Metabolic syndrome in patients with oral lichen planus and lichen planopilaris: a cross-sectional study

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Background: Lichen planus (LP) is a chronic inflammatory disease of unknown etiology. There is conflicting data on the link between LP and metabolic syndrome. This study evaluated the association of chronic subtypes of LP, namely oral lichen planus and lichen planopilaris (LPP), with metabolic syndrome.

Methods: In this cross-sectional study, 66 patients with oral and follicular LP were evaluated for metabolic syndrome based on the US National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) criteria and were compared against 66 healthy controls. Waist circumference, body mass index (BMI), systolic and diastolic blood pressure, fasting blood sugar (FBS), and lipid profile were measured for each individual.

Results: There was no significant difference in the prevalence of metabolic syndrome (13 [19.7%] vs. 8 [12.1%]; $P = 0.23$) and dyslipidemia (51 [77.3%] vs. 49 [74.2%]; $P = 0.68$) between the study groups. These findings remained statistically insignificant in both genders. The waist circumference ($P = 0.008$) and diastolic blood pressure (DBP) ($P = 0.02$) were significantly higher in the LP group than the healthy individuals. Our data showed that each unit increment in waist circumference and DBP leads to a 4.1% ($P = 0.02$) and 4.7% ($P = 0.03$) increase in the chance of LP, respectively.

Conclusion: Patients with oral LP and LPP do not have a higher prevalence of metabolic syndrome or dyslipidemia than healthy individuals. However, they are more vulnerable to central obesity and high diastolic pressure, for which they should be routinely screened.

Keywords: lichen planus follicularis, oral lichen planus, metabolic syndrome, dyslipidemia

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INTRODUCTION

Lichen planus (LP) is an idiopathic chronic inflammatory disease affecting about 0.5–1% of the general population [1,2]. It is a T-cell-mediated inflammatory disorder of unknown cause involving the skin (cutaneous LP), oral cavity (oral LP), genitalia (vulvar or penile LP), scalp (lichen planopilaris [LPP]), nails, or esophagus [3].

Systemic inflammation is a risk factor for the development of insulin resistance and alters lipid metabolism. Chronic systemic inflammation leads to an increase in very-low-density lipoprotein (VLDL) and triglyceride (TG), along with a decrease in high-density lipoprotein (HDL). Consequently, chronic systemic inflammation is associated with the formation of atherosclerotic plaques and, thus, a higher risk of cardiovascular disorders [4,5]. Prolonged

defective lipid metabolism causes an inflammatory state. Additionally, obesity, metabolic syndrome, and type 2 diabetes are kinds of inflammatory disorders [6,7].

Many inflammatory dermatologic disorders like psoriasis, vitiligo, alopecia areata, androgenic alopecia, systemic lupus erythematosus, skin tags, acanthosis nigricans, and skin malignancies are known to be associated with a higher risk of metabolic syndrome [8-13]. LP is also a chronic inflammatory disease, and chronic inflammation is regarded as a part of the metabolic disturbances. Previous studies have observed a strong link between LP and dyslipidemia [1,14]. Patients with LP are at greater risk for diabetes or pre-diabetes [15,16]. However, the association between LP and metabolic syndrome is controversial [1,17-22]. Additionally, most of the previous studies included only the patients with mucocutaneous involvement, and there is no data on the prevalence of metabolic syndrome in LPP. The prevalence of metabolic syndrome is reported to be about 31-36.9% in Iranian populations, relatively higher than the estimated prevalence around the world (10–84%) [17,23].

Hence, we aimed to evaluate the prevalence of metabolic syndrome and its components (dyslipidemia, diabetes, central obesity, and hypertension) in Iranian patients with chronic subtypes of LP including oral LP and LPP.

PARTICIPANTS AND METHODS

Study Design

This prospective cross-sectional study was performed in patients with a definite diagnosis of oral LP and LPP, the results of which were compared against age and sex-matched healthy individuals. The Ethics Committee of Tehran University of Medical Sciences approved the research protocol. The study was performed in accordance with the Declaration of Helsinki and the Medical Research Involving Human Subjects Act. All patients signed informed consent forms.

Participants

Sixty-six patients diagnosed with oral LP or LPP were recruited from a referral dermatology clinic between April 2018 to October 2018. The control group consisted of 66 age and sex-matched healthy volunteers who presented with cosmetic complaints. The simple random sampling method was used for sampling. Inclusion criteria were age > 18 years and a confirmed diagnosis of oral LP or LPP by an experienced dermatologist. Participants with any coexisting inflammatory disease other than LP/LPP or history of cardiovascular or immunosuppressive disorders were excluded.

Collection of Data

A dermatologist collected the demographic, biometric, and other relevant information. The data were recorded in predefined standard case report forms. Waist circumference (obesity), systolic blood pressure (SBP), diastolic blood pressure (DBP), weight (kg), and height $(m)^2$ were measured, and the body mass index (BMI) was calculated. A BMI above 30 signified obesity. Blood samples were drawn between eight and nine AM after a 12-hour fasting period to measure total cholesterol, TG, HDL, low-density lipoprotein (LDL), and fasting blood sugar (FBS).

Metabolic syndrome was diagnosed based on the US National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) criteria [24]. Any patient who had three of the five following items was diagnosed with metabolic syndrome: 1) abdominal obesity (waist circumference ≥ 102 cm in men and ≥ 88 cm in women); 2) a high TG level (≥ 150 mg/dL [1.7 mmol/L] or drug treatment for elevated triglycerides); 3) a low HDL cholesterol level (< 40 mg/dL [1 mmol/L] for men and < 50 mg/dL [1.3 mmol/L] for women); 4) high blood pressure (systolic ≥ 130 mm Hg or diastolic ≥ 85 mm Hg or drug treatment for elevated blood pressure); 5) a high fasting plasma glucose concentration (≥ 100 mg/dL [5.6 mmol/L] or drug treatment for elevated blood glucose). Presence of dyslipidemia was defined if one of the criteria was present: 1) TG > 150 mg/dL; 2) total cholesterol > 200 mg/dL; 3) LDL > 130 mg/dL; 4) HDL level < 40 mg/dL in males and < 50 mg/dL in females [24].

Statistical analysis

The statistical software SPSS 24.0.0. (SPSS Inc. Chicago, IL, USA) was used for data analysis. The

Shapiro-Wilk test was used to assess the normality assumption of continuous variables. In the case of the normal distribution of variables, the t-test was used for quantitative variables. Non-parametric tests such as the Mann-Whitney U test were used in case the distribution of data was not normal. The chi-squared test was used for qualitative variables. Univariate binary logistic regression analyses were applied to compute the crude odds ratios (with 95% CI for OR) of the association between the explanatory variables and metabolic syndrome. A P-value < 0.05 was significant.

RESULTS

The study included 66 patients with LP, including 49 (74.24%) with LPP and 17 (25.76%) with oral LP. Also, 66 age and sex and smoking status-matched healthy control subjects were included, among which 47 (71.21%) were men and 45 (68.18%) were women ($P = 0.7$). The mean age in the LP group was 50.33 ± 11.32 (mean ± standard deviation [SD]) years, which was comparable to that of controls (50.27 ± 11.13; $P = 0.97$) (Table 1).

Thirteen (19.7%) patients with LP and 8 (12.1%) controls met the criteria for diagnosis of metabolic syndrome, which was not significantly different ($P = 0.23$). These findings remained statistically insignificant in both genders (23 [48.94%] vs. 29 [64.44%] and $P = 0.13$ in females; 5 [26.32%] vs.7 [33.33%] and $P = 0.63$ in males) (Table 2).

The waist circumference (95.91 ± 11.67 vs. 90.76 ± 10.07 cm; $P = 0.008$) and DBP ($P = 0.02$) were significantly higher in the LP group compared with healthy individuals. However, there was no significant difference between the study groups regarding other components of the metabolic syndrome ($U_{FBS} = 1772$, $P_{FBS} = 0.06$; $U_{SBP} = 1975.5$, $P_{SBP} = 0.35$; $U_{HDL} = 2172$, $P_{HDL} = 0.97$; and $U_{TG} = 1980$, $P_{TG} = 0.36$). The BMI (U = 1966, $P = 0.33$), total cholesterol ($P = 0.58$), and LDL levels ($P = 0.83$) were also comparable between the two groups

Table 1. Baseline demographics, clinical characteristics, and laboratory findings of patients with lichen planus (LP) and healthy controls

Characteristic	Patients with LP (n=66)	Healthy controls (n=66)	*P*-value*
Gender, n (%)			
Female	47 (71.21%)	45 (68.18%)	0.70
Male	19 (28.79%)	21 (31.82%)	
Age, years	50.33 ± 11.32	50.27 ± 11.13	0.97
BMI	26.61 (24.22, 30.2); (23.7)	27.23 (24.25, 31.12); (18.71)	0.33
Abdominal circumference, cm	95.91 ± 11.67	90.76 ± 10.07	0.008
Type of LP, n (%)			
LPP	49 (74.24%)	-	-
Oral	17 (25.76%)	-	-
Duration of disease, years	3 (1.88, 5); (12.6)	-	-
Age at onset of disease, years	46.48 ± 10.83	-	-
Cutaneous involvement, n (%)	10 (15.15%)	-	-
Nail involvement, n (%)	1 (1.52%)	-	-
Systolic BP, mm Hg	120 (110, 130); (55)	113.5 (110, 130); (70)	0.35
Diastolic BP, mm Hg	80 (70, 85); (40)	80 (70, 80); (40)	0.02
FBS, mg/dL	93.5 (88, 104.5); (151)	91 (85, 100); (105)	0.06
Total cholesterol, mg/dL	192.24 ± 35.98	195.85 ± 38.76	0.58
LDL, mg/dL	117.71 ± 29.97	118.83 ± 32.93	0.83
HDL, mg/dL	47 (41, 56); (52)	48 (42, 56.25); (49)	0.97
TG, mg/dL	112 (86.75, 163.25); (327)	125 (96.25, 167.5); (279)	0.36
Metabolic syndrome, n (%)	13 (19.7%)	8 (12.1%)	0.23
Dyslipidemia, n (%)	51 (77.3%)	49 (74.2%)	0.68

Values are stated as mean ± SD or median (25^{th}, 75^{th} percentiles); (range) unless otherwise noted.
Abbreviations: LP, lichen planus; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; FBS, fasting blood sugar; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides
**P*-value for the comparison between the study groups.
Note: ATP III criteria define metabolic syndrome as the presence of any three of the following five traits: waist circumference ≥ 102 cm in men and ≥ 88 cm in women, blood pressure ≥130/85 mmHg, fasting triglycerides (TG) level ≥150 mg/dL, fasting high-density lipoprotein (HDL) cholesterol < 40 mg/dl in men and < 50 mg/dl in women and fasting plasma glucose ≥ 100 mg/dL

Table 2. Baseline demographics, clinical characteristics, and laboratory findings of patients with lichen planus (LP) and healthy controls by gender of participants

Characteristic	Female (n=92)			Male (n=40)		
	Patients with LP (n=47)	Healthy controls (n=48)	*P*-value	Patients with LP (n=19)	Healthy controls (n=18)	*P*-value
Age, years	52.62 ± 9.75	52.31 ± 9.65	0.87	44.68 ± 13.14	44.83 ± 13.15	0.97
BMI	27.68 (25.56, 31.25); (23.63)	27.07 (24.24, 31.62); (14.42)	0.52	24.22 (21.8, 26.78); (12.83)	27.92 (26.55, 30.21); (15.75)	0.002
Abdominal circumference, cm	98.64 ± 10.42	93.58 ± 15.11	<0.001	89.16 ± 12.11	91.90 ± 10.39	0.22
Type of LP, n (%)						
LPP	35 (74.47%)	0 (0%)		14 (73.68%)	0 (0%)	
Oral	12 (25.53%)	0 (0%)		5 (26.32%)	0 (0%)	
Duration of disease, years	3 (2, 6); (12.4)	-		2 (1, 5); (6.6)	-	
Age at onset of disease, years	48.36 ± 9.14	-		41.84 ± 13.34	-	
Cutaneous involvement, n (%)	9 (19.15%)	-		1 (5.26%)	-	
Nail involvement, n (%)	10 (21.28%)	-		6 (31.58%)	-	
Systolic BP, mm Hg	119.77 ± 13.88	116.56 ± 13.17	0.25	122.47 ± 14.99	122.61 ± 16.3	0.97
Diastolic BP, mm Hg	78.68 ± 10.34	75.83 ± 7.24	0.12	81.95 ± 8.71	77.33 ± 8.03	0.1
FBS, mg/dL	93 (88, 107); (151)	90 (83.5, 98.25); (40)	0.03	94 (88, 99); (71)	95 (86.5, 100); (105)	0.98
Total cholesterol, mg/dL	191.68 ± 36.37	198.13 ± 40.2	0.41	193.63 ± 35.92	189.78 ± 34.99	0.74
LDL, mg/dL	116.64 ± 29.68	121.33 ± 33.26	0.47	120.37 ± 31.32	112.17 ± 32.01	0.43
HDL, mg/dL	48 (41, 60); (52)	50 (44, 58.75); (49)	0.68	45.95 ± 8.7	43.61 ± 8.84	0.42
TG, mg/Dl	119 (86, 168); (327)	115 (91.75, 153); (279)	0.84	91 (87, 139); (221)	136 (100.75, 200.25); (232)	0.057
Metabolic syndrome, n (%)	23 (48.94%)	29 (64.44%)	0.13	5 (26.32%)	7 (33.33%)	0.63
Dyslipidemia, n (%)	38 (80.9%)	36 (75%)	0.5	13 (68.4%)	13 (72.2%)	0.8

Values are stated as mean ± SD or median (25^{th}, 75^{th} percentiles); (range) unless otherwise noted.

Abbreviations: LP, lichen planus; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; FPG, fasting plasma glucose; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides

**P*-value for the comparison between the study groups

Note: ATP III criteria define the metabolic syndrome as the presence of any three of the following five traits: waist circumference ≥ 102 cm in men and ≥ 88 cm in women, blood pressure ≥130/85 mmHg, fasting triglycerides (TG) level ≥150 mg/dL, fasting high-density lipoprotein (HDL) cholesterol < 40 mg/dl in men and < 50 mg/dl in women, and fasting blood sugar ≥ 100 mg/dL

(Table 1). Meanwhile, the female patients with LP had a significantly higher waist circumference (98.64 ± 10.42 vs. 93.58 ± 15.11 cm; $P < 0.001$) and FBS level (93 vs. 90 mg/dL; U = 841.5, $P = 0.03$) compared to the female controls. Surprisingly, the BMI (24.22 vs. 27.92 kg/m^2; U = 72, $P = 0.002$) was lower in males with LP than in the control male group (Table 2), which might be attributed to the low sample size.

The statistics showed no significant difference between the study groups regarding the presence of dyslipidemia (51 [77.3%] vs. 49 [74.2%]; $P = 0.68$). There was also no significant difference regarding the presence of dyslipidemia between the cases and controls in both genders (38 [80.9%] vs. 36 [75%] and $P = 0.5$ in females; 13 [68.4%] vs. 13 [72.2%] and $P = 0.8$ in males) (Table 2).

We enrolled variables with P-values less than 0.25 at univariate analysis into the multiple logistic regression analysis. These were the DBP, waist circumference, FBS, and cholesterol levels. Accordingly, the results showed a significant association between LP and each of DBP and waist circumference. That is, each centimeter increment in waist circumference led to a 4.1% increase in the chance of LP ($P = 0.02$), while each unit increment in DBP increased the chance of LP by 4.74 % ($P = 0.03$) (Table 3).

DISCUSSION

Our findings revealed that the prevalence of metabolic syndrome and dyslipidemia in LP patients was comparable to the control group. Although the mean of both DBP and waist circumference was significantly higher in the LP group compared to the healthy controls, there was no significant difference between LP patients and controls regarding other components of metabolic syndrome. It seems that the probability of having metabolic syndrome is not associated with gender since the same results with metabolic syndrome and dyslipidemia in the total population were found between males and females.

Table 3. Results of multivariate logistic regression analyses of the association between the presence of metabolic syndrome and other variables evaluated in patients with lichen planus

	P-value	EXP (B)	95% CI for EXP (B) Lower-upper
Waist circumference	0.02	1.041	1.006-1.078
Cholesterol	0.42	0.996	0.986-1.006
Fasting blood sugar	0.14	1.019	0.994-1.044
Diastolic blood pressure	0.03	1.047	1.003-1.093

Abbreviations: CI, confidence interval; EXP, the exponentiation of the B coefficient.

LP is a chronic inflammatory skin disorder that frequently affects the skin, hair, mucous membranes, or nails [2]. Activation of T-helper 1-mediated immune responses as well as antigen processing by Langerhans cells and presentation to T-lymphocytes are implicated in the pathogenesis of LP. The subsequent lymphocytic infiltrate attacks keratinocytes, resulting in the generation of reactive oxygen species and lipid peroxidases, which contribute to the development of LP. Keratinocytes release more cytokines such as tumor necrosis factor (TNF)-a, interleukin (IL)-6, IL-10, and IL-4, which attract more lymphocytes. The released cytokines are also involved in LP pathogenesis [1,25].

Chronic inflammation and inflammatory mediators (cytokines including TNF-α, IL-2, and IL-6) are associated with dyslipidemia and metabolic syndrome. Chronic mild inflammation in LP patients could explain the reported association between LP and dyslipidemia [14]. However, not all previous reports have confirmed the higher rate of metabolic syndrome and its components in LP patients [19-22].

Similar to our results, earlier studies did not show any significant difference in SBP or serum glucose between patients with oral LP and healthy individuals [26]. Later studies reported a higher prevalence of diabetes among LP patients [16], while our findings did not show any significant difference in glucose levels between patients and controls. Some previous studies have reported an association between dyslipidemia and increased cardiovascular risk in patients with LP [1,14]. It has been reported that the total cholesterol, triglycerides, and LDL levels are higher in LP patients than healthy individuals, while HDL is decreased in such patients [19,20]. A recent meta-analysis also has shown an increased risk of dyslipidemia (higher TG levels) in LP patients [27]. Saleh *et al.* demonstrated that all components of metabolic syndrome are significantly different in LP patients compared with controls [28]. Our findings showed a higher waist circumference and DBP in the LP group compared with the controls, though there was no significant difference between the cases and controls regarding

other criteria of metabolic syndrome.

The conflicting results regarding the link between metabolic syndrome and LP could be explained by differences in ethnicities, sampling, inclusion/exclusion criteria, and statistical methods. Interestingly, different criteria for defining metabolic syndrome, including the ATP III, International Diabetes Federation (IDF), and American Heart Association (AHA) criteria, have been used by previous studies, which could explain the inconsistent data on the prevalence of metabolic syndrome in LP patients. In addition, these definitions have been modified through time, limiting the accuracy of the older studies. The prevalence of metabolic syndrome is estimated higher with the AHA and IDF criteria as compared to the ATP III definition; the AHA and IDF definitions seem to be more sensitive in diagnosing metabolic syndrome [29].

Our study had some limitations. We could not measure the variables of insulin resistance or inflammatory cytokines relating to the pathogenesis of LP and metabolic syndrome. We also note diet, physical activity, and medications as confounding factors influencing the metabolic profile.

CONCLUSION

This study did not show any significant association between LP in male or female patients and dyslipidemia or metabolic syndrome. However, these patients are more vulnerable to central obesity and high DBP, which are risk factors for cardiovascular disorders. Hence, they need to be screened routinely for such risk factors.

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Conflict of interest: None declared.

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