Original Article

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Dentistry Section

Lipid Profile and Metabolic Syndrome Status in Patients with Oral Lichen Planus, Oral Lichenoid Reaction and Healthy Individuals Attending a Dental College in Northern India - A Descriptive Study

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ABSTRACT

Background: Chronic inflammation causes disturbances in the lipid metabolism. When this dyslipidemia becomes prolonged it increases the risk of cardiovascular disease. Recent literature reveals similar dyslipidemia in patients with lichen planus. However, the results were not compared with lichenoid reactions.

Objective: The aim of this study was to profile the lipid levels and metabolic syndrome status in patients with oral lichen planus (OLP), oral lichenoid reactions (OLR) and healthy individuals in order to evaluate their respective cardiovascular risk.

Materials and Methods: This case-control descriptive study included 32 adults from the OPD visiting the Department of Oral Medicine, 18 with either oral lichen planus or oral lichenoid reactions and 14 age and sex matched healthy controls. Ethical clearance and informed consent were obtained. Their lipid levels, body mass index and metabolic syndrome status were evaluated. Statistical analyses were performed with the SPSS version 16.0 software.P≤0.05 was considered significant.

Results: The key findings of this study were a) increased levels of S.cholesterol and LDL-C in OLP and OLR patients when compared to normal healthy individuals b) significantly higher S.triglyceride and VLDL in OLP when compared to OLR and c) lower HDL-C levels in OLP when compared to OLR. 2(18%) patients with OLP and 3(50%) with OLR were found to have high BMI suggestive of obesity whereas none of the normal individuals were obese.

Conclusion: There may be an association between chronic inflammation and dyslipidemia that increases the risk for cardiovascular disease. OLP and OLR patients have increased serum cholesterol and LDL-C when compared to normal adults. Further research on lipid levels in OLR are required to establish the findings of this study.

Keywords: Dyslipidemia, Lipid profile, Metabolic syndrome status, Oral lichen planus, Oral lichenoid reaction

INTRODUCTION

Lichen planus (LP) is a chronic mucocutaneous disease whose aetiology and pathogenesis still remains perplexing. However, current literature considers lichen planus to be a T cell mediated inflammatory condition [1]. The 6 Ps of LP are planar (flat-topped), purple, polygonal, pruritic, papules and plaques [2]. The classical presentation of LP are presence of flat violaceous polygonal papules or plaques on the skin of the wrists, thighs, abdomen, extremities and nails [3]. The prevalence of Oral Lichen Planus (OLP) is higher in the Indian population (2.6%) when compared to other ethnicities of the world (0.5-1.9%) [4]. OLP can present as any one of the 6 known clinical types. The hallmark of OLP is the presence of symmetrical lesions with the characteristic fine white striae known as the “Whickham striae”. Buccal mucosa, tongue and gingiva are the most commonly affected regions of the oral cavity. Rarely there may be involvement of the hard palate, larynx and oesophageal mucosa too [5]. Oral lichenoid reactions (OLR) may be considered as a variant of OLP due to drugs, dental materials, graft versus host disease or due to tobacco chewing [4].

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. Prolonged dyslipidemia, due to chronic inflammatory condition enhances the formation of atherosclerotic plaques and thereby augments the risk of cardiovascular disease in such patients [6].

A few skin diseases like androgenetic alopecia [1] and psoriasis [7-14] have been associated with lipid abnormalities and hence cardiovascular disease risk. A few recent case control studies have concluded that LP was associated with significant dyslipidemia [1]. High prevalence of glucose metabolism disturbance is also established in LP [3]. However, the lipid profile, blood glucose status, abdominal obesity or blood pressure in patients with OLP has not been compared with those in patients with OLR. Hence this study was planned to analyse cardiovascular risk factors (dyslipidemia and metabolic syndrome-MS) in patients visiting our clinics with OLP, OLR and healthy individuals.

MATERIALS AND METHODS

Study design

This single blinded, case-control study was conducted in the Department of Oral Medicine and Radiology, ITS – CDSR Muradnagar, Ghaziabad, Uttar Pradesh, India, between March 2012 and August 2013. Thirty two adult patients (males and females) aged between 18 to 65 y from our OPD were included in this study. Eighteen patients with either OLP or OLR were included in the case group and 14 age and sex matched healthy individuals were the control group. Ethical clearance was obtained from the institutional ethical committee. An informed written consent was a taken from all participants enrolled in the study. All patients were examined by a trained Oral Medicine specialist under optimal lighting with appropriate armamentarium. Diagnosis of OLP and OLR were

made on clinical examination and confirmed histopathologically by a punch biopsy. The diagnosis was in accordance to the modified WHO criteria proposed by van der Meiji EH et al., [15]. Clinically OLP was diagnosed when there were bilateral, symmetrical lesions with the presence of a lacelike network of slightly raised grey-white line for reticular type. Erosive, atrophic, bullous and plaque type OLP were accepted only when there was presence of the reticular lesion elsewhere in the oral cavity. Histological diagnosis of OLP was given when there was liquefaction degeneration of the basal epithelial cell layer, a well defined band of cellular infiltrate, mainly lymphocytes, in the connective tissue and absence of epithelial dysplasia. The term OLR was reserved for those cases that clinically resembled OLP but had an identifiable aetiology like an amalgam restoration, history of medication etc or were unilateral in presentation. Presence of plasma cells and neutrophils in the connective tissue were suggestive of lichenoid reaction [4]. Only untreated cases of OLP and OLR thus selected were included in the study. Previously treated patients, patients with hyperlipidemia or those undergoing treatment for the same, patients with co-existing systemic diseases (diabetes, hypertension, thyroid or cardiovascular disease), patients on any long term medications and those patients who did not accept for incisional biopsy were excluded from the study.

Dyslipidemia- Triglyceride>150mg/dl Total cholesterol>200mg/dl LDL>130mg/dl
Body mass index- Under weight<18.5 Normal weight 18.5-24.9 Over weight-25-29.9 Obesity >30 or more
Metabolic syndrome – (presence of any 3 or more of the following) • Abdominal circumference>102cm(males);88cm(females) • Hypertriglyceridemia >150mg/dl • HDL-C <40mg/dl (males);50mg/dl(females) • Blood pressure- systolic > 130mmHg;dialostic >85mmHg • Fasting blood glucose level >110mg/dl

[Table/Fig-1]: Adult Treatment Plan (ATP) III [16] criteria

Lipid profile	Diagnosis	Mean (mg/dl)±SEM	P value
S.Triglyceride	OLP	152.48±1.086	0.001*
	OLR	139.22±1.163	
S.Cholesterol	OLP	190.26±0.646	0.624
	OLR	190.75±0.613	
LDL-C	OLP	117.38±0.699	0.024
	OLR	119.34±0.519	
VLDL-C	OLP	31.23±0.219	0.001*
	OLR	27.79±0.231	
HDL-C	OLP	42.44±0.062	0.001*
	OLR	43.66±0.108	

[Table/Fig-2]: Comparison of lipid profiles between patients with OLP and OLR **P value significant*

Lipid profile	Diagnosis	Mean (mg/dl)±SEM	P value
S.Triglyceride	OLP	152.48±1.086	0.408
	Normal	150.71±1.760	
S.Cholesterol	OLP	190.26±0.646	0.001*
	Normal	184.00±0.868	
LDL-C	OLP	117.38±0.699	0.001*
	Normal	111.56±0.633	
VLDL-C	OLP	31.23±0.219	0.001*
	Normal	30.13±0.352	
HDL-C	OLP	42.44±0.062	0.059
		42.30±0.042	

[Table/Fig-3]: Comparison of lipid profiles between OLP patients and normal individuals, **P value significant*

Lipid profile	Diagnosis	Mean (mg/dl)±SEM	p-value
S.Triglyceride	OLR	139.22±1.163	0.001
	Normal	150.71±1.760	
S.Cholesterol	OLR	190.75±0.613	0.001
	Normal	184.00±0.868	
LDL-C	OLR	119.34±0.519	0.001
	Normal	111.56±0.633	
VLDL-C	OLR	27.79±0.231	0.001
	Normal	30.13±0.352	
HDL-C	OLR	43.66±0.108	0.001
	Normal	42.30±0.042	

[Table/Fig-4]: Comparison of lipid profiles between OLR patients and normal healthy individuals

Group	Body mass index (number of patients)				Metabolic syndrome Present in no.of pts
	Below normal	Normal	Above normal	Obesity	
OLP n=11	2 (18.2%)	6 (54.5%)	1 (9.1%)	2 (18.2%)	3 (27.27%)
OLR n=6	0	2(33.3%)	1(16.7%)	3(50%)	3(50%)
Normal n=14	2(14.3%)	10(71.4%)	2(14.3%)	0	2(14.28%)

[Table/Fig-5]: Frequency distribution of the patients' BMI and metabolic syndrome status among various groups.

Clinical data recorded

The patient's age, sex, weight (kg), height (cm sq), abdominal circumference (cm), blood pressure (mm Hg) were recorded and the body mass index (BMI) (weight/height) was calculated. Venous blood sample was collected the subsequent morning after the patient had fasted overnight for at least 8 h. Serum lipid profile-triglyceride, total cholesterol, LDL-C, VLDL-C, high density lipoprotein cholesterol (HDL-C), total cholesterol/HDL, LDL/HDL and fasting blood sugar levels were analysed. Operational definitions of dyslipidemia, metabolic syndrome and inference of body mass index were according to the Adult Treatment Plan (ATP) III [16], [Table/Fig-1].

STATISTICAL ANALYSES

SPSS version 16.0 was used. Student's t-test was done to compare the mean values of quantitative variables in patients with OLP, OLR and normal healthy individuals. To compare inter and intra group variables one-way-ANOVA was used. $p \leq 0.05$ was considered significant in all analyses.

RESULTS

A total of 32 patients were studied, 18 with either OLP or OLR and 14 age and sex matched controls. All the 18 patients had characteristic lesions in the oral cavity. Eleven patients had OLP, six had OLR. The mean age of the patients enrolled in this study was 33.09 y. The serum lipid profiles were compared between the OLP and OLR patients [Table/Fig-2]. There were no significant differences in the serum total cholesterol and LDL-C. However, the mean values of serum triglyceride and VLDL-C in OLP patients were significantly higher than the OLR counterparts ($p<0.001$). Interestingly, the HDL-C was lower in patients with OLP (42.44± 0.062) when compared to OLR (43.66±0.108). We also compared the lipid levels of patients with OLP and OLR individually with those of the normal healthy controls [Table/Fig-3&4]. Serum total cholesterol and LDL-C levels were significantly ($p<0.001$) higher in OLP and OLR patients when compared to the healthy individuals. Differences in the other values of lipid levels were not statistically significantly among OLP, OLR and healthy patients. The distribution of patient's BMI and MS status in the groups is given in [Table/Fig-5]. None of the normal individuals

were obese, but 2 (18.2%) patients with OLP and 3(50%) with OLR were obese. According to the ATP-III criteria, 3(27.27%) of OLP patients and 3(50%) OLR patients in our study had MS. However, Chi-square test showed no significant association between BMI and metabolic syndrome in patients with OLP, OLR and normal individuals.

DISCUSSION

Classical disturbances occur in lipid metabolism during the acute phase of an infection or inflammation including increased serum triglyceride and decreased HDL-C. Such alterations normally help to reduce the toxicity of the causative agent and aid in tissue repair. But if the inflammation becomes chronic, then the changes in the lipid profile become sustained and thereby augment the accumulation of cholesterol in cells and formation of lipid foam cells which in turn produce fatty streaks in the arterial walls. This eventually increases the occurrence of atherosclerotric plaques leading to cardiovascular disease in such patients [6]. Also, increased reactive oxygen species and lipid peroxides may play a role in the pathogenesis of lichen planus [17]. Studies have shown a strong correlation between diabetes, hypertension, hyperlipidemia and increased BMI in psoriatic patients. This association was significant in the severe form of psoriasis when compared to the milder forms [4]. Inflammatory mediators like cytokines (TNF-α, IL-2 and IL-6) have been related to the dyslipidemia and metabolic syndrome in these patients.

Psoriasis, another complex chronic inflammatory dermatological disorder like lichen planus, also presents with definite plasma lipid profile aberrations. Mallbris L et al., [8] investigated the plasma lipid, lipoprotein and apolipoprotein profile in 200 psoriatic patients.These patients had higher cholesterol concentrations in the VLDL-C and HDL-C fractions. Neimann AL et al., [7] concluded in their study that diabetes, hypertension, hyperlipidemia and increased BMI are associated with both mild and severe psoriasis.

Recently, in a hospital-based study Chalkoo AH et al., [18] concluded that serum cholesterol and LDL-C were significantly decreased whereas serum triglyceride and HDLC were increased in oral submucous fibrosis, strongly suggesting that there were alterations in the plasma lipid profile in oral precancerous conditions too. A few recent studies have documented dyslipidemia and increased cardiovascular risk factors in patients with lichen palnus [1,14]. Arias-Santiago S et al., in their case-control study found significant prevalence of dyslipidemia in patients with lichen planus. The male patients with lichen planus in their study presented higher significant total cholesterol/HDL-C (p=0.02) and LDL-C/HDL-C (p=0.01) [1].

The authors have however not compared patients with lichen planus and lichenoid reactions. The present study found significant differences between the lipid profiles of OLP and OLR patients. The important findings of this study were a) increased levels of S cholesterol and LDL-C in OLP and OLR patients when compared to normal healthy individuals b) significantly higher S triglyceride and VLDL in OLP when compared to OLR and c) lower HDL-C levels in OLP when compared to OLR. Although lichen planus is an immune-mediated disease, the keratinocytes are known to release more cytokines (TNF-α, IL-4,IL-6 and IL-10) during the lymphocytotoxic process [1]. Hence, the dyslipidemia seen in these subjects may be attributed to these proinflammatory cytokines. A current literature search shows no studies that have compared lipid profile and MS status between patients with OLP and OLR. Hence at the present moment the plausible reason for the dyslipidemia in patients with OLR may be similar to that of OLP i.e. chronic inflammation. Research on C-reactive proteins and specific cytokines in OLR may add to our knowledge in understanding the differences in pathogenesis of OLP and OLR. Very recently Sahin M et al., have found increased P-wave dispersion in patients with lichen planus [17]. This information further corroborates that lichen planus may be a marker for cardiovascular risk factors.

Potential confounding factors (like tobacco and alcohol consumption, gender predilections, sedentary lifestyle and familial history of cardiovascular disease) may have to be considered in future studies to better analyze the mechanisms underlying the increase in cardiovascular risk in patients with OLP and OLR. Long term prospective studies, on a larger sample size from the time of onset of the disease may be recommended to confirm our results.

CONCLUSION

Contemporary scientific literature emphasizes the strong association between chronic inflammation and increased cardiovascular disease. The findings of this study are important in that it adds to the growing evidence of a relation between OLP and cardiovascular risk factors like dyslipidemia and MS. Patients with OLP and OLR in our study showed increased levels of serum cholesterol and LDL-C when compared to normal healthy individuals. It also for the first time documents the differences in the lipid profiles of patients with OLP and OLR Higher levels of S triglyceride and VLDL-C, lower levels of HDL-C in OLP when compared to OLR also indicate that research in this field may further our existing knowledge of the two diseases. The results demonstrate the need for careful monitoring of patients with OLP and OLR in order to identify, prevent and modify their cardiovascular risk factors.

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