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Original Article

Dyslipidemia and metabolic syndrome in patients with lichen planus: A case-control study

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Abstract

Objectives 1) To study the lipid levels in patients with lichen planus and controls, to find the association of lichen planus with dyslipidemia and to find the association of lichen planus with metabolic syndrome.

Methods This was a case-control study involving a total of 100 patients, consecutively visiting the Outpatient Dermatology Department at Karnataka Institute of Medical Sciences Hubli, Karnataka. Men and women with age more than 18 years (50 cases with Lichen planus and 50 controls without lichen planus and had other skin diseases mainly nevi, seborrheic keratosis, verruca vulgaris).

Results We found significantly higher levels of triglycerides (153.03 vs 107.91 p value 0.008), total cholesterol (158.49 vs 143.47 p value 0.018), VLDL (30.61 vs 22.75 p value0.021) and significantly lower levels of HDL (38.86 vs 45.78 p value<0.001). Both TG/HDL ratio (4.26 vs 3.19) and LDL/HDL ratio (2.45 vs 1.78) were significantly higher with a p value of <0.0001. ATP-III criteria for metabolic syndrome were met by 6% of the patients with LP versus 2% of the controls (p value=0.617), suggesting no association between metabolic syndrome and lichen planus. The prevalence of dyslipidemia in patients with LP was 38% for cases and 6% for controls (p value< 0.001). A multivariate logistic regression model demonstrated that LP was associated with dyslipidemia, even after controlling for confounders, including age, gender, BMI and FBS levels (OR=11.53 95%, CI=2.80-47.55, p value<0.001).

Conclusion The results obtained in our study support the association of dyslipidemia in lichen planus which was seen even after controlling the confounding factors. The study also highlights the importance of routine screening of dyslipidemia since early intervention may reduce the risk and complications of cardiovascular disease later in life. However, there was no association seen between lichen planus and metabolic syndrome. Further studies are required to establish this finding.

Key words
Lichen planus, dyslipidemia, metabolic syndrome.

Introduction

Lichen planus (LP) is an inflammatory, papulosquamous disorder that may affect the

skin, mucous membranes, hair and nails. The name 'lichen planus' has been derived from the Greek word 'leichen' (tree moss) and the Latin word 'planus' (flat). The overall prevalence is believed to be somewhat around 1% of general population.[1] The classical presentation of LP is characterized by plane-topped, purplish, polygonal pruritic papules or plaques (6 Ps) distributed mainly on the flexor surfaces of extremities, particularly the wrists and ankles. The involvement of oral cavity, genitals, nails and scalp is not uncommon. Rarely, there is laryngeal, esophageal and conjunctival involvement.[2,3]

The exact etiopathogenesis of LP is poorly understood. Current concepts consider it to be a T cell-mediated inflammatory condition. Few of the associated factors and disease conditions implicated in LP include genetic polymorphism of different HLA markers, dental materials like silver amalgam, infections mainly hepatitis C virus, drugs, autoimmune diseases such as primary biliary cirrhosis, ulcerative colitis, myasthenia gravis and thymoma, stress and anxiety, and physical factors like radiation therapy.[4]

Cardiovascular risk factors have been assessed in some skin diseases such as androgenetic alopecia[5-7] and psoriasis.[8-10] Although lipid abnormalities have been studied in LP, case-control studies pertaining to the components of metabolic syndrome in LP are limited. The objective of this prospective case-control study was to study the lipid levels along with the components in the Adult treatment Plan (ATP)-III metabolic syndrome criteria and also to find out whether association between LP and metabolic syndrome exists.

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Methods

This was a case-control study involving a total of 100 patients, consecutively visiting the Outpatient Dermatology Department at Karnataka Institute of Medical Sciences Hubli, Karnataka. Men and women with age more than 18 years (50 cases with LP and 50 controls having skin diseases other than LP, mainly nevi, seborrheic keratosis, verruca vulgaris willing to give informed consent were included in the study. Patients receiving treatment for lichen planus like systemic corticosteroids, retinoic acid, methotrexate and patients with lichenoid drug eruptions were excluded from the study. Diagnosis of LP was based mainly on clinical findings. Biopsy was taken only from willing patients to confirm the clinical diagnosis.

Clinical parameters and lipid levels measurement

The weight, height and abdominal circumference of subjects were measured and their body mass index was calculated. Systolic and diastolic blood pressure was measured. The patients were instructed to visit the OPD after an overnight fasting period (10-12 hours) for studying the serum lipid profile (total cholesterol, triglycerides, high density lipoprotein cholesterol HDL-C, low density lipoprotein cholesterol LDL-C) and fasting blood sugar (FBS) levels. In addition, total cholesterol/HDL-C and LDL-C/HDL-C were calculated. These data were calculated before starting the treatment. Data were also gathered on age, sex, habits like smoking, alcohol consumption, and hypothyroidism, personal or family history of cardiovascular disease and whether the patients were on antihypertensive, cholesterol lowering and hypoglycemic drugs.

Prevalence of metabolic syndrome (MS) was calculated according to ATP-III criteria.[11] MS was defined by the presence of 3 of the following criteria: 1) Waist circumference > 102 cm or 40 inches (male), >88 cm or 35 inches (female); 2) Triglycerides ≥ 150 mg/dl; 3) Reduced HDL <40 mg/dl in males and <50 mg/dl in females; 4) Blood pressure ≥130/≥85 mmHg; and 5) Fasting plasma glucose ≥ 110 mg/dl).

The presence of dyslipidemia was defined if one of the following parameters were present: 1) Triglycerides >150 mg/dL; 2) Total cholesterol >200 mg/dL; 3) LDL-C>130 mg/dL; or 4) the patient received treatment for dyslipidemia.

Statistical Analysis

The statistical analyses were performed with the PASW Version 19. Continuous data were summarized as mean and standard deviation and categorical data was summarized as proportion. Independent sample student t test was used to compare mean values of quantitative variables. Qualitative variables were analyzed with chi-squared test and Fischer exact test. Binary logistic regression was used to measure the association between LP and dyslipidemia in a multivariate analysis. P <0.05 was considered significant in all analyses.

Results

A total of 100 patients were studied, 50 with LP and 50 controls. Except for one patient with oral lichen planus, all other patients presented with cutaneous LP.

In our study group, 28 cases were males and 22 cases were females. Age of the patients ranged from 19 years to 78 years. The mean age was 41.71 years for men with LP and 40.64 years for women with lichen planus. Mean time since the onset of LP was 7.73 months for men and 7.25 months for women. There were no significant differences between the two groups with respect to personal habits, hypothyroidism, personal or family history of cardiovascular disease. Moreover, no significant differences were found in antihypertensive, cholesterol lowering or hypoglycemic drugs intake between patients with LP and controls, respectively. We found significantly higher levels of triglycerides (153.03 mg/dl vs. 107.91 mg/dl, P value = 0.008), total cholesterol (158.49 mg/dl vs. 143.47 mg/dl, P value = 0.018), VLDL (30.61 mg/dl vs. 22.75 mg/dl, P value = 0.021) and significantly lower levels of HDL (38.86 mg/dl vs. 45.78 mg/dl, P value <0.001), [**Table 1**]. Both TG/HDL ratio (4.26 vs 3.19) and LDL/HDL ratio (2.45 vs 1.78) were significantly higher with a P value <0.0001. ATP-III criteria for metabolic syndrome were met by 6% of the patients with LP versus 2% of the controls (P value = 0.617).

The components of the criteria which were statistically significant were higher levels of triglycerides (P value = 0.008) and lower levels of HDL (P value <0.001). The prevalence of dyslipidemia in patients with LP was 38% for cases and 6% for controls (P value < 0.001). A multivariate logistic regression model demonstrated that LP was associated with dyslipidemia, even after controlling for confounders, including age, gender, BMI and FBS levels (OR=11.53, 95% CI=2.80-47.55, p value<0.001), **(Table 2)**.

Tables 3-5 compare the clinical and laboratory parameters studied in male and female and cases and controls.

Table 1 Clinical and laboratory parameters of patients with lichen planus and controls in both males and females.

	Cases (n=50)	*Controls (n=50)*	*P value*

Age (years)	41.24 ± 16.17	39.48 ± 11.36	0.530
Height (cm)	158.40 ±17.12	161.24 ±7.56	0.286
Weight (kg)	61.69 ± 10.97	59.97 ± 8.32	0.379
BMI (kg/m^2)	24.02 ± 4.29	23.07 ± 2.90	0.198
Waist circumference (cm)	89.25 ± 11.02	90.55 ± 9.78	0.534
Systolic blood pressure (mmHg)	118.44 ± 12.08	117.24 ± 5.46	0.524
Diastolic blood pressure (mmHg)	74.60 ± 10.62	76.68 ± 6.95	0.249
Fasting blood sugar (mg/dl)	87.17 ± 17.32	86.92 ± 10.45	0.931
Total cholesterol (mg/dl)	158.49 ± 33.91	143.47 ± 28.54	0.018
HDL (mg/dl)	38.86 ± 10.49	45.78 ± 7.63	<0.001
Triglycerides (mg/dl)	153.03 ± 99.77	107.91 ± 62.38	0.008
Very low density lipoproteins (mg/dl)	30.61 ± 19.95	22.75 ± 12.70	0.021
Low density lipoproteins (mg/dl)	88.74 ± 30.46	79.02 ± 20.17	0.063
TG/HDL ratio	4.26 ± 1.11	3.19 ± 0.73	<0.0001
LDL/HDL ratio	2.45 ± 1.17		

HDL – High-density lipoprotein, VLDL - Very low-density lipoproteins, LDL – Low-density lipoproteins.

Table 2 Binary logistic regression model for lichen planus.

	Odds ratio	*95% C.I.*		*P value*
Age (years)	1.009	0.976	1.044	0.595
Female (vs male)	1.142	0.475	2.746	0.767
BMI (kg/m^2)	0.912	0.791	1.053	0.209
Dyslipidemia (vs control)	11.842	2.919	48.043	0.001*
Fasting blood sugar (mg/dl)	1.021	0.988	1.056	0.213

* Significant P value.

Table 3 Characteristics of cases and controls.

Characteristics	*Cases*	*Controls*	*p value*
Mean age (years)	41.24 ± 16.17	39.48 ± 11.36	0.530
Waist circumference (cm) in males			
Normal	24 (85.71%)	25 (86.21%)	1.00
>102	4 (14.29%)	4 (13.79%)	
Waist circumference (cm) in females			
Normal	12 (54.55%)	19 (90.48%)	0.016
>88	10 (45.45%)	02 (9.52%)	
Triglycerides (mg/dl)			
Normal	35 (70%)	47 (94%)	0.002
>150	15 (30%)	03 (6%)	
Total cholesterol (mg/dl)			
Normal	43 (86%)	50(100%)	0.006
>200	07 (14%)	00 (0%)	
LDL (mg/dl)			
Normal	45 (90%)	50 (100%)	0.056
>130	05 (10%)	00 (0%)	
Reduced HDL (mg/dl) in males			
Normal	09 (32.14%)	23 (79.31%)	<0.001
<40	19 (67.86%)	06 (20.69%)	
Reduced HDL (mg/dl) in females			
Normal	07 (31.82%)	09 (42.86%)	0.454
<50	15 (68.18%)	12 (57.14%)	
Blood pressure (mm Hg)			
Normal	44 (88%)	44 (88%)	1.00
>=130/85	06 (12%)	06 (12%)	
Fasting blood sugar (mg/dl)			
Normal	46 (92%)	50 (100%)	0.117

>100	04 (8%)	00 (0%)	
Dyslipidemia			
Present	19 (38%)	03 (6%)	<0.001
Absent	31 (62%)	47 (94%)	
Metabolic syndrome			
Present	03 (6%)	01 (2%)	0.617
Absent	47 (94%)	49 (98%)	
TC/HDL ratio			
>3.5	40 (80%)	15 (30%)	<0.001
<3.5	10 (20%)	35 (70%)	
LDL/HDL ratio			
>2.5	17 (34%)	03 (6%)	
<2.5	33 (66%)	47(94%)	<0.001
On antihypertensive drugs			
Yes	03(6%)	00(0%)	0.242
No	47(94%)	00(100%)	
On hypoglycemic drugs			
Yes	01(2%)	00(0%)	1.000
No	49(98%)	50(100%)	
History of smoking			
Absent	36 (72%)	35(70%)	0.826
Present	14 (28%)	15(30%)	
History of alcohol consumption			
Absent	39 (78%)	38(76%)	0.812
Present	11 (22%)	12(24%)	

Table 4 Clinical and laboratory parameters in patients with lichen planus and controls in males.

	Cases (n=28)	*Controls (n=29)*	*P value*
Age (years)	41.71 ± 16.50	41.10 ± 11.83	0.873
Height (cm)	162.50 ± 22.05	165.10 ± 6.41	0.545
Weight (kg)	65.95 ± 10.16	63.34 ± 7.04	0.264
BMI (kg/m^2)	24.00 ± 4.27	23.25 ± 2.35	0.411
Waist circumference (cm)	88.38 ± 11.17	95.38 ± 9.48	0.013
Systolic blood pressure (mmHg)	120.57 ± 8.25	117.45 ± 4.17	0.075
Diastolic blood pressure (mmHg)	76.07 ± 8.53	77.10 ± 7.08	0.621
Fasting blood sugar (mg/dl)	86.00 ± 17.89	87.55 ± 11.93	0.759
Total cholesterol (mg/dl)	152.19 ± 35.07	149.56 ± 29.37	0.018
HDL (mg/dl)	37.37 ± 8.55	44.29 ± 6.33	0.001
Triglycerides (mg/dl)	168.65± 118.17	124.10± 68.36	0.086
Very low density lipoproteins (mg/dl)	33.73 ± 23.63	25.27± 13.72	0.103
Low density lipoproteins (mg/dl)	80.60 ± 29.78	82.88 ± 22.91	0.746
TG/HDL ratio	4.18 ± 1.00	3.43 ± 0.80	0.003
LDL/HDL ratio	2.26 ± 1.07		0.141

HDL – High-density lipoprotein, VLDL - Very low-density lipoproteins, LDL – Low-density lipoproteins.

Table 5 Clinical and laboratory parameters in patients with lichen planus and controls in females.

	Cases (n=22)	*Controls (n=21)*	*P value*
Age (years)	40.64 ±16.11	37.23 ± 10.48	0.419

Height (cm)	153.18 ± 2.77	155.90 ± 5.58	0.05
Weight (kg)	56.27 ± 9.67	55.31 ± 7.81	0.722
BMI (kg/m^2)	24.04 ± 4.42	22.82 ± 3.56	0.327
Waist circumference (cm)	90.36 ± 10.98	83.88 ± 5.30	0.019
Systolic blood pressure (mmHg)	115.73 ± 15.46	116.95 ±6.97	0.741
Diastolic blood pressure (mmHg)	72.73 ± 12.76	76.10 ± 6.88	0.291
Fasting blood sugar (mg/dl)	88.66 ± 16.87	86.05 ± 8.17	0.525
Total cholesterol (mg/dl)	166.50 ± 31.34	135.06 ± 25.70	0.001
HDL (mg/dl)	40.76 ± 12.49	47.85 ± 8.88	0.039
Triglycerides (mg/dl)	133.14 ± 67.34	85.56 ± 45.68	0.01
Very low density lipoproteins (mg/dl)	26.63 ± 13.47	19.26 ± 10.47	0.052
Low density lipoproteins (mg/dl)	99.11 ± 28.71	73.69 ± 14.52	0.001
TG/HDL ratio	4.37 ± 1.25	2.85 ± 0.45	<0.001
LDL/HDL ratio	2.70 ±1.27	1.58 ± 0.39	<0.001

HDL – High-density lipoprotein, VLDL - Very low-density lipoproteins, LDL – Low-density lipoproteins.

Table 6 Altered lipid levels in lichen planus: A comparison with previous studies.

Authors	*Year*	*TG*	*TC*	*HDL*	*LDL*	*VLDL*	*TC/HDL*	*LDL/HDL*
Arias-Santiago *et al*. [14]	2011	S	S	S	S	-	S	S
Arias –Santiago *et al.* [15]	2011	S	S	S	S	-	S	S
Krishnamoorthy *et al.* [12]	2014	NS	S	NS	S	S	-	-
Polic [16]	2014	NS	NS	NS	NS	-	-	-
Our study	2014	S	S	S	NS	S	S	S

S=statistically significant with *p* value <0.05, NS=Not statistically significant, *p* value>0.05.
TG - Triglycerides, TC - Total cholesterol, HDL - High-density lipoproteins, LDL - Low-density lipoproteins, VLDL -Very low-density lipoproteins,

Discussion

Chronic inflammation causes disturbances in lipid metabolism such as decrease in high-density lipoproteins – cholesterol (HDL-C), increase in very low-density lipoprotein - cholesterol (VLDL-C) and hypertriglyceridemia. This dyslipidemia if prolonged enhances the formation of atherosclerotic plaques and thereby augments the risk of cardiovascular disease in such patients. This fact has been observed in psoriasis.

LP is an idiopathic inflammatory disease of skin and mucous membranes. Cell-mediated immunity plays an important role in its pathogenesis. Both CD8 cytotoxic T cells and CD4 helper cells are stimulated in the process to combat the antigens presented by Langerhans cell. This stimulated lymphocytic infiltrate attacks keratinocytes and results in generation of free radicals. During this process, cytokines like IL-2, IL-4, IL-6, IL-10, and IFN-gamma, TNF-alpha are released and these cytokines are implicated in causing dyslipidemia.[4,12]

Dyslipidemia plays an important role in the development of cardiovascular diseases, which has become the leading cause of death in most developed and developing countries.[13] In our study, we found significantly higher levels of triglycerides (153.03 vs 107.91 mg/dl, P value = 0.008), total cholesterol (158.49 vs 143.47 mg/dl, P value = 0.018), VLDL (30.61 vs 22.75 mg/dl, P value = 0.021) and significantly lower levels of HDL (38.86 vs 45.78 mg/dl, P value <0.001). This is concordant with the study done by Arias-Santiago *et al.*[14] **(Table 6)** except for LDL levels which were not significantly higher (88.74 vs 79.02 mg/dl, P value = 0.063).

The levels of total cholesterol were elevated in 7 (14%) patients with LP and none in controls which showed a significant association (P value = 0.006). Nineteen males with LP (67.9%) and 6

males in controls (20.7%) had low HDL levels which was highly significant (P value <0.001). However, there were 15 females with LP (68.2%) and 12 females in control group (57.1%) showing no significant statistical difference (P value = 0.454), (**Table 4** and **5**).

Though increased LDL-C/HDL-C ratio (>2.5) is a sensitive predictor of cardiovascular risk, recently, total cholesterol/HDL-C (>3.5) has been found to be a better predictor for cardiovascular risk. The ratio of total cholesterol/HDL and LDL/HDL more than 3.5 and 2.5, respectively is dangerous.[17,18] We found TC/HDL ratio (4.26 vs 3.19) and LDL/HDL ratio (2.45 vs 1.78) to be significantly higher with a P value of <0.0001.

Studies like Atefi *et al.*[19], Seyhan *et al.*[20] and Lowe *et al.*[21] have shown significantly altered glucose levels in LP. But our study did not find significant prevalence of altered glucose levels (P value = 0.117) as only 2 females and 2 males with Lichen planus had FBS>110mg/dL. Hypertensives were equally distributed in cases (12%) and controls (12%), (p value=1). Males and females differed in the prevalence of abdominal obesity. Abdominal obesity was seen in 10 females with LP (45.45%) as compared to 2 females in controls (9.52%) which was statistically significant (p value=0.016); but it was equally distributed in males (p value=1). Metabolic syndrome, according to ATP-III criteria is associated with a higher risk of cardiovascular events. In our study, only 3 (6%) patients with LP fulfilled the criteria for metabolic syndrome and the association was not statistically significant. (p=0.617)

Conclusion

The results obtained in our study support the association of dyslipidemia in lichen planus which was seen even after controlling the confounding factors. The study also highlights the importance of routine screening of dyslipidemia since early intervention may reduce the risk and complications of cardiovascular disease later in life. However, there was no association seen between lichen planus and metabolic syndrome. Further studies are required to establish this finding.

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