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# **Original Research**

# Correlation of Serum Lipids, Lipoprotein and the Status of Oxidants-Antioxidants with Atherogenic Risk Markers in Psoriasis Patients

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#### ABSTRACT

**Background & Objectives:** Psoriasis represents a recurrent hyper-proliferative dermal condition frequently associated with the generation of free radicals, deviations in lipid metabolism, and heightened inflammatory secretions, which collectively contribute to an elevated cardiovascular risk among affected individuals. The objective of the current study was to assess the levels of serum lipids, lipoproteins, and oxidant-antioxidant statuses, as well as to elucidate their correlation with atherogenic risk markers— specifically oxidized low-density lipoprotein (oxLDL) and high-sensitivity C-reactive protein (hsCRP)—in individuals diagnosed with psoriasis.

**Methods:** The research was undertaken involving 300 patients diagnosed with psoriasis and 300 healthy control subjects who were matched in age and sex. Fasting blood samples, collected after an overnight fast, were procured for the purpose of analyzing lipids, lipoproteins, products of lipid oxidation and peroxidation (including oxidized low-density lipoprotein, oxLDL, and malondialdehyde, MDA), antioxidant enzyme levels (such as reduced glutathione, GSH, and total antioxidant status), and for the determination of high-sensitivity C-reactive protein (hsCRP) levels.

**Results:** The mean concentrations of atherogenic lipids, such as total cholesterol (P<0.001) and triacylglycerol (P<0.01), as well as lipid peroxidation products (P<0.001), oxidized low-density lipoprotein (oxLDL), and high-sensitivity C-reactive protein (hsCRP) levels (P<0.001), were observed to be significantly elevated in patients with psoriasis when compared to healthy control subjects. Conversely, the ferric-reducing ability of plasma (FRAP, P<0.001) and the activities of antioxidant enzymes, such as reduced glutathione (GSH, P<0.01), were observed to be significantly diminished in comparison to the healthy control group. In this cohort of patients, a positive correlation was observed between plasma oxLDL levels and both LDL cholesterol (P<0.001) and MDA (P<0.001) concentrations, while a negative association was noted with antioxidant status. Serum levels of malondialdehyde (MDA), ferric reducing ability of plasma (FRAP), and oxidized low-density lipoprotein (oxLDL) demonstrated a correlation with the risk of atherosclerosis in patients suffering from psoriasis. Nonetheless, no statistically significant association was observed between the levels of reduced glutathione (GSH) and high-sensitivity C-reactive protein (hsCRP).

**Conclusions:** The findings of the study indicate that the oxidation of low-density lipoprotein (LDL) along with reactive oxygen species, in conjunction with inflammatory markers, may play a critical role in the induction of atherosclerosis in individuals afflicted with psoriasis.

Key words: Antioxidants, glutathione high sensitivity C-reactive protein, ferric-reducing ability of plasma, psoriasis, malondialdehyde oxidative stress,

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# INTRODUCTION

Psoriasis constitutes an autoimmune inflammatory dermatological condition. Numerous exogenous and endogenous factors, in conjunction with additional biochemical and genetic parameters, have been identified as influencing the severity of the disease; however, the precise mechanism underlying the disease remains unknown. T-lymphocytes, in conjunction with other immune and phagocytic cells, possess reduced nicotinamide adenine dinucleotide phosphate (NADPH), which subsequently generates reactive (ROS) oxygen species in conditions of immunocompromise. A sedentary lifestyle, in conjunction with emotional and behavioral factors such as alcoholism and smoking habits, has the potential to exacerbate these inflammatory responses, thereby further promoting the production of free radicals. The endogenous antioxidant defense system of the body is unable to adequately repair the damage, and the adverse skin metabolism exacerbates the condition in individuals with psoriasis. Peroxynitrite and hydroxyl radicals, generated as a result of lipid peroxidation, specifically through malondialdehyde (MDA) pathways, lead to damage of cellular membranes, lipoproteins, and a multitude of lipid molecules. The assimilation of the oxidation product of low-density lipoprotein (oxLDL) by macrophages within the vascular wall has the potential to precipitate the onset of atherosclerosis [5,6]. In addition to being a dermatological condition, psoriasis is also characterized as a systemic inflammatory disease that can contribute to the development of atherosclerosis. Various crosssectional and case-control studies conducted nationwide have indicated an increased prevalence of cardiac risk among patients with psoriasis. Khunger et al. (2023) reported a 22% increase in the risk of metabolic syndrome (MS) among patients with psoriasis in comparison to healthy controls [9,10]. Given that the onset age for psoriasis can occur as early as 15 years, coinciding with early adolescence, it is of heightened importance to focus on the underlying mechanisms of the disease that contribute to an elevated risk of cardiac conditions in this patient population. Recent biomedical research has demonstrated that psoriasis, along with other inflammatory diseases such as rheumatoid arthritis and systemic lupus erythematosus, frequently corresponds with a heightened occurrence of atherosclerosis [11]. This correlation is attributed to shared pathogenic mechanisms, including oxidative stress. dvslipidaemia. and inflammation [7]. Nonetheless, conflicting findings have also been documented. Low-density lipoprotein (LDL) particles of a smaller size have the capacity to accumulate within the tunica intima, thereby instigating the onset of atherosclerosis [12]. The low-density lipoprotein (LDL) particles undergo oxidative modification, resulting in

the formation of oxidized LDL (oxLDL), which may subsequently be internalized by macrophages. This process leads to their transformation into foam cells, contributing to the progression of atherosclerotic plagues [12]. The derivatives of oxidized low-density lipoprotein (oxLDL) may induce vascular wall cells to secrete cytokines and inflammatory mediators, thereby facilitating low-grade inflammation and the progression of atherosclerotic plaques. High-sensitivity C-reactive protein (hsCRP) is recognized as an inflammatory mediator with atherogenic properties[13]. The current investigation was conducted to assess the levels of circulating oxidized low-density lipoprotein (oxLDL) and high-sensitivity C-reactive protein (hsCRP) in relation to the oxidant/antioxidant status in individuals diagnosed with psoriasis. The impact of disease severity on the association between oxidative stress and atherogenic parameters was likewise assessed.

#### **MATERIAL & METHODS**

A cohort of three hundred consecutive psoriasis patients, all aged over 18 years, who presented at the outpatient departments of Medicine and Dermatology at Rama Medical College, Hospital and Research Centre in Kanpur, Uttar Pradesh, India, during the period from 2023 to 2024 and met the specified inclusion and exclusion criteria, were enrolled in the study. An equal number of age- and gender-matched healthy volunteers, consisting of hospital staff members free from any systemic diseases, were also included. The measurable confounding variables-namely, age, gender, and body mass index (BMI)-were controlled for in the analysis. Individuals undergoing pharmacological treatment for any systemic illness and those receiving retinoid therapies were excluded from participation in the study. This research received approval from the Institutional Ethical Committee, and written informed consent was secured from all participating patients and control subjects. Anthropometric and clinical data relevant to disease, as well as family history of cardiovascular disease and/or psoriasis in first and second-degree were collected from patients relatives. upon recruitment. The historical use of medications and the presence of additional comorbidities were systematically examined, with a particular focus on dyslipidaemia, type 2 diabetes mellitus, and depression [14]. Data pertaining to lifestyle factors, encompassing physical activity, dietary habits, smoking, and alcohol was from consumption, gathered patients. parameters, Anthropometric and physiological including weight, height, waist circumference, and blood pressure, were assessed during the physical examination [3]. The Body Mass Index (BMI) was determined by employing the standard formula BMI = weight in kilograms divided by height in meters squared. The Psoriasis Area Severity Index (PASI) was

employed as a tool to evaluate the severity of the disease. Patients presenting with a Psoriasis Area and Severity Index (PASI) score exceeding 20 were categorized as having severe psoriasis [15].

Assav for biochemical parameters: Fasting blood samples (5 ml) were obtained from these patients for the purpose of conducting laboratory analyses, with a focus on lipid profiling and blood glucose measurement, as previously described [16]. In accordance with the guidelines [17] stipulated by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), total cholesterol (TC) levels equal to or exceeding 200 mg/dl, and/or low-density lipoprotein cholesterol (LDL-C) levels equal to or exceeding 160 mg/dl, and/or high-density lipoprotein (HDL) cholesterol, are considered significant. The evaluation of metabolic risk was predicated upon the presence of three or more conventional risk factors, as delineated by the American Heart Association Guidelines. These factors include smoking index, hypertension, central obesity, dyslipidemia, and diabetes [18]. The concentration of oxidized low-density lipoproteins (OxLDL) in both patients and healthy control subjects was assessed utilizing the methodology established by Ahotupa and colleagues. Malondialdehyde (MDA) was employed as an indicator of oxidative stress, and its concentration in serum samples was determined using the method established by Satoh [19]. The concentration of reduced glutathione (GSH) in blood was quantified utilizing a method devised by Beutler et al [20]. , which relies on the formation of a stable yellow color upon the addition of 5,5'-dithiobis(2-nitrobenzoic acid) to a sulfhydryl compound. The ferric-reducing ability of plasma (FRAP) method is predicated upon the reduction of the ferric tripyridyltriazine complex to form the ferrous tripyridyltriazine [Fe (II)-TPTZ] by a reductant under conditions of low pH. The Fe(II)-TPTZ complex, characterized by its blue coloration, was observed at a wavelength of 593 nm. The evaluation of serum highsensitivity C-reactive protein (hsCRP) levels was conducted utilizing an Enzyme-Linked Immunosorbent Assay (ELISA) Kit provided by DRG International, Inc., United States.

**Statistical Analysis:** The statistical analysis was conducted utilizing SPSS software, version 22. 0 (IBM Corp., Armonk, NY, USA). The assumption of normality for continuous data was evaluated utilizing the Kolmogorov–Smirnov test. The comparison between the cases and controls was conducted through the application of Student's t-test. Continuous variables were reported as mean±standard deviation, whereas categorical variables were represented as percentages. Distinct patient cohorts were subjected to comparative analysis utilizing a one-way ANOVA, succeeded by Tukey's test for post hoc multiple comparisons. Pearson's correlation analysis was employed to ascertain the relationship between high-sensitivity C-reactive protein (hsCRP) and oxidative parameters.

# RESULT

A total of 300 individuals (183 males and 117 females) diagnosed with psoriasis, along with an equivalent number of controls matched for age, gender, and body mass index (BMI), participated in the study. The age range of the enrolled participants spanned between 20 and 70 years (patients; 38±12 year verses controls;  $37\pm11$  year). The majority of the patients belonged to the age group of 31 to 40 years. An early exacerbation was noted in 19 percent of the population afflicted with the disease. A total of 86.3% (n=129) of patients were diagnosed with the predominant variant of psoriasis, namely psoriasis vulgaris, also known as plaque psoriasis. The next prevalent phenotype observed was guttate psoriasis (n=27, 9.0%), followed sequentially by erythrodermic psoriasis (n=9, 3.0%) and pustular psoriasis (n=5, 1.7%). The mean Psoriasis Area and Severity Index (PASI) score was determined  $15.6\pm10.3$  for the cohort of patients.

Table No.1: Distribution of clinical variables of the psoriasis patients (n=300)								
Variables	Number of cases	Percentage (%)						
	Gender							
Male	183	61.0%						
Female	117	29.0%						
Clinical type of psoriasis								
Plaque psoriasis	259	86.3%						
Guttate psoriasis	27	9.0%						
Erythrodermic psoriasis	9	3.0%						
Pustular psoriasis	5	1.7%						
Cardiac risk factors								
Central obesity	73	24.3%						
Dyslipidaemia	79	26.3%						
Smoking	58	19.3%						

Alcohol consumption	47	15.7%
Smoking+ Alcohol consumption	62	20.7%
Hypertension	54	17.9%
Diabetes	28	9.3%

Upon assessing the anthropometric factors of the two groups (patients;  $26.3 \pm 3.2$  verses controls  $25.4 \pm 3.6$  kg/m<sup>2</sup>), no statistically significant difference was identified in the Body Mass Index (BMI) values between them. Among patients with psoriasis, the diastolic blood pressure was observed to be significantly elevated. Twenty-one percent of the patient population exhibited more than three traditional cardiac risk factors, thereby increasing their susceptibility to metabolic syndrome (MS). Table No.2 provides an analysis of the lipid profiles for the two groups under investigation. In patients, the levels of total cholesterol (TC) (*P*<0.001) and triglycerides (TG) (*P*<0.01) were significantly elevated in comparison to those observed in healthy control subjects.

Table No.2: Serum Biochemical parameters of psoriasis cases and healthy controls				
Serum Biochemical parameters	Psoriasis cases (n=300)	Healthy control (n=300)		
Fasting glucose (mg/dl)	92.3±10.8	83.2±14.7		
Postprandial glucose (mg/dl)	132.6±18.9	108.9±14.8		
Total cholesterol (mg/dl)	201.8±22.4	149.6±21.7		
HDL-C (mg/dl)	35.9±7.4	45.8±7.9		
LDL-C (mg/dl)	136.8±23.1	129.4±27.9		
oxLDL (µmol/l)	47.2±8.3	39.2±5.1		
oxLDL/LDL-C (µmol/l)	13.3±3.7	11.4±3.1		
Triglycerides (mg/dl)	123.6±22.1	92.7±24.8		
hsCRP (mg/l)	6.8±2.1	2.1±0.8		
P- *<0.01, **<0.001 compared to controls, HDL-C – high density lipoprotein-cholesterol, LDL-C – Low				
density lipoprotein-cholesterol, oxLDL – oxidized LDL, hs CRP – high sensitive C-reactive protein				

Though the difference in serum LDL of the two groups was not significant, plasma oxLDL (P<0.01) levels and oxLDL to LDL ratio (P<0.01) were significantly higher in psoriasis patients. Plasma oxLDL was also found to be associated with oxLDL/LDL ratio (r=0.69, P<0.001) and LDL levels (r=0.87, P<0.001) in psoriasis patients. A significant increase was observed in levels of hsCRP (P<0.001) of psoriasis patients when compared with healthy controls. Psoriasis patients had significantly higher serum MDA (P<0.001) levels and decreased reduced GSH (P<0.01) and FRAP (P<0.001) level as compared to healthy controls (Table No.3).

Table No.3: Comparison of oxidative stress parameters of cases and controls				
Variables	Mean ± SD			
	Cases (n=300)	Controls (300)		
MDA (nmole/ml)	3.7±0.8**	$1.83{\pm}0.4$		
Reduced glutathione (mg/dl)	35.1±4.2*	39.3±4.2		
FRAP (µmol/l)	531±71.2**	741.2±76.1		
<i>P</i> *<0.01, ** < 0.001 compared to controls; FRAP – ferric reducing ability of plasma; MDA –				
malondialdehyde; <b>SD</b> – standard deviation				

When categorizing the patients with psoriasis according to the severity index, as displayed in Table No. 4, into mild (PASI: 1-10), moderate (PASI: 11-20), and severe (PASI:  $\geq 21$ ) groups, it was observed that the levels of oxidized low-density lipoprotein (oxLDL) were significantly elevated in individuals with severe psoriasis compared to those with mild (P < 0.001) and moderate (P < 0.001) forms of the disease. An increase in serum MDA levels was observed in correlation with the severity. The FRAP activity demonstrated a significant reduction in patients exhibiting a high severity index in comparison to those presenting a low PASI score. Nevertheless, glutathione levels were found to be comparable among individuals diagnosed with moderate to severe psoriasis. Serum high-sensitivity C-reactive protein (hsCRP) concentrations were elevated in individuals with severe cases relative to those presenting mild to moderate severity.

Table No.4: Serum level of MDA, reduced glutathione, FRAP and oxLDL in different types of psoriasis					
Variables	Mild psoriasis (n=121)	Moderate psoriasis (n=98)	Severe psoriasis (n=81)		
FRAP (µmol/l)	2.53±0.92	2.75±1.62	3.18±0.93^#		
MDA (nmol/ml)	35.54±5.13	33.25±6.24	33.13±5.26##		
oxLDL (µmol/l)	594±43.13	516.13±61.36	508.43±62.23##		
Reduced glutathione (mg/dl)	43.67±8.15	45.26±8.73	51.72±7.18^^##		
* $P < 0.05$ compared to mild psoriasis cases; $P \sim 0.01, \sim 0.001$ compared to moderate psoriasis cases; $P \# < 0.01$ ,					
##<0.001 compared to mild psoriasis cases					

A significant (P<0.001) association was observed between oxLDL and serum MDA across various patient groups. A negative correlation between reduced glutathione (GSH) (moderate: P<0.05; severe: P<0.001) and ferric reducing ability of plasma (FRAP) (P<0.001) with oxidized low-density lipoprotein (oxLDL) was identified among the three distinct subgroups of psoriasis patients, as presented in Table 5.

Table No.5: Correlation analysis between oxidative stress markers and ox LDL in different groups of patients of psoriasis						
Variables	Mild psoriasis (n=121)		Moderate psoriasis (n=98)		Severe psoriasis (n=81)	
	r	Р	r	Р	r	Р
FRAP (µmol/l)	-0.64	< 0.001	-0.37	< 0.001	-0.49	< 0.001
MDA (nmol/ml)	0.36	< 0.001	0.36	< 0.001	0.41	< 0.001
Reduced glutathione (mg/dl)	-0.16	>0.5	-0.27	< 0.05	-0.35	< 0.001
FRAP – ferric reducing ability of plasma; MDA – malondialdehyde, oxLDL – Oxidized Low density						
lipoprotein-cholesterol						

A positive correlation was observed between plasma oxidized low-density lipoprotein (oxLDL) and serum highsensitivity C-reactive protein (hsCRP) (r=0.35, P<0.01). A correlation between serum malondialdehyde (MDA) and plasma ferric reducing ability of plasma (FRAP) levels with oxidized low-density lipoprotein (oxLDL) and highsensitivity C-reactive protein (hsCRP) was observed. Nevertheless, an association was not observed between reduced glutathione (GSH) and serum high-sensitivity C-reactive protein (hsCRP), as indicated in Table 6.

Table No.6: Correlation analysis between oxidative stress markers and hsCRP in different groups of patients of psoriasis						
Variables	Mild psoriasis (n=121)		Moderate psoriasis (n=98)		Severe psoriasis (n=81)	
	r	Р	r	Р	r	Р
FRAP (µmol/l)	-0.48	< 0.001	-0.38	< 0.001	-0.41	< 0.001
MDA (nmol/ml)	0.34	< 0.001	0.46	< 0.001	0.51	< 0.001
Reduced glutathione (mg/dl)	-0.17	>0.5	-0.24	>0.05	-0.23	>0.05
FRAP – ferric reducing ability of plasma; hs CRP – high sensitive C-reactive protein; MDA –						
malondialdehyde						

# DISCUSSION

Psoriasis is recognized to be influenced by a range of exogenous and endogenous factors; however, the etiology of the disease remains not yet fully comprehended. Research has indicated that psoriasis exhibits a close pathological association with other chronic inflammatory diseases as well as atherosclerosis [7,11,12]. Therefore, it can be hypothesized that the susceptibility to atherosclerosis in individuals with psoriasis is contingent upon the capacity of the intrinsic antioxidant system to mitigate oxidative stress conditions. Reactive oxygen species generated as a result of the inflammatory process contribute to the formation of lipid oxidation and peroxidation products, including oxidized low-density lipoprotein (oxLDL) and malondialdehyde (MDA). In the current study, dyslipidaemia was identified, as evidenced by elevated levels of total cholesterol (TC) and triglycerides (TG) in patients with psoriasis [23]. Nevertheless, no significant difference was observed in the levels of HDL between the patient group and the control group. Praveenkumar et al. [24] observed a significant reduction in HDL levels among patients with psoriasis in comparison to healthy control subjects. Prior research conducted within our laboratory has demonstrated that individuals with psoriasis who exhibit an aberrant apolipoprotein profile-specifically, diminished levels of apoAcontaining lipoproteins and elevated levels of apoBcontaining lipoproteins—are predisposed to subclinical atherosclerosis. The results of our study were congruent with those of previous research (see reference 24), as the levels of LDL cholesterol observed in the study groups did not exhibit significant differences. The current research indicates that the oxLDL/LDL ratio serves as a more effective predictor of atherosclerotic risk in comparison to LDL. Previous studies [26] have documented an increase in serum MDA levels. Nonetheless, certain studies have indicated an absence of significant alteration in serum MDA levels; however, they have documented an elevation of MDA levels in tissue and red blood cells among psoriasis patients [27,28]. Within our study, notable increases was observed in plasma oxLDL levels, alongside a significant reduction in antioxidant activity, as indicated by reduced GSH and FRAP measurements, among various cohorts of psoriasis patients in comparison to healthy controls. These findings align with the results reported by Kadam et al. [29]. Consistent with findings from previous research [30,31], an increase in LDL oxidation and peroxidation products in psoriasis patients has been shown to correlate with elevated hsCRP levels. Nevertheless, the study conducted by Balci et al. [32] did not reveal any significant differences in hsCRP levels among patients diagnosed with mild-to-moderate psoriasis. A limitation of the present study was the small sample size.

# CONCLUSION

In conclusion, the results of our study indicate that an imbalance between antioxidants and oxidants in psoriasis may be linked to inflammatory responses in the condition, potentially elevating the risk of premature atherosclerosis in these patients. Therefore, the implementation of a dietary regimen, modification of lifestyle practices, and pharmacological interventions for the management of psoriasis ought to promote an antioxidant response against both endogenous and exogenous oxidative stress. The observation of oxidative damage in these patients may contribute to the development of novel and effective therapeutic approaches addressing both psoriasis and atherosclerosis.

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