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ASSOCIATION BETWEEN LICHEN PLANUS AND DYSLIPIDEMIA: AN EXPERIENCE FROM NORTH INDIA

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Abstract

Association between lichen planus (LP) and dyslipidaemia and other cardiovascular risk factors has been reported in many studies in the past, with variable results between studies.

The aim: this study was undertaken to study the association of lichen planus with dyslipidaemia.

Methods: this was a prospective hospital-based case control study conducted over a period of three years, on 105 prospective newly diagnosed male patients of lichen planus and equal number of age and sex matched controls. Fasting serum lipid profile including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) were measured, and comparison done between cases and controls.

Results: dyslipidaemia was found in 44 (41.9 %) lichen planus patients (cases) as compared to 28 (26.7 %) controls, the difference being statistically significance ($p < 0.020$). Triglycerides, total cholesterol, LDL cholesterol and VLDL cholesterol were significantly higher in cases than controls, whereas difference in the values of abdominal circumference and body mass index (BMI), although more in cases than controls was not statistically significant. Similarly, HDL-cholesterol values were less in cases than controls, but without statistical significance.

Conclusion: dyslipidaemia was more common in lichen planus (LP) patients, as compared to controls, suggesting that LP patients are at a higher risk of developing derangements of serum lipids and should be routinely and regularly monitored for dyslipidaemia and other cardiovascular risk factors, to detect cardiovascular diseases well in time. The result of present study strengthens the evidence of association between LP and dyslipidaemia.

Keywords: lichen planus, dyslipidaemia, triglycerides, total cholesterol, LDL cholesterol, VLDL cholesterol, cardiovascular risk.

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1. Introduction

Lichen planus (LP) is a chronic inflammatory papulo-squamous disorder that affects skin, mucous membranes, hair and nails. It has around 1 % prevalence in general population [1]. Lesions of LP are distributed mainly on the flexor surfaces of extremities, particularly the wrists and ankles, along with other body parts. The involvement of oral cavity, genitals, nails, and scalp is not uncommon. LP may also manifest with laryngeal, oesophageal and conjunctival involvement [2, 3].

LP is considered as T-cell mediated inflammatory disorder, although exact pathogenesis remains unknown. 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].

It has been demonstrated that inflammation, as also in LP, triggers changes known as acute-phase response (APR), which may influence lipid metabolism, as seen with increased serum triglyceride and low-density lipoprotein (LDL) cholesterol levels and decreased high-density lipoprotein (HDL) cholesterol levels in LP patients in various studies. Thus, the lipid disturbances linked to chronic inflammation in LP may increase the cardiovascular (CV) risk associated with hyperlipidemia [5, 6–15].

Various studies in the past have reported association between lichen planus and dyslipidaemia, with variable results. Very few studies in the literature have reported this relationship especially in males, as prevalence/incidence of LP has been more commonly reported among females. Keeping this fact in mind, we designed this study to compare lipid levels of male LP patients with that of healthy male controls.

The aim of present study was to see the association between lichen planus and dyslipidaemias in males and compare it with the age and sex matched controls.

2. Material and methods

Study design: this study was a prospective hospital-based case control study, conducted simultaneously in the department of dermatology at two tertiary care hospitals in Union territory of Jammu and Kashmir in North India, over a period of three years from January 2019 to December 2021.

Study population: the cases included consecutive LP patients visiting respective outdoors of dermatology department of our hospitals and controls were selected from healthy attendants of the patients, with same population source for both cases and controls.

Inclusion criteria: cases included ≥ 18 years old male lichen planus patients and willing to participate in the study, diagnosed mainly clinically, with occasional histopathological confirmation in doubtful cases. The control group comprised of same number of age and sex matched healthy male patients, accompanying the patients.

Exclusion criteria: we excluded the following group of patients for the study: those with age less than 18 years; female gender; LP with other concomitant skin diseases known to be associated with dyslipidaemia such as psoriasis; patients with systemic diseases associated with dyslipidaemia such as thyroid disorders, familial dyslipidaemias, chronic renal failure; patients on drugs that are known to cause dyslipidaemia; patient with lichenoid drug eruptions and also those with hypertension, diabetes and liver diseases.

Data collection: a detailed relevant history from each study participant was documented in a proforma regarding name, age, occupation, duration of disease, age of onset, history of cardiovascular disorder, diabetes, hypertension, thyroid dysfunction, liver and kidney disease, in patient or family, and also about personal habits like smoking, alcohol intake, tobacco consumption and history of any drug intake. Written informed consent was taken for participation in the study.

General physical and systemic examination was performed. Weight, height, abdominal circumference of subjects was measured and body mass index calculated. The patients were instructed to visit the hospital after an overnight fasting period (10-12 hours) and samples sent to the hospital laboratory for serum lipid profile, viz total cholesterol, triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C) and fasting blood sugar (FBS) levels.

Serum Triglycerides levels > 150 mg/dL, Total cholesterol > 200 mg/dL, LDL-C > 130 mg/dL, HDL-C < 40mg/dl, VLDL-C > 30mg/dL were taken as abnormal readings. Same laboratory standards were ensured for all the samples of the study participants.

We ensured that the study subjects have a choice for voluntary participation and patient confidentiality and human subject protection was ensured. Ethical guidelines of the declaration of Helsinki of 1975, as revised in 2000 were followed in all aspects of the study.

Approval was taken from local bioethics committee of our institute namely Government Medical College Baramulla, with number GMC/BLA/2019/39, dated 22.01.2019.

Statistical analysis: the collected data was compiled in Microsoft excel sheet. SPSS 18.00 (Statistical Package for Social sciences; SPSS Inc., Chicago, IL, USA) for windows was used for data analysis.

Results were presented as number percentage for qualitative variables and mean ± standard deviation (± SD) was used for quantitative variables. Chi square (χ^2) test and two-sample independent *t* tests were applied for determining any statistical difference in the variables between the two groups. Probability value $P < 0.05$ was considered significant in all analyses.

3. Results

A total of 105 prospective male LP patients and equal number of age and sex matched controls were studied.

The age of the patients ranged from 18–55 years with Mean ± SD of 35.86 ± 10.5 years. The age of the control group ranged from 18–60 years with Mean ± SD of 35.78 ± 11.1 years.

Most of the cases, 38 (36.2 %) were in the age group 30–40 years, followed by 25 (23.8 %) and 19 (18.1 %) in groups 40–50 and 20–30 respectively. No statistically significant difference was observed in the age distribution of cases and controls (**Table 1**).

Table 1

Age distribution characteristic of study population

Age group (years)	Cases (*n* = 105)	Control (*n* = 105)	*p* value
≤ 20	13 (12.4 %)	15 (14.3 %)	0.934 (Not significant)
21–30	19 (18.1 %)	17 (16.2 %)	
31–40	38 (36.2 %)	40 (38.1 %)	
41–50	25 (23.8 %)	21 (20.0 %)	
> 50	10 (9.5 %)	12 (11.4 %)	

The duration of disease was in range of minimum of one month to maximum of 13 years and most of the patients, 63 (60 %) had duration of 6 months to 5 years. Along with cutaneous involvement found in all the LP patients, mucosal involvement was found in 16 (15.75 %) patients, nail involvement in 6 (6.3 %) and scalp involvement in 4 (4.2 %) LP patients.

Dyslipidaemia was found in 44 (41.9 %) cases and 28 (26.7 %) controls and this difference was statistically significant ($p < 0.020$). Parameters such as Triglycerides, Total cholesterol, LDL-cholesterol and VLDL-cholesterol were significantly more deranged in LP cases as compared to controls, as depicted in **Table 2**.

Table 2

Comparison of lipid profile parameters and other variables between cases and controls

Parameter/Variable	Cases (*n* = 105)	Control (*n* = 105)	P value
Dyslipidaemia	44 (41.9 %)	28 (26.7 %)	0.020*
Triglycerides (mg/dl)	153.6 ± 37.1	138.6 ± 28.4	0.013*
Total cholesterol (mg/dl)	176.9 ± 34.2	167.4 ± 29.7	0.033*
LDL cholesterol (mg/dl)	115.9 ± 28.4	108.1 ± 21.5	0.026*
VLDL cholesterol (mg/dl)	27.4 ± 6.4	24.2 ± 9.6	0.005*
HDL cholesterol (mg/dl)	45.2 ± 14.7	46.1 ± 18.4	0.696
Abdominal circumference (cm)	78.4 ± 16.2	77.1 ± 15.9	0.558
BMI (Kg/m^2)	24.6 ± 8.5	23.2 ± 9.2	0.253

** Statistically significant; LDL: Low-Density Lipoprotein; VLDL: Very Low-Density Lipoprotein; HDL: High-Density Lipoprotein; BMI: Body Mass Index*

Lower overall levels of HDL-cholesterol were found in cases than controls and similarly higher overall values of abdominal circumference and BMI were found in cases than controls, but this difference was not statistically significant.

4. Discussion

Chronic inflammation leads to disturbances in lipid metabolism and may result in dyslipidaemia changes such as decrease in high-density lipoprotein cholesterol (HDL-C), increase in very low-density lipoprotein cholesterol (VLDL-C) and hypertriglyceridemia. Long standing dyslipidaemia enhances the formation of atherosclerotic plaques, thereby enhancing the risk of cardiovascular disease in patients suffering from various inflammatory diseases, including dermatological inflammatory diseases, a fact well reported in psoriasis.

LP is an idiopathic inflammatory disease of skin and mucous membranes, with cell-mediated immunity playing an important role in its pathogenesis. Stimulation of both CD8 cytotoxic and CD4 helper T cells occurs to deal with the antigens presented by Langerhans cells. Subsequent generation of free radicals by the stimulated lymphocytic infiltrate cause keratinocytes to release various cytokines like IL-2, IL-4, IL-6, IL-10, IFN-gamma and TNF-alpha, which are believed to be responsible for causing dyslipidaemia [4, 5]. Chronic inflammation is also related to visceral obesity and increased adipocytokines, such as TNF-α, IL-1, and IL-6 [16]. High IL-6 levels have been observed in adipose tissues of obese patients and it plays an important role in various metabolic processes and actions of adipocytes [17]. A case report in 1994 by Kurgansky et al, was probably the first in the literature to propose an association of LP with dyslipidaemia [12]. In subsequent years, studies started to be undertaken to find out evidence-based association between LP and dyslipidaemia [18].

In the present study 41.9 % of LP patients showed derangement of one or the other parameter of lipid profile as compared to 26.7 % controls, the difference being statistically significant. Individual parameters of serum lipid viz TG, TC, LDL-C, VLDL-C were also significantly more in LP patients as compared to controls. These findings are consistent with most of the previously done studies.

Arias-Santiago et al conducted a case-control study to evaluate lipid levels in adult males and females with LP compared to healthy controls. LP Patients showed higher triglycerides, total cholesterol, and LDL levels, along with lower HDL levels in comparison with the controls [16].

Dreiher et al conducted a case control study investigating association between LP and dyslipidaemia in Israel, including 1477 patients and 2856 controls. The prevalence of dyslipidaemia was significantly higher in LP patients, as compared to the controls [18]. It was found that LP was significantly associated with dyslipidaemia even after controlling for confounders such as age, sex, smoking, hypothyroidism, diabetes, hypertension, obesity, and socioeconomic status.

Panchal et al conducted a case control study to evaluate the status of lipid disturbances in LP patients and controls. Analysis of serum lipid profile revealed significantly higher level of total cholesterol (TC), triglycerides, and low-density lipoprotein cholesterol (LDL-C) in LP patients as compared to controls, along with decreased levels of high-density lipoprotein cholesterol (HDL-C) and significantly higher atherogenic index in LP patients [11].

A recent case control study in North India by Mushtaq et al also found significant association between dyslipidaemia and lichen planus [19].

There are only few studies in the literature where in no significant association was seen between LP and dyslipidaemia, as that by Azeez et al [19].

Hence, present study strengthens the evidence of association between LP and derangements of serum lipids, and we lay emphasis on the importance of evaluating LP patients for dyslipidaemia and other cardiovascular risk factors. This will help in early and timely detection of any associated cardiovascular disease, so that preventive and therapeutic management strategies are adopted well in time.

Study limitations. One of the major limitations of the present study was a smaller number of study subjects. One of the main reasons for less enrolment was COVID-19 related restrictions and confinements, decreasing the overall patient attendance to the hospitals.

Prospects for further research. The present study emphasizes the need for evaluating lichen planus patients for associated dyslipidaemia as well as other risk factors for cardiovascular diseases. There is a definite scope for carrying forward this research aspect on larger study subjects, so that definite association between lichen planus and dyslipidaemias as well as other risk factors for cardiovascular diseases is well established.

5. Conclusion

In the present study, dyslipidaemia was found more common in LP patients as compared to the control population. This lays emphasis on the fact that LP should be taken as multisystem inflammatory disorder and LP patients should be routinely evaluated for lipid disorders and other risk factors for cardiovascular diseases, as growing evidence over time, including the present study, has shown the existence of an association between LP and lipid abnormalities. This will help in timely detection of cardiovascular diseases and LP patients should be counselled for adopting appropriate healthy lifestyle, to correct their modifiable risk factors and prevent any future cardiovascular catastrophic events.

Conflict of interests

The authors declare there are no conflicts of interest.

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