A case-control study to evaluate the levels of non-HDL-Cholesterol in lichen planus patients to rule out the risk of cardiovascular events

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Background: Multiple studies indicate the correlation between lichen planus (LP) and certain systemic disorders. Data suggest an increased incidence of dyslipidemia with LP. Abnormal lipid levels are major risk factors for developing atherosclerotic changes and cardiovascular disorders (CVD). Non-high-density lipoprotein cholesterol (non-HDL-C) is a reliable marker for cardiovascular events. If non-HDL-C levels are raised in LP patients, it would mean that these individuals are high-risk patients and should be investigated periodically. We aimed to find non-HDL-C serum levels in cases of lichen planus and compare them with controls.

Methods: We compared lipid profiles between 100 cases of LP and 50 healthy controls.

Results: Non-HDL-C levels were significantly higher in cases than controls ($P = 0.002$). The non-HDL-C level was elevated in 67% of LP cases, compared to 42% of controls.

Conclusions: We demonstrated higher levels of non-HDL-C in LP patients than in controls, confirming the increased risk of CVDs in LP patients.

Keywords: cardiovascular disease, correlation, dyslipidemia, lichen planus, non-HDL-C

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INTRODUCTION

Lichen planus (LP) affects 0.22 to 4% of the general population [1,2]. It is associated with various systemic and metabolic disorders for which dermatologists commonly refer these patients to other specialists. [3] The available data proves the association of metabolic syndrome with autoimmune dermatological disorders like vitiligo and psoriasis [4,5]. Similarly, LP has an autoimmune etiology, meaning that it may be associated with other systemic disorders. Studies indicate an association of LP with diabetes mellitus, hypertension (HTN), obesity, and hepatic disorders [6-8].

Dyslipidemia has also been associated with LP in recent studies [9]. Dyslipidemia is considered one of the major risk factors for CVDs [10], often indicated by low-density lipoprotein cholesterol (LDL-C) levels. While LDL-C represents the amount of cholesterol within low-density lipoproteins, it does not provide any information regarding size, structure, or quantity. Moreover, other lipoproteins, such as chylomicrons, very

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low-density lipoproteins (VLDL-C), and lipoprotein remnants, also possess atherogenic properties. These have Apo-B, can accumulate in the vessel wall, and may lead to inflammation [11]. Another disadvantage is that LDL-C is calculated using Friedewald's equation, which gives an approximate value [12].

Non-high-density lipoprotein cholesterol (non-HDL-C) has recently emerged as an alternative predictor of CVD. It represents the complete atherogenic burden of cholesterol in transport. Values of all potentially atherogenic lipoproteins like intermediate-density lipoproteins, VLDL-C, LDL-c, and remnant lipoproteins are reflected by non-HDL-C estimation. Several studies have shown that non-HDL-C levels are a more reliable indicator of cardiovascular risk than LDL-C [13]. Its detection in LP patients will more specifically reveal the association of LP with dyslipidemia and hence CVDs.

METHODS

We conducted a case-control study with 100 cases of LP and 50 sex and age-matched controls. The study was conducted at the Outpatient Department of Dermatology, Venereology, and Leprosy at our college after approval by the institution's ethics committee (IEC- 992). Patients of LP above 18 years of age were included in the study. Patients on medications like retinoids, oral steroids, or lipid-lowering agents, along with pregnant women, were excluded from the study. Firstly, informed consent was taken from the study subjects, followed by a detailed history of present illness, disease duration, occupation, family history, treatment history, and personal history. All the subjects were then subjected to complete physical and dermatological examinations.

Patients were investigated for complete lipid profile after overnight fasting for at least 8 hours. Our study considered non-HDL-C values of more than 130 mg/dl abnormal. Qualitative variables were compared between case and control groups using chi-squared analysis. Confidence intervals (CIs) and odds ratios (ORs) were calculated with logistic regression. A *P*-value of ≤ 0.05 was considered significant.

RESULTS

In the study group with 100 LP patients, the mean age was 42.02 ± 13.82 years, ranging from 18 to 81 years. Most patients (35%) belonged to the age group of 41 to 50 years. The mean age in the control group was 40.72 ± 10.83 years, ranging from 20 to 64 years. The sex ratio in cases was 1.5:1, comparable to the control group ($P = 0.813$). The disease duration in most patients (34%) was greater than six months.

On comparing the lipid profile values among the two groups, higher lipids values were found in the case group. The mean total cholesterol was 203.96 ± 49.633 mg/dl in LP cases compared to 175.3 ± 40.217 mg/dl in controls ($P < 0.05$). Mean non-HDL-C was 156.09 ± 52.8 mg/dl in cases and 129.08 ± 41.974 mg/dl in controls, respectively. This difference was also statistically significant ($P < 0.05$) (Table 1).

In our study, 50% of cases and 24% of controls

Table 1. Mean values of main study lipid outcomes compared between lichen planus patients and controls

Serum lipids (mg/dl)	Cases		Controls		*P*-value
	Mean	SD	Mean	SD	(*t*-test)
Total cholesterol	203.96	49.633	175.3	40.217	0.0001
HDL-C	47.87	13.462	46.22	11.523	0.22
Non-HDL-C	156.09	52.805	129.08	41.974	0.002

Abbreviations: HDL-C, high-density lipoprotein cholesterol; Non-HDL-C, non-high-density lipoprotein cholesterol; SD, standard deviation

Table 2. Number and percentage of lichen planus patients with altered lipid levels compared with controls

Abnormal parameter	No. of Cases (%)	No. of Controls (%)	*P*-value
TC (> 200 mg/dl)	50 (50)	12 (24)	0.003
HDL-C (< 40 mg/dl)	29 (29)	17 (34)	0.53
LDL-C (> 130 mg/dl)	38 (38)	8 (16)	0.007
VLDL-C (> 30 mg/dl)	43 (43)	5 (10)	0.0002
TG (> 150 mg/dl)	44 (44)	13 (26)	0.034
Non-HDL-C (> 130 mg/dl)	67 (67)	21 (42)	0.004

Abbreviations: TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol; TG, triglycerides; Non-HDL-C, non-high-density lipoprotein cholesterol

had elevated total cholesterol levels. LDL-c was high in 38% of cases and 16% of controls. However, as high as 67% of cases of LP patients had increased non-HDL-C values compared to 42% of controls (Odds ratio = 2.8038; 95% CI = 1.39 – 5.64). The difference was statistically significant, with a P value of 0.0039 (Table 2).

DISCUSSION

Lichen planus (LP) is a chronic inflammatory disorder of skin and mucous membranes in which a patient suffers from pruritic plane-topped violaceous lesions. A slight male preponderance was seen in our study, which does not correspond with other published studies [1,6]. The male preponderance could be due to the higher percentage of male patients visiting our outpatient department. Our patients' mean age was 42.02 years, ranging from 18 to 81 years. Similarly, in a study by Omal PM *et al.* [1], most patients with LP were 40–60 years old.

Cutaneous inflammatory disorders like LP are associated with systemic derangements [6-8]. LP is an autoimmune inflammatory disorder mediated by T-cells. Inflammation leads to disturbed lipid metabolism, causing increased levels of triglycerides or decreased HDL-C. Such deranged lipid levels increase the risk of cardiovascular events [14].

The present study found dyslipidemia in 65% of cases compared to 38% of controls, representing a significant difference ($P = 0.002$). In a study by Arias-Santiago *et al.*, the prevalence of dyslipidemia in patients with LP was 61% compared to 33% in controls [9]. López-Jornet *et al.* observed that 58% of patients suffering from oral LP had dyslipidemia [15]. Dreiher *et al.* found that dyslipidemia was prevalent in 42.5 % of Israeli patients with LP [16]. However, in these studies, non-HDL-C was not taken into account. Non-HDL-C provides a broader picture of lipid abnormality and hence, serves as a better marker for CVDs [13,17].

Limitations

High levels of triglycerides can interfere with the levels of non-HDL Cholesterol. This confounding factor may have affected our results.

CONCLUSION

In our study, raised non-HDL-C values were found in 67% of the cases of LP compared to 42% of controls, which was significant. This analysis means that roughly two-thirds of patients are at future risk of CVD morbidity. Thus, clinicians should be aware and attentive to the symptoms of dyslipidemia in LP patients, and timely screening is essential. These findings may help us formulate guidelines for investigating and properly managing such patients.

Authors contributions

All authors have been personally and actively involved in substantial work leading to the paper and take public responsibility for its content.

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REFERENCES

1. Omal PM, Jacob V, Prathap A, et al. Prevalence of oral, skin, and oral and skin lesions of lichen planus in patients visiting a dental school in southern India. Indian J Dermatol. 2012; 57(2): 107–9.
2. Usatine RP, Tinitigan M. Diagnosis and treatment of lichen planus. Am Fam Physician. 2011; 84(1):53-60.
3. Singla R, Ashwini P K, Jayadev B. Lichen planus and metabolic syndrome: Is there a relation? Indian Dermatol Online J. 2019;10:555-9.
4. Akay BN, Bozkir M, Anadolu Y, et al. Epidemiology of vitiligo, associated autoimmune diseases and audiological abnormalities: ankara study of 80 patients in Turkey. J Eur Acad Dermatol Venereol. 2010; 24(10):1144-50.
5. Cohen AD, Sherf M, Vidavsky L, et al. Association between psoriasis and the metabolic syndrome. A cross-sectional study. Dermatology. 2008; 216(2):152-5.
6. Naldi L, Sena P. Lichen planus and liver diseases: a multicentre case-control study. Gruppo Italiano Studi Epidemiologici in Dermatologia (GISED). Br Med J. 1990; 300 (6719): 227–30.
7. Atefi N, Majedi M, Peyghambari S, et al. Prevalence of diabetes mellitus and impaired fasting blood glucose in patients with lichen planus. Med J Islam Repub Iran. 2012; 26 (1):22-6.
8. Lodi G, Pellicano R, Carrozzo M. Hepatitis C virus infection and lichen planus: a systematic review with meta-analysis. Oral Dis. 2010; 16(7):601-12.

9. Arias-Santiago S, Buendía-Eisman A, Aneiros-Fernández J, et al. Lipid levels in patients with lichen planus: a case-control study. J Eur Acad Dermatol Venereol. 2011; 25(12):1398-401.
10. Musunuru K. Atherogenic dyslipidemia: cardiovascular risk and dietary intervention. Lipids. 2010;45:907-14.
11. Fruchart JC, Davignon J, Hermans MP, et al. Residual risk reduction initiative (R3i). Residual macrovascular risk in 2013: what have we learned? Cardiovasc Diabetol. 2014;13:26.
12. Fukuyama N, Homma K, Wakana N, et al. Validation of the friedewald equation for evaluation of plasma LDL-Cholesterol. J Clin Biochem Nutr. 2008; 43(1):1–5.
13. Barbalho SM, Tofano RJ, de Oliveira MB, et al. HDL-C and non-HDL-C levels are associated with anthropometric and biochemical parameters. J Vasc Bras. 2019;18:e20180109.
14. Grattagliano I, Palmieri VO, Portincasa P, et al. Oxidative stress-induced risk factors associated with the metabolic syndrome: a unifying hypothesis. J Nutr Biochem. 2008;19:491-504.
15. Lopez-Jornet P, Camacho-Alonso F, Rodríguez-Martínes MA. Alterations in serum lipid profile patterns in oral lichen planus: a cross-sectional study. Am J Clin Dermatol. 2012;13:399-404.
16. Dreiher J, Shapiro J, Cohen AD. Lichen planus and dyslipidaemia: a case-control study. Br J Dermatol. 2009;161:626-9.
17. Arias-Santiago S, Buendía-Eisman A, Aneiros-Fernández J, et al. Cardiovascular risk factors in patients with lichen planus. Am J Med. 2011; 124(6):543-8.