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Short Communication

Potential implication of serum lipid levels as predictive indicators for monitoring oral lichen planus

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Abstract Compelling evidence indicates that dyslipidemia is positively associated with oral lichen planus (OLP). The types and magnitude of lipid metabolism disturbance in peripheral blood of OLP patients have been investigated in different studies. Yet, consensus on how these different lipid components varied in levels for the development of OLP lesions has not been reached so far. Herein, a total of 8 eligible studies were recognized, which enrolled 533 cases of OLP and 499 healthy controls. The analysis showed that the average total triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) levels were considerably higher, and high-density lipoprotein cholesterol (HDL-C) levels were significantly lower in OLP patients compared to healthy controls. Collectively, the lipid profile panel maybe serve as the potential predictive indicator for screening OLP.

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Introduction

Oral lichen planus (OLP) is a chronic inflammatory oral mucosal disorder, and can affect around 1% of the global adult population with a higher prevalence in middle-aged women.¹ There are six clinical forms of OLP: plaque-like, reticular, bullous, papular, atrophic, and erosive or ulcerative.² The reticular form, the most common subtype, is often asymptomatic. While the erosive form, the most

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advanced subtype, usually manifests as erosions and ulcerations of the mucosa surrounded by atrophic or erythematous lesions. The erosive OLP has a serious impact on the quality of life of afflicted individuals, interfering with the patients' feeding and swallowing. Despite the precise etiology of OLP is not fully understood, it is believed that this disease represents a condition of T cell-mediated immunologic dysregulation, leading to the apoptosis of basal keratinocyte in the epithelium induced by auto-cytotoxic CD8⁺ T cells.³ Besides, a great number of risk agents including viral infections, food allergies, genetic predisposition, psychologic anxiety, local trauma, internal neoplasm, and immunodeficiency have been identified as eliciting factors.⁴

Previous studies have verified a relationship between OLP and metabolic syndrome (MS).⁵ MS is a constellation of metabolic conditions, including hypertension, central obesity, hyperglycemia, atherogenic dyslipidemia, insulin resistance and prothrombotic and proinflammatory states, which were regarded as cardiovascular risk factors.⁶ Patients with abdominal obesity and hyperlipidemia are more prone to suffer from autoimmune or inflammatory diseases, caused by the release of various cytokines.⁷ Increasing evidence has shown high occurrence of dyslipidemia in some dermatological conditions such as vitiligo, psoriasis, lichen planus and pemphigus compared to the general population.^{8–11} Currently, scientific investigations on the abnormal lipid elements among individuals with OLP have been conducted, but the results are inconsistent. Some studies suggested an evident correlation between OLP and dyslipidemia^{2,12–15} however, other studies observed no significant increase in the prevalence of impaired lipid metabolism in OLP patients.^{16–18}

Therefore, the comprehensive evaluation on this issue is needed to clarify the role of lipid variation involved in the progression of OLP. This article attempts to overview these medical literature reports focused on the significantly altered lipid components of participants with OLP. It might serve as a reference source for scholars to perform further research in this particular field.

Materials and methods

This article was performed following the Cochrane Handbook and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement 2020.¹⁹ The literature on lipid metabolism of patients with OLP was searched for in Pubmed, the Cochrane Library and Web of Science with the limit to English language. Different medical terms used were "oral lichen planus", "lipid", "dyslipidemia", "LDL", "HDL", "hyperlipidemia", "cholesterol", "triglyceride", and their synonyms.

The following inclusion criteria were utilized to choose relevant articles: cohort, cross-sectional, or case-control studies, which involved subjects of any age with previous diagnosis of OLP; laboratory measurements of serum lipid levels or incidence of dyslipidemia; healthy cohorts with no history of OLP; and analysis of the relationship between OLP and dyslipidemia. Then, the references of identified primary papers and related information were searched manually. All eligible articles up to Nov 9, 2023 were

included in this study. Two independent investigators (X.X. and S.L.) retrieved and screened the titles, abstracts, or full text of all publications, and subsequently analyzed the included studies. A third author (Z.S.) reached a consensus in case of disagreement.

Lipid level variables included: total triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C). The presence of dyslipidemia were based on the National Cholesterol Education Program Adult Treatment Panel III criteria.⁵ It was established as one of the following four parameters: TG > 150 mg/dl; TC > 200 mg/dl; LDL-C > 130 mg/dl; HDL-C < 40 mg/dl, and Castelli's atherogenic index (TC/HDL-C of ≥ 5.1 for men and ≥ 4.5 for women).

All the observational association studies about the quantitative difference of peripheral blood lipid values between OLP patients and healthy controls were reviewed and recorded the following significant information: authors, the year of publication, country of origin, the number of OLP patients, the number of healthy control subjects, gender, mean age of both groups, the types of study design, diagnostic criteria of dyslipidemia, and significant lipid levels.

Results

Characteristics of participant cohorts

The preliminary search screened 191 literature, and 182 were excluded with some reasons. As illustrated in Fig. S1, eight eligible studies were selected for further analysis.^{2,12–18} The detailed information of these documents were summarized in Table 1. There were seven case-control studies^{2,12–14,16–18} and one cross-sectional study.¹⁵ Five studies were performed in Asia^{2,12–14,18} while the rest were in Romania,¹⁷ Croatia,¹⁶ and Spain.¹⁵ These studies were comprised of 533 cases of OLP subjects and 499 healthy volunteers.^{2,12–18} The subjects in both groups were matched in relation to gender and age. The clinical forms of OLP patients were classified as atrophic-erosive or non-erosive subtypes in most studies^{2,13,15–18} involving 171 cases of atrophic-erosive forms and 244 cases of non-erosive forms.

Aberrant serum lipid profile

Five studies^{2,12–15} (408 OLP patients, 374 healthy controls) showed that mean TG, TC, LDL-C values were significantly higher, and mean HDL-C values were relatively lower in OLP group compared to healthy controls. Although the rest three studies^{16–18} (125 OLP cases, 125 controls) indicated that no statistically important difference could be found between the two groups, the tested lipid indexes were more elevated in OLP participants than in the normal healthy individuals. Moreover, two studies^{2,15} (260 OLP subjects, 230 control volunteers) revealed TC/HDL-C were markedly higher in OLP cohorts than control group. In addition, only one study¹⁵ (200 cases, 200 controls) verified that TG levels were considerably increased in atrophic-erosive types than in the reticular-papular forms of OLP.

Table 1 Characteristics of included studies on serum lipid profile in patients with oral lichen planus.

References	Study design	OLP group			Control group			OLP subtypes	Dyslipidemia criteria	Significant lipid levels
		n	Age (mean $\pm$ SD, y)	F/M	n	Age (mean $\pm$ SD, y)	F/M			
Li et al., 2023; China ¹²	Case-control	100	46.11 $\pm$ 9.54	71/29	100	46.17 $\pm$ 9.22	66/34	NA	(1) TG > 150 mg/dl (2) TC > 200 mg/dl (3) LDL-C > 130 mg/dl (4) HDL-C < 40 mg/dl	TG $\uparrow$, TC $\uparrow$, LDL-C $\uparrow$, HDL-C $\downarrow$
Radic et al., 2022; Croatia ¹⁶	Case-control	63	62.62 $\pm$ 9.47	54/9	63	62.21 $\pm$ 10.75	49/14	50 erosive 13 non-erosive	NA	No statistically significant differences (parameters elevated)
Toader et al., 2021; Romania ¹⁷	Case-control	18	NA	15/3	18	NA	9/9	10 erosive 8 non-erosive	NA	No statistically significant differences (parameters elevated)
Ozbagcivan et al., 2020; Turkey ²	Case-control	60	NA	40/20	30	47.47 $\pm$ 7.98	18/12	36 erosive 24 non-erosive	(1) TG > 150 mg/dl (2) TC > 200 mg/dl (3) LDL-C > 130 mg/dl (4) HDL-C < 40 mg/dl	TG $\uparrow$, TC $\uparrow$, LDL-C $\uparrow$, HDL-C $\downarrow$, TC/HDL-C $\uparrow$, LDL-C/HDL-C $\uparrow$, CRP $\uparrow$
Aniyan et al., 2018; India ¹⁸	Case-control	30	NA	18/12	30	NA	16/14	8 atrophic 22 non-erosive	(1) TG > 150 mg/dl (2) LDL-C > 130 mg/dl (3) HDL-C < 40 mg/dl	No statistically significant differences (parameters elevated)
Mehdipour et al., 2015; Iran ¹³	Case-control	44	NA	19/25	44	36.6 $\pm$ 11.7	23/21	22 erosive 22 non-erosive	NA	TG $\uparrow$, TC $\uparrow$
Krishnamoorthy et al., 2014; India ¹⁴	Case-control	18	NA	NA	14	NA	NA	NA	(1) TG > 150 mg/dl (2) TC > 200 mg/dl (3) LDL-C > 130 mg/d (4) HDL-C < 40 mg/dl	TC $\uparrow$, LDL-C $\uparrow$
Lopez-Jornet et al., 2012; Spain ¹⁵	Cross-sectional	200	57.34 $\pm$ 12.65	166/34	200	57.88 $\pm$ 13.65	156/44	45 erosive 155 non-erosive	(1) TG > 150 mg/dl (2) TC > 200 mg/dl (3) LDL-C > 130mg/(4) HDL-C < 40 mg/dl (5) TC/HDL-C of $\geq$ 5.1 for men and $\geq$ 4.5 for women	HDL-C $\downarrow$, TC/HDL-C $\uparrow$

Abbreviations: OLP, oral lichen planus; F, female; M, male; NA, not available; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; CRP, complement-reactive protein; SD, standard deviation.

Discussion

Growing evidence indicates that a delayed hypersensitivity autoimmune responses are involved in the pathogenesis of OLP, in which cytokines and chemokines released by T helper (Th) –1 or Th-2 cells have been suggested to play a central role.⁴ Multiple proinflammatory cytokines (IL-2, IL-4, IL-6, IL-10, TNF- α , IFN- γ) induced the destruction of the keratinocytes and the generation of reactive oxygen species, leading to cell membrane destruction and lipid peroxidation.²⁰ Otherwise, oxidized LDL-C, in turn, enhanced the secretion of cytokines and contributed to a state of chronic low-grade inflammation throughout the body, thus triggering or exacerbating OLP lesions.²¹ The chronic systemic inflammation stimulates disrupted lipid metabolism since it endeavors to reduce the damage and repair tissue injury by redistributing nutrients to cells involved in the host defense. The activation of inflammatory cascade instigates a decrease in HDL that could induce compensatory response such as an augmented accumulation of cholesterol and triglycerides, which binds bacterial products or other toxic agents, leading to hyperlipidemia.¹⁸ Therefore, the increased oxidative stress, prolonged systemic inflammation, and sustained dyslipidemia as risk factors could facilitate the occurrence and development of OLP. The underlying inflammatory condition might elucidate the reciprocal cause-effect relationship between OLP, dyslipidemia, and other metabolic derangements, since chronic inflammation has been considered as a part of MS.

In most previous reports^{2,12-15} patients with OLP were found to have higher prevalence of dyslipidemia compared to the general population. While, in other studies¹⁶⁻¹⁸ they also presented a tendency of increased concentrations of TC, TG, LDL-C and decreased values of HDL-C with no significant difference. Besides, elevated LDL-C/HDL-C ratio and TC/HDL-C ratios had also been shown as sensitive predictors for cardiovascular complications in a large research.²² In a study conducted by Ozbacivan et al.,² both ratios were found in higher values in the cases than controls. These lipid metabolism disturbances associated with chronic inflammation dedicated to the incremental risk of cardiovascular disorders linked to dyslipidemia. Therefore, raising HDL-C and lowering TG, TC or LDL-C concentrations could decrease the risk of cardiovascular events.

The magnitude of lipid aberration could have pivotal clinical implications as predictive indicator for screening the disease activity status of OLP, and these patients would benefit from monitoring and consequent pharmaceutical treatment of dyslipidemia. However, in view of the limited number and comparative heterogeneity of the included studies available for this analysis, prospective longitudinal clinical trials with a larger sample size would be required to assess and clarify the roles of the lipid profile panel in the detection of OLP. And physicians should be recommended to manage lipid anomalies for these individuals.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jds.2023.12.026>.

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