Alterations of serum lipids in patients with classic cutaneous lichen planus

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Background: Lichen planus (LP) is a chronic inflammatory disease involving the skin, mucous membranes and appendages. Like other chronic inflammatory diseases, it may be associated with metabolic disorders and dyslipidemia. Due to the discrepancies in the results of previous studies and lack of a similar study on an Iranian population, we decided to investigate and compare the serum lipid levels of LP patients and normal healthy subjects.

Methods: In this case-control study, 71 patients with lichen planus confirmed by clinical and pathological examination who referred to dermatology clinic were recruited; further included were 71 subjects selected from attendants without any skin diseases matched for age, gender and BMI.with patients; the well-being of the healthy subjects was confirmed by laboratory tests, physical examination and medical history..After filling the questionnaire, triglyceride, cholesterol, HDL and LDL levels were measured for patients and healthy subjects..The collected data were then analyzed.

Results: Mean age of patients in the case group was 40.63 ± 11.41 years, 50.6% of whom were men, while 49.4% were women. Cholesterol, triglyceride and LDL levels in patients were significantly higher than the control group; it was only regarding HDL levels that no significant difference was observed between the two groups. HDL and triglyceride levels were significantly higher in patients with generalized disease. There was a recognizable correlation between elevated levels of LDL and cholesterol and disease duration.

Conclusions: In this study, a disrupted lipid profile was observed in LP patients, which can be associated with disease severity. This study proposes measuring lipid serum levels prior to commencing the treatment in all known cases of lichen planus so as to preclude cardiovascular diseases if there is a problem with the lipid profile.

Keywords: lichen planus, dyslipidemia, cholesterol, triglyceride, HDL, LDL

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INTRODUCTION

Lichen planus (LP) is a chronic inflammatory disease involving the skin, mucous membranes, hair and nails [1-3]. Epidermal cells in LP show abnormal enzymatic activity and defective expression of carbohydrates. Diabetes and glucose intolerance have been observed in patients with LP. Therefore, LP and psoriasis may be associated with metabolic disorders [4]. During the destruction

of keratinocytes by lymphocytes, the latter release more cytokines recruiting further lymphocytes, which are involved in the pathogenesis of LP and account for dyslipidemia with a similar mechanism to psoriasis [5,6]. Dreiher et al studied 1477 LP patients and showed that dyslipidemia was significantly higher in LP patients in comparison with the controls [4]. In the study of Arias_Santiago, LP patients had a significantly higher TG, total cholesterol and LDL levels but lower HDL levels [7]. On the other hand, in a study on oral lichen planus, the levels of TG, Chol and LDL did not differ between the case and control [8]. Furthermore, Polic found no difference in serum lipid levels between LP patients and the control group [9]. No study has been conducted on an Iranian population concerning dyslipidemia in LP patients and conflicting results have been observed in previous studies, hence the objective of the present to compare the serum levels of lipids in LP patients and healthy control group.

MATERIALS & METHODS

Participants and study design

In this case-control study, we enrolled 71 patients with lichen planus, confirmed by clinical and pathological examination in dermatology Clinics of Imam Reza and Ghaem Hospitals in Mashhad University of Medical Sciences. Seventy-one healthy subjects with no skin diseases and matched with patients regarding age, sex and body mass index (BMI) were randomly selected from attendants of other patients. After confirming their health status by laboratory testing, clinical examination and medical history, they were included as controls.

Inclusion criteria were classic cutaneous lichen planus by clinical and pathological examination as well as filling out the informed consent form. Exclusion criteria for both patients and controls were consumption of systemic steroids or methotrexate for treatment of lichen planus over the past six months, topical treatments during last four weeks, lichenoid drug reaction in histopathologic evaluation, smoking and alcohol consumption, hypothyroidism and hyperthyroidism, diabetes, chronic renal and hepatic disease, cancer and hypertension, use of lipid-lowering drugs, retinoids, thiazides, cyclosporine, beta-blockers, corticosteroids, comorbidity with other inflammatory skin diseases and family history of hyperlipidemia.

After filling out the written informed consent form approved by regional ethics committee, 5 ml venous blood was taken, between 8-9 AM, from the brachial vein of patients and controls following 12 hours of fasting; further measured were total cholesterol and triglyceride, HDL, LDL, fasting blood sugar (FBS), alanine aminotransferase (ALT), aspartate aminotransferase (AST),alkaline phosphatase (ALP), thyroid-stimulating hormone (TSH), bilirubin, creatinine and blood urea nitrogen (BUN) levels. Those meeting the exclusion conditions in the laboratory study and medical history were excluded, and 142 patients were ultimately enrolled.

Blood pressure of patients was measured upon admission and after five minutes of rest; the average value was recorded as the final blood pressure. The height and weight of patients was measured, and BMI was calculated and recorded in the questionnaires. The data collected in questionnaires were encoded and fed into SPSS software.

Statistical methods

SPSS for windows (version 11.5) (SPSS Inc., Chicago, II, USA) was used for data analysis. The quantitative and qualitative data were described using central tendency; dispersion indices and mean SD were used to express these values. Chi-square test was used to evaluate the correlation between qualitative variables. Distribution of quantitative variables in the subgroups of qualitative variables was analyzed using student t-test. Prior to conducting the statistical tests, normal distribution of quantitative variables was measured by Kolmogorov–Smirnov test, where if the distribution of a variable was not normal, the equivalent non-parametric tests were done. $P < 0.05$ was considered as statistically significant.

Ethical considerations

A written informed consent was obtained from all participants.

RESULTS

In this cross-sectional case-control study, conducted over three years (Jan 2012- Jan 2014)

to determine and compare serum lipid levels in healthy subjects and lichen planus patients, 142 individuals including 71 LP patients and 71 healthy volunteers were evaluated. The mean age of patients (36 males (50. 7%) and 35 females (49.3%)) in the case group was 40.63 ± 11.41 years. The mean age of the control group was 40.24 ± 11.41 years, where 37 were males (52.1%) and 34 were females (47.8%). Only 11.3% of patients had a generalized form of the disease, 70.4% of the patients had oral lesions, and nail lesion was only observed in one case. None of the patients had scalp lesion. Mean disease duration in patients was 6.59 ± 8.75 months. Chi-square test showed no difference in sex distribution between the two groups (P = 0.931).

Mean age of subjects in the two groups indicated no significant difference concerning Mann-Whitney test (P = 0.762). Student T-test showed no significant difference regarding height, weight, BMI, systolic and diastolic blood pressure (P > 0.05).

The lipid profile included TG, Chol, HDL and LDL, the mean values of which can be seen in Table 1. Chol, LDL and TG levels were significantly higher in patients with lichen planus. Mean HDL level in the case group was not significantly different compared to the control group. Cholesterol, LDL, HDL and TG levels were not significantly different between women and men with lichen planus.

There was no significant difference between cholesterol and LDL levels of patients with generalized disease and patients with localized type of the disease; however, triglyceride level was significantly higher in the group with generalized disease than the group with localized disease (P = 0.003); moreover, HDL level was significantly lower in the group with generalized disease (P = 0.003).

The level of cholesterol, triglycerides and LDL in patients having oral mucosal involvement was not significantly different from those lacking oral mucosal disease; only HDL level was associated with the presence or absence of oral lesion, hence the fact that its mean value was higher in patients with oral lesion (Table 2).

Pearson's correlation coefficient showed that the increase in the disease duration augmented

Table 1. Review and comparison of the lipid profile between case and control groups

Groups	Variables	Min	Max	Mean	SD
Lichen plan patients	Chol (mg/dl)	128	288	199.028	33.778
	TG (mg/dl)	55	776	154.338	104.329
	HDL (mg/dl)	30	68	52.112	13.379
	LDL (mg/dl)	63	178	120.816	26.756
Healthy controls	Chol (mg/dl)	124	239	164.485	22.250
	TG (mg/dl)	52	313	106.028	55.867
	HDL (mg/dl)	35	65	48.042	9.338
	LDL (mg/dl)	63	152	94.900	18.769
P value		**Chol**	**TG**	**HDL**	**LDL**
		<0.001	<0.001	0.164	<0.001

Table 2. Comparison of Chol, TG, HDL and LDL serum levels in LP patients based on gender, disease severity and presence of mucosal lesions

Variables in lichen plan patients	Chol		TG		HDL		LDL	
Sex	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Male	202.75	30.90	157.83	76.56	51.97	17.70	125.36	25.19
Female	195.20	36.55	150.74	127.86	52.25	10.14	116.14	27.85
P value	0.350		0.1794		0.150		0.149	
Oral lesions	**T student**		**Mann-Whitney**		**Mann-Whitney**		**T student**	
Yes	201.42	33.264	140.86	68.19	55.24	15.48	122.72	26.23
No	193.33	35.130	186.42	158.64	44.66	7.30	116.28	28.08
P value	0.361		0.09		0.004		0.359	
Disease severity	**T student**		**Mann-Whitney**		**Mann-Whitney**		**T student**	
Localized	198.49	31.91	137.03	67.14	53.31	14.41	121.11	26.12
Generalized	203.25	48.66	290.62	212.12	42.62	10.50	118.50	33.24
P value	0.710		0.003		0.005		0.836	

the cholesterol levels. The correlation coefficient between these two factors was equal to 0.345, and the p-value obtained by Pearson's correlation coefficient was equal to 0.003. Furthermore, the increase in the duration of the disease augmented LDL levels, which was significant given the correlation coefficient of 0.352 and p-value of 0.003. Pearson correlation coefficient did not show any significant association between triglyceride and HDL levels and disease duration (P = 0.404 and r = -0.101, P = 0.163 and r = 0.167, respectively) (Figures 1,2).

DISCUSSION

Psoriasis, lichen planus, connective tissue disease, granuloma annulare, pemphigus and histiocytosis have been reported to be associated with dyslipidemia. They are mainly chronic inflammatory diseases, and the release of pro-inflammatory cytokines is a possible mechanism of hyperlipidemia [5].

Lichen planus is an immune-mediated inflammatory disease in which the antigens processed by Langerhans cells are presented to T-cells. The stimulated T-cells are epidermotropic and release cytokines that recruit inflammatory cells and destroy keratinocytes via cell-mediated cytotoxicity. During this lymphocytotoxic process, the keratinocytes release more cytokines which

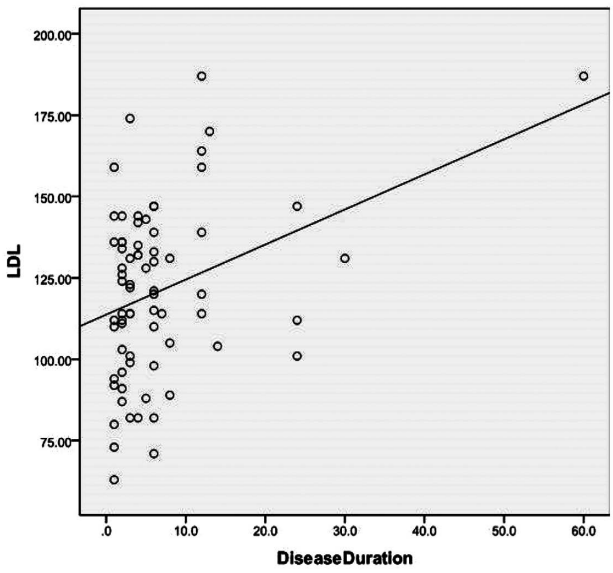

Figure 1. Relationship between LDL levels and duration of disease

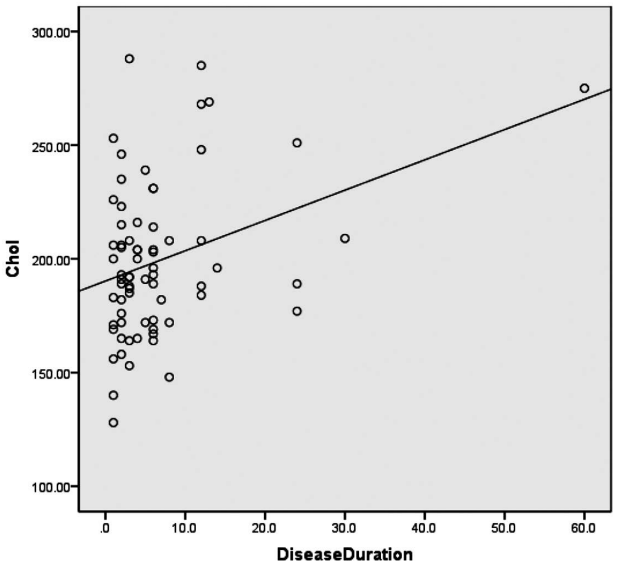

Figure 2. Relationship between cholesterol levels and duration of disease

will attract further cells. The released cytokines such as TNF-α, IL-6, IL-10 and IL-4 may explain the correlation between LP and dyslipidemia [3,6]. Inflammatory cytokines, including TNF-α, IL-1, IL-6, IFN γ and monocyte chemo-attractant protein-1 reduce the activity of lipoprotein lipase (LPL) via antibodies. For the first time, a study in 2009 in Israel indicated major dyslipidemia in 1477 LP patients of Jewish or Arab descent [4]. In this study, however, we did not mention the exclusion of patients with lichenoid drug reactions and those treated with retinoids and systemic steroids, lipid serum levels of patients, lichen planus type, BMI of patients and history of drug. In addition, several other studies have indicated the correlation between lichen planus and risk factors of cardiovascular disease, including dyslipidemia [4,7,10], diabetes [11] and increased oxidative stress [12].

In the present study, the variables of LDL, cholesterol and triglyceride were significantly higher in the patient group (P < 0.001), yet HDL level was not significantly different between the case and control (P = 0.164). Given the similarity between the two groups regarding other interfering factors in serum lipid levels and the elimination of other causes of dyslipidemia in the exclusion criteria, the predominant difference in lipid levels between the two groups can be attributed to lichen planus, which is in line with Panchal [14].

In the study of Arias Santiago, LP patients

(80 cases) showed significantly higher levels of triglyceride, total cholesterol, LDL, total chol/HDL and LDL/HDL ratios as well as lower levels of HDL compared to the control group [7]. In another study on 100 patients with LP, Arias Santiago showed a significant difference in the serum levels of TG and HDL-c between patients and controls. LP patients had a higher frequency of metabolic syndrome compared to the controls [6].

In the study of Dreiher, the correlation between LP and dyslipidemia was indicated even after controlling interfering factors such as age, sex, socioeconomic status, smoking, obesity, diabetes and hypertension [4]. Saleh showed that HDL, LDL, TG, Chol/ HDL and HDL/LDL ratios were significantly different in patients with cutaneous LP compared to the control group [13]. Sahin studied 58 LP patients, where LDL and triglyceride level was higher in the case group relative to the control [10].

In the study of Lopez jorent on oral LP patients, HDL level was lower compared to control group, yet other lipids were not significantly different between the two groups. In this study, other risk factors of hyperlipidemia such as hypothyroidism, chronic renal and hepatic disease, smoking and hypertension were not mentioned and diabetic patients bearing the risk factor for hyperlipidemia were not excluded either [8]. Polic found no difference between serum lipid level of patients and controls, probably due to the selection of control group from among patients treated for other skin diseases (other inflammatory diseases that may be associated with hyperlipidemia) and a lower sample size (30 vs 71) [9].

Arias Santiago reported that dyslipidemia was more severe in men [7]. In the study of Saleh, HDL level was lower in men [13], while Lopez jorent demonstrated that men with oral LP had significantly lower HDL and higher total cholesterol to HDL ratio [8]. In the present research, the mean cholesterol, LDL and TG was higher in men and HDL was higher in women; however, the differences were not significant, and the increase in the sample size may cause this difference to be significant.

Furthermore, triglyceride level was significantly higher in patients with generalized disease, but HDL was significantly lower in this group, which may be due to the higher severity of the disease and inflammation in these patients.

In our study, HDL level in patients with classic lichen planus without oral lesions was significantly lower than patients with oral lesions, an association not evaluated in similar studies. Lopez jorent showed lower HDL levels in patients with oral LP relative to control group [8], which is not in accordance with the present, since they studied the patients lacking skin lesions. In the study of Arias Santiago, no significant difference was observed regarding the level of lipids in patients with oral Lp and cutaneous LP [7]. In this study, increasing the disease duration augmented cholesterol and LDL, which can be justified by the impact of prolonged inflammation on the development of dyslipidemia.

Similar to other studies, lichen planus patients in our study had a higher lipid profile underlying cardiovascular disorders, an association which might be explained by the chronic inflammation in this disease. Therefore, it is suggested that the level of plasma lipids be routinely measured, not only for treatment but also for the prevention of cardiovascular events.

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Conflict of Interest: None declared.

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