OXIDIZED LDL AS A CARDIOVASCULAR RISK MARKER IN PSORIASIS PATIENTS

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Abstract:

Background:

Psoriasis is a common, genetically determined, inflammatory and proliferative dermatological disorder that affects skin, nails & joints characterized by keratinocyte hyperplasia leading to erythematous oval plaques with adherent silvery scales and has various systemic involvements. Psoriasis has been associated with an increased risk of atherosclerosis, including coronary artery disease (CAD) and stroke, for decades. Recent evidence suggests that oxidation (Ox) of LDL plays an important role in the pathogenesis of atherosclerosis and cardiovascular diseases. Our study therefore aims to assess ox-LDL and lipid profile in patients with psoriasis with an objective to observe and report any significant deviations in the same as compared to healthy controls.

Materials & Methods:

Fifty (50) clinically diagnosed cases of psoriasis and fifty age and gender-matched healthy controls from the general population were enrolled in the study. Estimation of lipid profile was assayed by standard photometric methods in auto analyzer ERBA-XL (EM-200) using commercially available kits and VLDL cholesterol was calculated using the formula adopted by Friedewald's and colleagues.[12] Estimation of Human Ox-LDL (Oxidized Low Density Lipoprotein) was done by using ELISA Kit (Elabscience, USA).

Results:

Significant increase in the lipid levels (TC, TG, LDL and VLDL) and significant decrease in the HDL cholesterol was observed in psoriasis patients when compared with the controls ($p<0.001$). Similarly, oxidized low-density lipoprotein (Ox-LDL) was significantly increased in the patients with psoriasis when compared with the control subjects ($p<0.001$).

Conclusion:

Our study clearly showed the association of psoriasis with higher OxLDL levels and risk changes in lipid profile. Similarly, increased levels of (TC, TG, LDL, and VLDL) and decreased HDL representing an alarming sign for psoriasis towards the progression of cardiovascular risk was also observed in psoriatic patients. Furthermore, the psoriasis patients presented significantly higher circulating level of oxLDL combined with the previous studies supports that the harmful effects of oxLDL, triggers a chronic inflammatory reaction, which is associated with plaque and thrombosis formation and may lead CVD risk. Therefore, we suggests early screening of serum lipid profile in psoriatic patients at the time of presentation as well as follow-up for evaluating risk and treatment of hyperlipidemia to modify and prevent the progression to future cardiovascular diseases.

Key words: psoriasis oxidized LDL, lipid profile, cardiovascular disease, atherosclerosis.

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DOI: - 10.48047/ecb/2023.12.si5a.0547

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease affecting 2–3% of the population worldwide.[1, 2] In India, the prevalence of psoriasis varies from 0.44% to 2.8%.[3] It commonly affects individuals in their third or fourth decade with males being affected two times more common than the females.[4]

Psoriasis is a multigenic inflammatory disease and more than 20 predisposition genes have been identified. The role of environmental factors such as infection, drugs, stressful events and smoking has been suggested. The association of psoriasis with cardiovascular disease dates back from 1961.[5] Psoriasis has been associated with an increased risk of atherosclerosis, including coronary artery disease (CAD) and stroke, for decades.[6-8] Patients with psoriasis have a 5-year shorter life expectancy, most frequently due to CVD causes.[9] Recent evidence suggests that oxidation (Ox) of LDL plays an important role in the pathogenesis of atherosclerosis and cardiovascular diseases.[10] Oxidized LDL induces atherosclerosis by stimulating monocyte infiltration, smooth muscle cell migration and proliferation. It contributes to atherothrombosis by inducing endothelial cell apoptosis, and thus plaque erosion, by impairing the anticoagulant balance in endothelium, stimulating tissue factor production by smooth muscle cells, and inducing apoptosis in macrophages.[11]

Hence, the present study was taken up with the purpose of evaluating the relationship of oxidized LDL levels and cardiovascular disease risk in patients with psoriasis.

MATERIALS & METHODS

This Study was carried out in the Department of Biochemistry and Dermatology of SGT Medical College, Hospital & Research Institute, Gurugram, Delhi-NCR, India. The Ethical clearance was obtained from the Institutional Ethical Committee of SGT University, Gurugram, Delhi-NCR. Written and informed consent was taken from both the subjects prior to the sample collection.

Fifty (50) clinically diagnosed cases of psoriasis and fifty age and gender-matched healthy controls from the general population were enrolled in the study.

Clinically diagnosed psoriatic patients without any concomitant cardiovascular disorder with the age above 18 years were included in the study. Similarly, the subjects with CVD, steroid and hormonal therapy & drugs affecting lipid levels and renal disorders were excluded from the study.

Study Design: - Hospital based observational study Anthropometric parameters including BMI of all the subjects were measured. After 12-14 hours of fasting, 5 ml of venous blood was collected in plain vial taking all aseptic precautions and serum was separated by centrifuging at 3000 rpm for 10-15 minutes. The lipid profiles of the subjects were estimated immediately and one aliquot was preserved at –20°C for the estimation of Oxidized LDL (Ox-LDL) within 1 month of collection of sample.

Estimation of serum total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL) and high-density lipoprotein cholesterol (HDL) was assayed by standard photometric methods in auto analyzer ERBA-XL (EM-200) using commercially available kits and VLDL cholesterol was calculated using the formula adopted by Friedewald's and colleagues.[12] Estimation of Human Ox-LDL (Oxidized Low Density Lipoprotein) was done by using ELISA Kit (Elabscience, USA).

Statistical Analysis:

The data obtained was entered into the spreadsheet and the statistical analysis was performed by using Statistical Package for the Social Sciences (SPSS) version 21.0. Continuous variables were summarized in the form of means and standard deviations. Graphical data was presented by bar diagrams. Student's independent t-test was applied for comparative study of lipid profile and ox-LDL between Psoriatic patients and the healthy controls. The *p*-value ($p < 0.05$) was considered statistically significant for all the parameters.

RESULTS

The results of our study suggested that there were disturbances in the lipid profile and oxidized low-density lipoprotein (Ox-LDL) in psoriasis patients as compared to healthy controls. The psoriasis patients (n=50) and the healthy controls (n=50) were above the age of 18 years. The mean age of the psoriasis patients was (29.04 ± 6.19) years and for healthy controls (27.38 ± 4.63) years. The anthropometric parameters like body mass index (BMI) and the waist-hip ratio (WHR) was significantly raised in psoriatic cases ($p<0.001$) compared to controls (Table 1).

Table 1: Comparison of anthropometric measurements between psoriasis patients and the controls.

Parameters	Cases (Mean ± SD)	Controls (Mean ± SD)	t-value	p-value
Age (years)	29.04 ± 6.19	27.38 ± 4.63	1.51	0.13
BMI (Kg/m^2)	25.10 ± 3.41	20.60 ± 2.39	7.63	0.001**
WHR	0.86 ± 0.05	0.77 ± 0.04	8.48	0.001**

Our results showed significant increase in the lipid profile (TC, TG, LDL and VLDL) of the Psoriasis patients (**p<0.001) when compared with healthy controls. However, HDL cholesterol was significantly decreased in cases (**p<0.001) when compared with the controls. Similarly, oxidized low-density lipoprotein (Ox-LDL) was significantly increased in the patients with psoriasis when compared with the control subjects (p<0.001) (Table 2 & Figure 1,2).

Table 2: Comparison of lipid profile & oxidized LDL between psoriasis patients and the controls.

Parameters	Cases (Mean ± SD)	Controls (Mean ± SD)	t-value	p-value
TC (mg/dL)	198.23 ± 26.48	141.45 ± 14.75	13.24	0.001**
TG (mg/dL)	161.92 ± 33.99	91.96 ± 21.54	12.29	0.001**
HDL (mg/dL)	36.01 ± 4.45	46.56 ± 4.07	-12.34	0.001**
LDL (mg/dL)	113.42 ± 24.77	82.94 ± 12.55	7.76	0.001**
VLDL (mg/dL)	32.38 ± 6.79	18.39 ± 4.30	12.29	0.001**
Ox-LDL (ng/mL)	1.55 ± 0.71	0.40 ± 0.32	10.32	0.001**

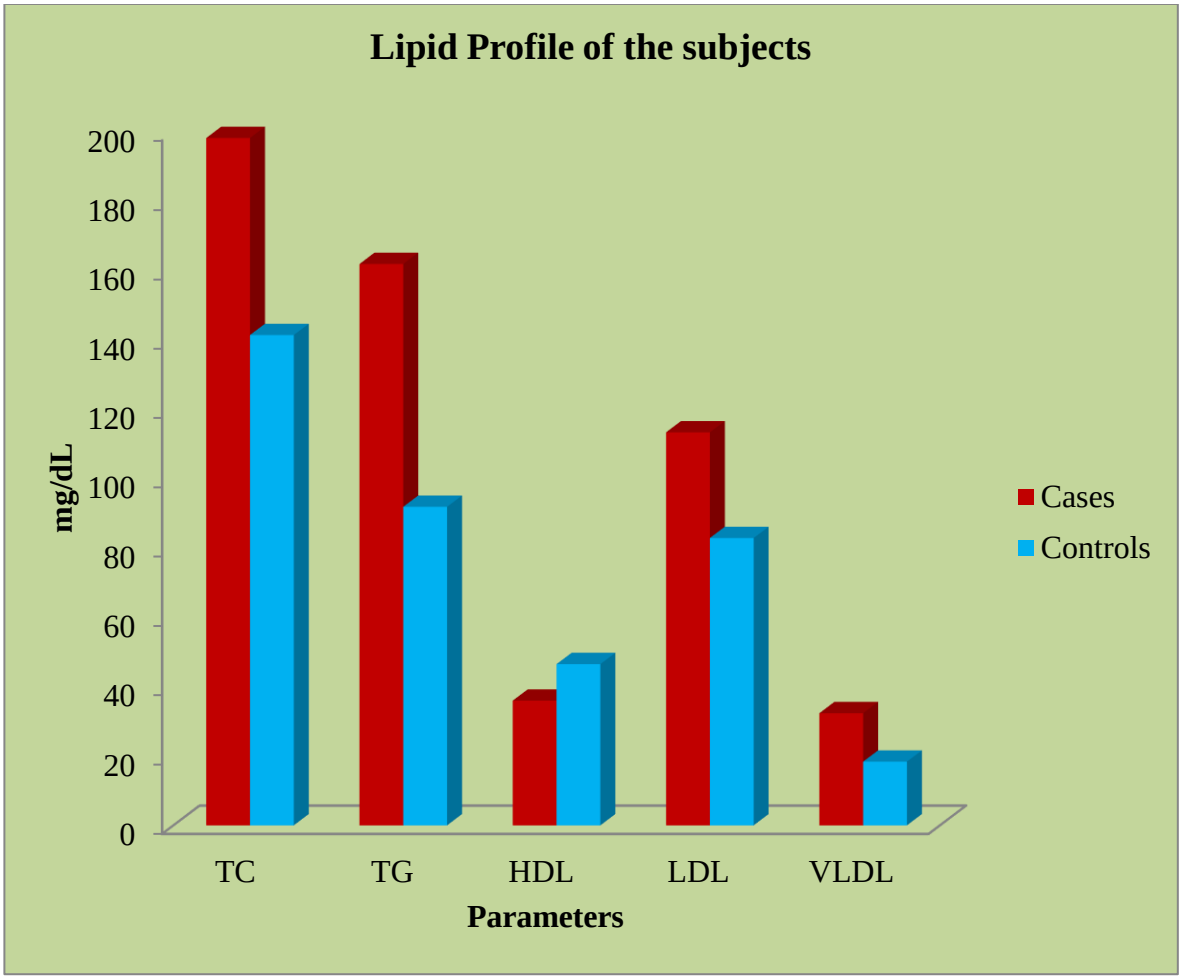

Figure 1: Graph showing lipid profiles of the psoriasis patients and controls.

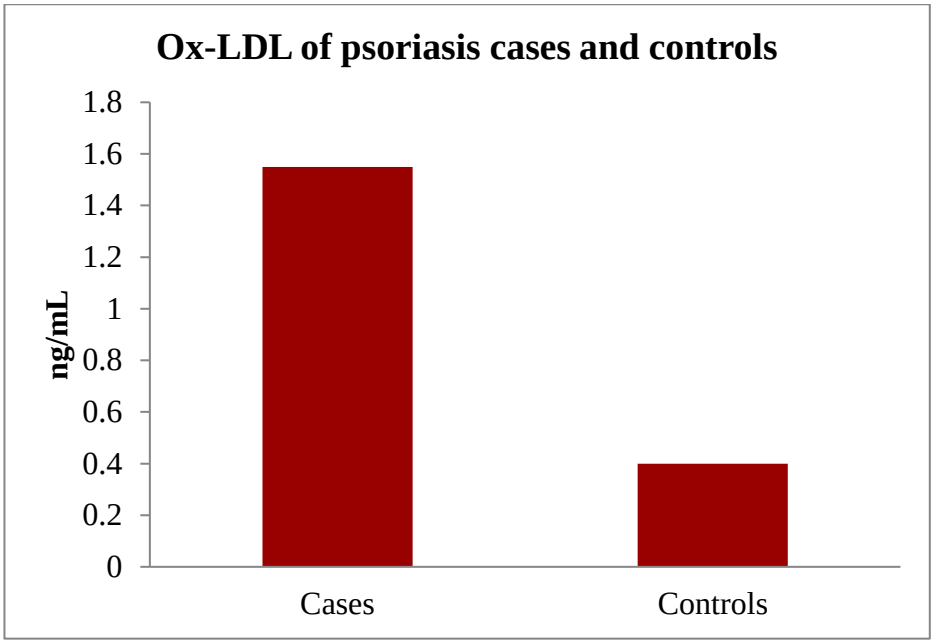

Figure 2: Graph showing oxidized low-density lipoprotein (Ox-LDL) of the psoriasis patients and controls.

DISCUSSION

Psoriasis is a common and chronic inflammatory disease of the skin which can be associated with various comorbidities such as myocardial infarction and stroke.[13] additionally, the prevalence rates of cardiovascular risk factors are increased, including hypertension, diabetes mellitus, dyslipidemia, obesity, and metabolic syndrome. Consequently, increased mortality rate and decreased life expectancy have been found in patients with psoriasis, as compared to the general population.[14]

Obesity is a significant and growing problem worldwide. Body Mass Index (BMI) is a widely used tool to measure obesity, where BMI of (18.5–24.9) is considered as normal, BMI of (25–29.9) as overweight and BMI of ≥30 as obese. Waist circumference may be a more accurate measurement of abdominal obesity and its measurements, >40 inches (102 cm) in men and >35 inches (88 cm) in women increases the risk of morbidity from conditions associated with obesity.[15]

In the present study, body mass index (BMI) and the waist-hip ratio (WHR) were significantly raised in psoriatic cases ($p<0.001$) compared to controls. Our results were similar to the previous findings.[16-21] However, there were contradictory findings by previous authors who did not find significant differences in BMI between psoriasis patients and the control groups.[22-26]

Abnormalities in lipid metabolism play an important role in the pathogenesis of psoriasis.[27] recently; the association of psoriasis with metabolic syndrome has been extensively established that contains a variety of cardiovascular risk factors, such as atherosclerosis, dyslipidemia, and obesity.[17, 28, 29] In the present study, dyslipidemia was observed characterized by significant increase in the levels of lipid profile (TC, TG, LDL and VLDL) in psoriasis patients ($p<0.001$) and significant decrease in the HDL cholesterol level (($p<0.001$) when compared to controls. Our findings were consistent with the previous studies.[26, 30-32] On the contrary, Jones SM et al. (2000)[33], Pietrzak A et al. (2002)[22], found significantly lower total cholesterol and LDL cholesterol than their controls.

HDL cholesterols has anti-oxidative, anti-inflammatory, anti-apoptotic and anti-thrombotic functions hence its importance goes much beyond reverse cholesterol transport and are of pivotal importance in atherosclerosis.[34] Disturbances in HDL level may play a role in atherogenesis and vascular disease associated with psoriasis.[35]

Oxidized LDL is of great importance in the development and progression of atherosclerosis including activation of monocytes, leading to their infiltration and smooth muscle cell proliferation.[36] Atherosclerosis is initiated by the accumulation of oxidatively modified LDL within plaques, which release ROS. Accumulation of ox-LDL in psoriatic skin also plays a role in the immune inflammatory events resulting in progressive skin damage.[24] During the initial stage of atherosclerosis ox-LDL can activate endothelial cells through the lectin-like oxidized low-density lipoprotein receptor-1

(LOX-1) leading to an up-regulation of many different signaling pathways including the CD40/CD40L pathway.[37, 38]

In our study, Ox-LDL was significantly increased in the patients with psoriasis when compared with the control subjects ($p<0.001$). Similar results were found by Coimbra S et al. (2009)[19], Coimbra S et al. (2010)[20], Sunitha S et al. (2016)[39], Asha K et al. (2017)[40] and Pietrzak A et al. (2019)[26]. This is in contrast to other studies conducted by Gerdes S et al. (2014)[41] and Sorokin AV et al. (2018)[42] who were not able to show differences in the serum levels of ox-LDL in the patient groups.

CONCLUSION

In the present study, our data clearly showed that psoriasis is associated with higher OxLDL levels and risk changes in lipid profile. Thus, this profile seems to be independent of the severity and duration of psoriasis.

Similarly, significantly increased levels of (TC, TG, LDL, and VLDL) and decreased HDL is an alarming sign that psoriasis is progressing towards cardiovascular risk and may be responsible for higher prevalence of cardiovascular accident in psoriatic patients. Furthermore, the psoriasis patients presented significantly higher circulating level of oxLDL combined with the previous studies supports that the harmful effects of oxLDL, triggers a chronic inflammatory reaction, which is associated with plaque and thrombosis formation and may lead CVD risk.

Therefore, we suggests early screening of serum lipid profile in psoriatic patients at the time of presentation as well as follow-up for evaluating risk and treatment of hyperlipidemia to modify and prevent the progression to future cardiovascular diseases.

Acknowledgement:

Conflict of interests: Nil.

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