients and compare them with healthy controls.

Methods: Forty-four patients aged older than 18 years old with histopathologically confirmed classical cutaneous LP, and 44 age- and gender-matched healthy controls admitted to the dermatology outpatient clinic between June 2022 and March 2023 were included in the study. All patients' demographic features, serum triglyceride, total cholesterol (TCOL), low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL) values, and Castelli-1 (TCOL/HDL) and Castelli-2 (LDL/HDL) risk indexes are recorded in the case report files.

Results: The number of patients with normal LDL values in the study group is significantly lower than in the control group (13.6% vs. 36.4%, $P = .034$). And also, 38 (86.4%) patients in the study group have higher Castelli-1 risk indexes than the controls ($P = .014$).

Conclusion: Lichen planus has a systemic, chronic inflammatory process. As a result of sharing common inflammatory processes, CVD and dislipidemia may be associated with LP. Therefore, serum lipid levels should be checked in the first evaluation and follow-up of LP patients.

Keywords: Cardiovascular disease, dislipidemia, lichen planus

Introduction

Lichen planus (LP) is a chronic inflammatory cutaneous disease that develops because of T cell-mediated autoimmune response to keratinocytes. It is most common between the third and sixth decades, with a slight predominance in perimenopausal women. It can affect the skin, skin appendages, and mucosa. It is classified into subtypes according to the morphology and localization of the lesions, such as cutaneous LP and oral LP. Cutaneous LP is characterized by pruritic, purple, polygonal, flattened papules and plaques, preferably on the flexor surfaces of limbs, however, it can be widespread.[1]

Serum lipids are a group of fats and fat-like substances and essential biomolecules for numerous biological functions. They are measured through their carrier lipoproteins, namely high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (TCOL), and triglyceride (TRIG). The concentration of blood lipids is a major factor in cardiovascular diseases (CVD).[2] Furthermore, constructed indices of these molecules such as the Castelli-1 risk index (TCOL/HDL), and Castelli-2 risk index (LDL/HDL) are good predictors of CVD events.[3]

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Because of the presence of chronic systemic inflammation in the pathogenesis of LP, comorbid diseases linked with chronic inflammatory processes such as dyslipidemia, CVD, and metabolic syndrome can often accompany patients with LP. Recent studies showed that the accompanying dyslipidemia was frequently examined in patients with cutaneous and oral LP; however, the results showed regional and habitual differences.[4-7]

In this study, it is aimed to examine dyslipidemia and CVD indexes in cutaneous LP patients and compare them with healthy controls.

Methods

Study Design

This study is a descriptive, retrospective, and case–control study. It was carried out in a tertiary dermatology center after the ethics committee's approval from Kütahya Health Sciences University (Approval No: 2023/07-01, Date: May 30, 2023). Forty-four patients aged older than 18 years old with histopathologically confirmed classical cutaneous LP without a history of cardiac disease, and 44 age- and gender-matched healthy controls admitted to the dermatology outpatient clinic between June 2022 and March 2023 were included in the study. The informed consent form was obtained from all patients. The exclusion criteria were lichenoid drug eruptions or contact reactions, hypothyroidism, and patients that received systemic drugs such as systemic corticosteroids, retinoid acid, or lipid-lowering drugs in the last 6 months.

Data Collection

All patients' age, gender, body mass index (BMI), smoking habits, serum TRIG, TCOL, LDL, HDL values after a 12-hour fasting

at the time of diagnosis were obtained from the hospital registry system and recorded in the case report files. Then, Castelli-1 (TCOL/HDL) and Castelli-2 (LDL/HDL) risk indexes were calculated. Serum levels of TRIG, TCOL, HDL, and LDL were measured by using a photometric autoanalyzer (Beckman Coulter AU 5800) and its standard kits. The cut-off values of hyperlipidemia were assessed in terms of the National Cholesterol Education Program Adult Treatment Panel III criteria (serum TRIG >150 mg/dL, TCOL >200 mg/dL, LDL >130 mg/dL, HDL <40 mg/dL for male, HDL < 50 mg/dL for females, Castelli-1 risk index <3, Castelli-2 risk index <3.5).

Statistical Analysis

Statistical analysis was done with The Statistical Package for Social Sciences version 20.0 software (IBM Corp.; Armonk, NY, USA). Numerical variables were given as mean ± SD or median (25th-75th percentile). Categorical variables were given as frequency (percentage). Relationships between categorical variables were evaluated by chi-square analysis. The Kolmogorov–Smirnov test was used to examine the uniform distribution of the data. Two samples' student's *t*-test was used to compare mean values of normally distributed quantitative variables. In the testing of 2-sided hypotheses, $P < .05$ was considered sufficient for statistical significance.

Table 1. Demographic Characteristics of the Study and Control Groups

	Study Group (n = 44)	Control Group (n = 44)	*P*
Mean age ± SD (years)	54.4 ± 15.9	55.18 ± 12.2	.800
Median duration of the disease (25%-75%) (months)	7.5 (6-12)		
Gender			
Female	28 (63.6%)	24 (54.5%)	
Male	16 (36.4%)	20 (45.5%)	1.000
Smoking			
Present	10 (22.7%)	12 (27.3%)	
Absent	34 (77.3%)	32 (72.7%)	.627
Body mass index ± SD	27.2 ± 4.96	26.99 ± 3.73	.754
Additional systemic disease			
Hypertension	11 (25%)	12 (27.3%)	
Diabetes mellitus	10 (22.7%)	10 (22.7%)	.694

Results

A total of 88 patients, 44 patients with LP and 44 healthy controls, participated in the study. The study group consisted of 28 (63.6%) females and 16 (36.4%) males. The mean age of the patients was calculated as 54.4 ± 15.9 years. The median disease duration of the study group was 7.5 (6-12) months. The mean BMI of the patients was 27.2 ± 4.96 kg/m^2. Eleven (25%) patients had hypertension, and 10 (22.7%) had diabetes mellitus as an additional systemic disease in the study group. Ten patients (22.7%) were active smokers in the study group. None of the patients with LP and the healthy control used alcohol. There was no difference between the 2 groups in terms of mean BMI and smoking habits ($P = .754$; $P = .627$, respectively). Table 1 shows that the study group was homogeneous and matched with the control group with regard to age, sex, and other demographic features.

Twenty-four (54.5%) patients had hypertriglyceridemia, 30 (68.2%) patients had hypercholesterolemia, 16 (36.4%) patients had a low level of HDL, and 12 (27.3%) patients' Castelli-2 risk index was high in the study group. However, there was no statistical difference with the control group ($P = .523$; $P = .221$; $P = .469$; $P = .622$, respectively). On the other hand, the number of the patiens with normal LDL values in the study group was significantly lower than in the control group. In addition, 38 (86.4%) patients in the study group had a significantly higher Castelli-1 risk index than the control group ($P = .014$). (Table 2)

Discussion

In this study, there was no difference in terms of serum TRIG, TCOL, HDL levels, and Castelli-2 risk index between the study group and control group. However, the number of patients with normal LDL values in the study group was significantly lower than in the control group. In addition, the Castelli-1 risk index was markedly higher in the study group than the control group.

The link between LP and dyslipidemia and CVD was previously reported. Dreiher et al[4] declared that patients with LP had a higher prevalence of dyslipidemia than controls. However, serum lipid levels were not studied separately, and it is unknown whether the patients used lipid-lowering drugs in this study.[4] In this study, the patients using lipid-lowering drugs were excluded and the serum lipid levels of the patients were examined separately, and the number of patients with normal LDL values in the study group was significantly lower than in the control group.

The relationship between LP and CVD has been investigated in many studies in the literature.[8,9] Sahin et al[8] reported that LP patients had higher LDL, TRIG, and high sensitive C reactive protein levels and high electrocardiographic P wave duration than controls. They stated that there is an increased risk of CVD in LP patients, but they did not examine Castelli indexes in their participants.[8] In this study, the electrocardiographic findings of LP patients and controls were not investigated, however cardiac risk indexes of the patients were calculated and the Castelli-2 risk index was significantly higher in the study group.

Ozbagcivan et al[9] compared serum lipid levels in patients with cutaneous LP and oral LP, cutaneous + oral LP, and controls in their study. TRIG, TCOL, and LDL values, Castelli-1, and Castelli-2 risk indexes were significantly higher, and HDL values were significantly lower in all LP subtypes compared to the controls. Among LP subtypes, although the differences were not statistically significant, TRIG, TCOL, and LDL values were higher in patients with oral mucosa involvement compared to patients with only cutaneous involvement. Patients with oral mucosa involvement also showed significantly higher Castelli-1 and Castelli-2 risk indexes compared to patients with only cutaneous involvement.[9] In this study, serum TCOL, TRIG, and HDL levels were not significantly different between groups. This could be because of the exclusion of the patients with hypothyroidism from the study and none of the patients and controls used alcohol. However, the difference between LP subtypes was not examined due to an insufficient number of patients.

LP is based on autoimmune response. The most important cells of this inflammatory response are cytotoxic T-cells. These autoimmune cytotoxic T-cells attack keratinocytes, and this inflammatory process leads to release of reactive oxygen species and cytokines. The cytokines mostly released in LP pathogenesis, such as TNF-α,

Table 2. Evaluation of Lipid Profiles and Cardiovascular Disease Risk Factors of the Study and Control Groups

	Study group (n = 44)	Control group (n = 44)	*P*
TRIG			
<150 mg/dL	20 (45.5%)	24 (54.5%)	
≥150 mg/dL	24 (54.5%)	20 (45.5%)	.523
TCOL			
0-199 mg/dL	14 (31.8%)	22 (50%)	
200-249 mg/dL	16 (36.4%)	12 (27.3%)	
>250 mg/dL	14 (31.8%)	10 (22.7%)	.221
LDL			
<130 mg/dL	6 (13.6%)[a]	16 (36.4%)[b]	
130-159 mg/dL	14 (31.8)[a]	8 (18.2%)[a]	
>160 mg/dL	24 (54.5%)[a]	20 (54.5%)[a]	.034*
HDL			
<40 mg/dL male <50 mg/dL female	16 (36.4%)	13 (29.5%)	
≥40 mg/dL Male ≥50 mg/dL Female	28 (63.6%)	31 (70.5%)	.469
Castelli-1 risk index			
<3.5	6 (13.6%)	16 (36.4%)	
≥ 3.5	38 (86.4%)	28 (63.6%)	.014*
Castelli-2 risk index			
<3	32 (72.7%)	34 (77.3%)	
≥3	12 (27.3%)	10 (22.7%)	.622

TRIG, triglyceride; TCOL, total cholesterol; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.
a-b: Bonferroni adjustment*:p<0.05

IL-6, IL-10, and IL-4, are also involved in the pathogenesis of dyslipidemia and CVD.[10] Georgescu et al[11] reported that higher lipid peroxidation, carbohydrate peroxidation, protein peroxidation, and reactive oxygen-nitrogen species occur in LP patients than in controls. In this study, the anti-oxidant status of the patients was not measured. However, in light of these findings, it can be thought that LP, dyslipidemia, and CVD have similar pathological pathways that lead to increased oxidant status.

The main limitation of the study was the limited number of patients. The serum lipid levels and antioxidant status of LP subgroups also could not compared. However, the strengths of the study were examining the LP patients from a different region, being a case–control study, and evaluating LP's real effect on dyslipidemia and CVD by excluding the patients with hypothyroidism. And, none of the patients used alcohol, which affects both dyslipidemia and CVD.

Consequently, LP has a chronic inflammatory process and shares common cytokines with CVD in pathogenesis. As a result, it can be concluded that there may be an association between CVD and dyslipidemia in LP patients. Thus, serum lipid levels should be checked in the first evaluation of LP patients and before systemic treatments such as systemic steroids and acitretin. If necessary, multidisciplinary follow-up should be performed with the cardiology and endocrinology departments.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Kütahya Health Sciences University (Approval No: 2023/07-01, Date: May 30, 2023).

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

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