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## Association Between Neopterin And Oxidative Stress in Patients with Psoriasis

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### Abstract

**Background:** Recent literature has focused on the oxidative stress and inflammatory biomarkers to play an important role in the pathogenesis and clinical course of psoriasis. **Objectives:** The study was designed to evaluate serum levels of neopterin and selected oxidative stress biomarkers (lactate dehydrogenase (LDH), malondialdehyde (MDA) and thiobarbituric acid reactive substances (TBARS)) in psoriasis patients and their correlation with disease severity and interrelationships in the context of the role of oxidative stress in psoriasis pathophysiology. **Methods:** This case-control cross-sectional study was conducted on 62 patients with clinically diagnosed psoriasis and 48 apparently healthy persons as a control group recruited from the Central Laboratory of Al-Sadr Medical City, Al-Najaf, Iraq during the period from June 2025 to January 2026. Patients were categorized into mild, moderate and severe psoriasis groups according to disease severity evaluated by the Psoriasis Area and Severity Index (PASI). **Results:** The levels of serum neopterin, LDH, MDA and TBARS in patients with psoriasis were significantly higher than those in healthy controls ( $p < 0.01$ ). A statistically significant trend for increasing biomarker levels according to disease severity was noted, with maximum values being recorded in patients with severe psoriasis. Pearson correlation analysis showed that neopterin was significantly positively correlated with both LDH ( $r = 0.341$ ,  $p = 0.002$ ) and MDA ( $r = 0.487$ ,  $p = 0.008$ ). On the other hand, neopterin showed a positive, although non-significant, correlation with TBARS ( $r = 0.168$ ,  $p = 0.121$ ). **Conclusion:** Serum neopterin and biomarkers of oxidative stress were significantly increased in patients with psoriasis and the levels progressively elevated according to disease severity. The observed positive peaks between neopterin and oxidative stress markers suggest that the immune activation do trigger the oxidative damage synergistic and mutual with each other in psoriasis pathogenic versus.



**Keywords:** Psoriasis, Neopterin, LDH, MDA, TBARS

## Introduction

Plaque psoriasis is a chronic, immune-mediated inflammatory skin disease that has considerable effects on patients' physical, psychological and social well-being (Armstrong et al., 2024). The disease (affecting around 2–3% of the general population) is linked with multiple systemic comorbidities, in particular cardiovascular disease and metabolic syndrome as well as obesity, diabetes mellitus and depression. The precise etiology of psoriasis remains poorly defined; it is thought to occur due to complex interactions between predisposing genetic factors, environmental triggers, immune dysregulation and oxidative stress (Pleńkowska et al., 2020).

Recent development in immunopathology has shown that psoriasis is mainly activated by dendritic cells (DCs), T lymphocytes, keratinocytes, and pro-inflammatory cytokines including tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-17 (IL-17) and interleukin-23 (IL-23). All these inflammatory factors can stimulate abnormal keratinocyte proliferation and differentiation, resulting in chronic inflammation and epidermal hyperplasia (Lin & Huang, 2016). Besides immune abnormalities, accumulating evidence suggests that oxidative stress contributes to the initiation and persistence of psoriasis. Oxidative Stress is the condition that arises when there is an imbalance between amount of reactive oxygen species (ROS) and reactive nitrogen species (RNS), which produces oxidative damage because it surpasses the mechanisms of antioxidant protection.

Reactive oxygen species are associated with lipid peroxidation, protein oxidation, DNA damage, and mitochondrial dysfunction that can lead to inflammation and local tissue injury in psoriatic lesions. Higher concentrations of oxidative stress markers were detected in patients with psoriasis including malondialdehyde (MDA), nitric oxide, and lipid peroxides, while many antioxidant molecules like superoxide dismutase, catalase, glutathione peroxidase, and total antioxidant capacity are often decreased (Cannavò et al., 2019). Multiple other studies have also shown a positive correlation of oxidative stress biomarkers with the Psoriasis Area and Severity Index (PASI) score establishing an association of oxidative imbalance with severity of disease (Bakić et al., 2024).

Neopterin is one of the new biomarkers correlated to inflammatory and oxidative scenarios in recent review articles. Neopterin is a pteridine derivative that is produced mainly by activated macrophages and monocytes after stimulation by the T

cell cytokine IFN- $\gamma$ , which is secreted from activated Th1 lymphocytes (Pingle et al., 2008). Neopterin Elevated neopterin concentrations are regarded as markers for cellular immune activation and systemic inflammation. Finally, neopterin is closely related to oxidative stress, as enhanced generation of reactive oxygen intermediates by activated immune cells leads to its increased production. As a result, neopterin has been suggested as an interesting parameter in a number of inflammatory, autoimmune, infectious and malignant diseases (Chuang et al., 2016).

Neopterin has recently become an increasingly attractive focus of effort to understand the relationship between psoriasis and immune function. Psoriasis is a result of continuous T lymphocyte and macrophage activation with excessive cytokine release and inflammatory signaling (Sánchez-Regana et al., 2000). Moreover, this persistence of the inflammatory milieu may induce synthesis of neopterin, leading to increased circulating levels in affected patients. Neopterin levels have not previously been monitored in order to evaluate the significance of psoriasisform lesions, although earlier studies from our group have characterized markedly higher serum neopterin concentrations in psoriasis patients compared to healthy controls and postulated its potential role as a biomarker of disease activity reflecting systemic immune dysregulation (Kemeriz et al., 2019). Moreover, neopterin may promote oxidative stress enhancement by inducing free radical generation and each oxidative injury in cell. Thus, investigating the correlation of neopterin with oxidative stress biomarkers may shed new lights for better understanding regarding molecular mechanisms involved in psoriasis pathogenesis (Giesege et al., 2018).

Oxidative stress has been highlighted by recent studies in relation to the pathogenesis of psoriasis including its comorbidities. Lack of oxidation-reduction homeostasis is responsible for enhanced cutaneous inflammation as well as endothelial dysfunction, lipid peroxidation and cardiovascular risk in psoriatic patients (Sorokin et al., 2020). Additionally, excessive mitochondrial ROS generation and mitochondrial dysfunction have been found to increase itchy psoriasis progression pathogenesis in only for the past few years. in which they emphasize the role of redox imbalance seemed to be significant role in pathogenesis of disease. These observations lend support to the hypothesis that biomarkers of oxidative stress may be relevant clinical indicators for monitoring disease activity and response to therapy (Jamil & Abdul Karim, 2024).

Despite considerable effort in deciphering the immunopathogenesis of psoriasis, little is understood about the relationship between neopterin and oxidative stress parameters in



psoriatic patients. Integrated associations of inflammatory cytokines or oxidative biomarkers have not been assessed simultaneously in most previous studies. The investigation of this association would be an adjunct to identify new biomarkers for disease severity assessment, early detection of systemic complications and therapeutic response monitoring. The interplay between neopterin and oxidative stress may also provide insights into the development of specific antioxidant and immunomodulatory drugs to diminish inflammatory burden and/or optimize clinical outcomes.

Accordingly, the aim of this study is to examine the relationship between serum neopterin and oxidative stress in psoriasis patients. Assessing the correlation of these biomarkers may help in revealing the inflammatory and oxidative mechanisms associated with psoriasis, as well as gain insights into possible diagnostic and prognostic markers for the patients.

## Methods

### *Patients and data collection*

This case–control cross-sectional study was conducted in the Central Laboratory of Al-Sadr Medical City, Al-Najaf, Iraq within a period from June 2025 to January 2026. This study enrolled a total of 110 participants, including 62 patients clinically diagnosed with psoriasis and 48 control subjects apparently healthy without any previous enrollment in related studies.

Patients were recruited from the Dermatology Outpatient Clinic of Al-Sadr Medical City. Psoriasis was diagnosed by specialist dermatologists based on clinical presentation and dermatological examination. Disease severity was assessed by Psoriasis Area and Severity Index (PASI), which enabled the categorization of groups into mild, moderate, and severe disease, thereby allowing subgroup analysis of biomarker changes as a function of disease activity.

Healthy age- and sex-matched volunteers with negative psoriasis, autoimmune disorders, chronic inflammatory diseases or malignancy within three months prior to study participation; renal dysfunction; hepatic disease; cardiovascular disease including diabetes mellitus; and antioxidant therapy in the past three months formed the control group.

### *Inclusion Criteria*

Study participants were included based on a few criteria:

1. Adults aged between 15–60 years

2. Clinically confirmed diagnosis of psoriasis
3. Absence of active bacterial or viral infections within 4-weeks preceding randomization
4. No systemic antioxidant therapy within 3 months
5. Written informed consent was provided prior to participation

### *Exclusion Criteria*

Exclusion criteria are following:

1. Chronic Physiologic: CLRG metabolic (diabetes mellitus, hypertension, chronic kidney disease)
2. Malignancy or history of cancer
3. Acute infection or sepsis
4. Other autoimmune or inflammatory disorders
5. Pregnancy or lactation
6. Smoking or alcohol consumption
7. Recent immunosuppressive or biological therapy

### *Clinical Data Collection*

Demographic and clinical data were collected through standardized questionnaires and medical records. The information collected included age, sex, BMI, illness duration, family history of psoriasis and treatment history including PASI score and disease duration. At sampling, clinical examination was undertaken by board-certified dermatologists.

### *Blood Collection and Sample Preparation*

Approximately 5 mL of venous blood was collected aseptically from each of the participants with sterile disposable syringes after overnight fasting. Blood samples were collected in sterile plain tubes and left at 20–30 °C for 20–30 min for clotting. Serum was then obtained by centrifugation of the samples at 3000 rpm for 10 minutes.

Serum was separated, aliquoted into sterile Eppendorf tubes and stored at –20°C until the day of biochemical determination. To avoid freeze–thaw cycles that may compromise biomarker stability, plasma samples were aliquoted and stored at –80 °C.

## Measurement of Serum Biomarkers

### Neopterin



Concentrations of serum neopterin were measured with an ELISA kit (from a commercial source; see Sources Section for details) according to the manufacturer's instructions. Absorbance was measured at 450 nm using a microplate reader, and concentrations were determined from standard calibration curves.

**Lactate Dehydrogenase (LDH)**

Spectrophotometric determination of serum LDH activity the activities of serum lactate dehydrogenase (LDH) were determined by an enzymatic, colorimetric assay kit. This assay is based on the enzymatic conversion of lactate to pyruvate coupled with reduction of nicotinamide adenine dinucleotide (NAD<sup>+</sup>) and subsequent monitoring of absorbance changes according to the kit protocol.

**Malondialdehyde (MDA)**

Lipid peroxidation was assessed by measuring the levels of serum malondialdehyde (MDA) using thiobarbituric acid (TBA) reaction method. In an acidic and high temperature environment, MDA interacts with thiobarbituric acid to produce a colored complex that is then measured spectrophotometrically at 532 nm.

**Thiobarbituric Acid Reactive Substances (TBARS)**

Serum thiobarbituric acid reactive substances (TBARS) concentrations were assessed as an indirect measure of oxidative stress by the use of a colorimetric method to quantify lipid peroxidation. The chromogen formed depended on the reaction between thiobarbituric acid and lipid peroxidation products, which were quantified spectrophotometrically at 532 nm.

**Ethical Considerations**

This study protocol was reviewed and approved by the Research Ethics Committee of Al-Sadr Medical City, Al-Najaf, Iraq in

2025. All participants provided written informed consent before enrollment. All experimental procedures were performed in accordance with the ethical standards of the Declaration of Helsinki.

**Statistical Analysis**

Statistical analysis was conducted using IBM SPSS Statistics v26. Data were reported as mean ± standard deviation (SD) for continuous variables, and frequencies and percentages for categorical variables. Comparing the biomarker levels in patients with psoriasis and healthy matched controls, independent sample t-test was applied. Biomarkers used were compared among the psoriasis severity groups by one-way analysis of variance (ANOVA) group based on PASI classification. Results: Pearson correlation analysis showed that serum neopterin levels were positively correlated with oxidative stress biomarkers. Categorical variables were analysed using Chi-square test. Statistical significance was defined as p-value <0.05.

**The Results**

Demographics of psoriasis patients and healthy control subjects are illustrated in Table 1. To further investigate, participants have been classified into age groups to determine the proportion of psoriasis patients and controls in each category and examined whether the distributions differed statistically (chi-squared test) with no differences observed (P = 0.345), suggesting appropriate matching for age between cases and controls. Likewise, gender distribution was similar between groups (males constituted a slightly greater fraction of the population for psoriasis patients; however, this difference was statistically non-significant P = 0.547). For residence, again no significant association was observed with disease status (P = 0.652) with regards to both groups being from urban areas mostly.

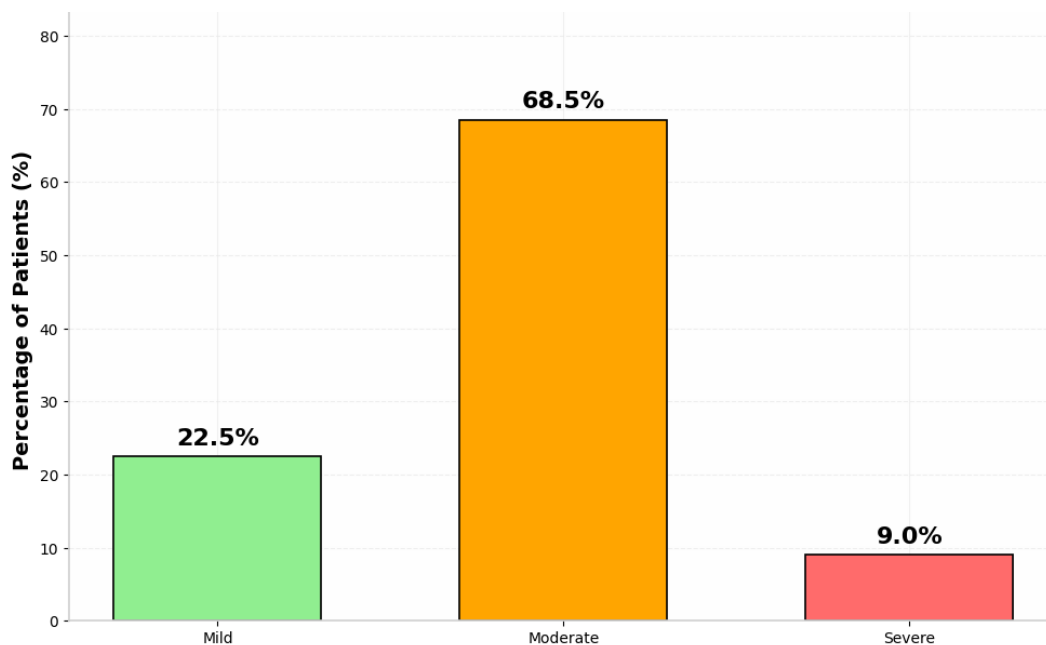
**Table 1. Assessment of age, gender and residence in both Psoriasis Patients and control**

Items		Psoriasis Patients (N= 62)		Control (N= 48)		(P value)
		Freq.	%	Freq.	%	
Age	16-25	14	22.6	13	27.1	0.345
	26-35	18	29	11	22.9	
	36-45	17	27.4	14	29.2	
	> 45	13	21	10	20.8	



Gender	Male	36	58.1	25	52.1	0.547
	Female	26	41.9	23	47.9	
Residence	Rural	24	38.7	16	33.3	0.652
	Urban	38	61.3	32	66.7	

The distribution of patients according to disease severity demonstrates that moderate psoriasis was the predominant clinical presentation, accounting for 68.5% of the studied cases, whereas mild disease activity represented 22.5%, and severe disease constituted only 9% (figure 1)



**Figure 1. Distribution of psoriasis Patients according to the severity of the disease**

Comparison of serum neopterin and oxidative stress biomarkers between patients with psoriasis and healthy controls (Data are presented as Means standard error) In patients with psoriasis, neopterin was significantly higher than in the control group ( $P < 0.003$ ), indicating increased immune activation and inflammatory response characteristic of psoriatic skin lesions development. In a similar manner, the serum LDH levels of psoriasis patients were markedly elevated than those in health ( $P < 0.004$ ). Moreover, the levels of oxidative stress markers as MDA and TBARS were significantly higher in psoriasis compared with healthy control ( $P < 0.003$  and  $P < 0.002$  respectively).

**Table 2. Comparison of neopterin and oxidative stress between psoriasis Patients and healthy control**

Biomarkers	Psoriasis Patients (N= 62)		Control (N= 48)		(P value)
	Mean	SD	Mean	SD	
Neopterin (nmol/L)	14.82	3.41	8.67	2.15	< 0.003*
LDH (U/L)	286.45	48.72	198.36	35.64	< 0.004*
MDA (nmol/mL)	5.91	1.26	3.12	0.88	<0.003*
TBARS (nmol/mL)	6.74	1.38	3.84	0.95	< 0.002*

\* High Significant at P value &lt;0.01

Comparison of Serum Neopterin and Its Oxidative Stress Biomarkers Between Psoriasis Patients With Different Severity grades (Table 3) The results showed a stepwise increase of serum neopterin levels from psoriasis mild to severe, with significant differences between severity groups ( $P < 0.022$ ). In parallel, LDH levels were also significantly elevated in patients with more severe psoriasis compared to those with mild and moderate cases ( $P < 0.023$ ). Most notably, markers of oxidative stress (MDA) increased significantly in trial subjects with severer psoriasis severity ( $P < 0.034$ ). While TBARS levels exhibited a gradual increase across disease severity categories, the association did not attain statistically significant ( $P < 0.12$ ).

**Table 3. Comparison of neopterin and oxidative stress among psoriasis patients classified according to disease severity**

Biomarkers	Mild (N= 14)		Moderate (N= 42)		Severe (N= 6)		(P value)
	Mean	SD	Mean	SD	Mean	SD	
Neopterin (nmol/L)	11.34	2.12	15.08	2.95	18.76	3.41	< 0.022*
LDH (U/L)	241.62	34.51	289.43	41.88	336.75	46.22	< 0.023*
MDA (nmol/mL)	4.76	0.84	5.98	1.05	7.11	1.24	<0.034*
TBARS (nmol/mL)	5.88	1.11	6.83	1.26	7.35	1.47	< 0.12

\* Significant at P value &lt;0.05

\Pearson correlation analysis of serum neopterin levels and oxidative stress biomarkers among psoriasis patients are shown in Table 4. Consequently, those results showed highly significant positive correlation between neopterin, and LDH levels ( $r = 0.341$ ,  $P = 0.002$ ), showing that higher immune activation indicates higher degree of cellular damage and tissue turnover among psoriasis patients. Moreover, serum neopterin displayed a moderate positive correlation with MDA levels ( $r = 0.487$ ,  $P = 0.008$ ), indicating an intimate connection between immune activation processes and lipid peroxidation. This finding corroborates the hypothesis that oxidative stress and immunomodulated inflammation are intimately linked in the pathogenesis of psoriasis. On the other hand, the association between neopterin and TBARS was weak and statistically non-significant ( $r = 0.168$ ,  $P = 0.121$ ).

**Table 4. Pearson correlation coefficient between neopterin and oxidative stress markers**



Markers	Neopterin	
	r	P value
LDH (U/L)	0.341	0.002*
MDA (nmol/mL)	0.487	0.008*
TBARS (nmol/mL)	0.168	0.121

\* High Significant at P value <0.01

## Discussion

The current study examined the relationship between neopterin and oxidative stress markers in patients with psoriasis, and showed for the first time that sera levels of increased significantly higher than control groups ( $p < 0.001$ ) in patient compared to healthy controls by using measurement in LDH, MDA or TBARS; both stronger association for serum proteins as biomarkers of oxidative stress in such disease can confirmed by both methods. In addition, neopterin levels and oxidative stress markers increased progressively with the severity of the illness and significant positive correlations were found between these 2 parameters with both LDH and MDA. These findings reinforce the idea that immune activation divides closely with oxidative stress in psoriasis pathogenesis and disease progression. Increased neopterin production has been shown to indicate activation of macrophages and T-helper 1 lymphocytes which play a major role in psoriasis immunopathogenesis. Kemeriz et al. (2019) found that serum neopterin levels correlated positively and significantly with PASI scores which suggests that the concentrations of neopterin increased with worsening disease severity. Moreover, strong positive correlation between serum neopterin and PASI score was also observed but the most astounding finding on this research work was that increased level of serum neopterin in severe psoriasis were significantly higher than mild to moderate form of the disease which makes us suggesting about its impactful role as a promising biomarker for inflammatory burden and disease activity specially in psoriasis. In addition, neopterin was shown to be reduced in a cohort of patients treated with narrowband ultraviolet B (UVB) therapy, suggesting its potential use as a laboratory marker for monitoring of therapeutic response and disease progression (Kemeriz et al., 2019).

No statistically significant differences in the demographic characteristics were observed between patients with psoriasis and healthy controls in terms of age, sex and residence (Table 1). This degree of inter year similarity reduces the potential for

demographic confounding effects on any biochemical outcome and reinforces the validity of the associations observed. Psoriasis affects people of all ages and both sexes, although a slight male predominance has been found in some studies, consistent with the present findings (Rendon & Schäkel, 2019).

The most important conclusion of our study was the enhanced concentration of serum neopterin in patients with psoriasis compared to healthy subjects. Neopterin is secreted by activated macrophages stimulated by interferon-gamma released from activated T helper lymphocytes, particularly Th1 cells. Hence, neopterin has a reflective role in regard to the extent of cellular immune activation and chronic inflammation. Psoriasis is a classical immune-mediated inflammatory disease, involving excessive activation of dendritic cells, macrophages and T lymphocytes leading to the release of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-17 and IL-23 (Boehncke & Schön, 2015). The raised levels of neopterin in this study may thus reflect ongoing immune activation in psoriasis patients.

These results are consistent with other studies, which found elevated serum neopterin levels in inflammatory and autoimmune diseases Rocha-Pereira et al (2004). Lastly, Nagy et al. (2004) showed that levels of neopterin were significantly increased in psoriasis patients and proposed that it might be a valuable marker of disease activity and immune dysregulation. Similarly, Kaskas et al. (2009) referred that neopterin levels correlated significantly with both psoriasis severity and systemic inflammation in a previous study. Indeed, in the current study, neopterin levels progressively increased from mild to severe psoriasis — supporting longitudinal disease exacerbation/inflammatory burden potential.

The second finding in this study was the increase of oxidative stress markers including MDA, and TBARS among psoriasis patients. Oxidative stress occurs when reactive oxygen species production exceeds the antioxidant defensive capacity of the body and leads to injury at cellular and molecular levels. In psoriasis, excessive reactive oxygen species secreted by activated



immune cells and keratinocytes cause damage to lipids through peroxidation, DNA through direct genotoxic effects and oxidative DNA damage and protein Lipo-oxidation that enhance inflammation pathways (Lin & Huang, 2016)

Malondialdehyde is thought to be one of the most dependable indicators of lipid peroxidation and oxidative membrane injury. Compared with the controls, the much higher levels of MDA found in this study also support our theory that psoriasis patients have greater oxidative damage. These findings are similar to those reported by Cannavò et al. (2019), who reported highly elevated MDA levels in psoriatic subjects compared to healthy controls and suggested oxidative stress is a seminal event in the pathogenesis of psoriasis. The high levels of TBARS in our current study also reinforce the occurrence of raised lipid peroxidation in psoriasis. Our results showed that TBARS levels were gradually increased in parallel with the disease severity, although this association did not reach statistical significance possibly because of a small sample size of severe psoriasis cases.

The results also indicated higher serum LDH levels among patients with psoriasis as well. Lactate dehydrogenase (LDH) is an intracellular enzyme stored in different types of cells and released into the blood when cell injury and tissue damage occur. Elevated LDH levels may represent accelerated keratinocyte turnover and epidermal hyperproliferation, two key pathological findings in psoriasis. Zhou et al (2021) also reported similar observations, revealed elevated levels of LDH activity in psoriasis patients, it is associated with disease severity and inflammatory activity.

One critical finding in the current study was the highly positive association between serum neopterin with LDH and MDA. The association of neopterin with LDH indicates that immunoactivation is a factor for enhanced tissue damage and cell turnover in psoriasis. Meanwhile, the moderate positive correlation between neopterin and MDA show a close interaction of the inflammatory immune responses and oxidative stress mechanisms. Moreover, activated macrophages and T lymphocytes not only produce neopterin but also trigger the generation of reactive oxygen species as an additional mechanism that enhances oxidative damage and maintains chronic inflammation (Murr et al., 2002). These findings confirm the theory of dual interactions underlying psoriasis progression (oxidative stress and immune dysregulation).

The lack of correlation between neopterin and TBARS may be resulted from biological variability within participants or differences in the sensitivity and specificity of measurement of TBARS compared with MDA. TBARS is used extensively as a

marker of lipid peroxidation, however it is affected by multiple interfering substances and may not always directly correlate with oxidative status (Moselhy et al.,2013).

The results of the present study combined point to the significant role played by oxidative stress and immune activation in psoriasis pathogenesis. Neopterin, LDH, MDA and TBARS are upregulated as psoriasis progresses, indicating ongoing inflammatory and oxidative processes that persist throughout the disease course in patients with psoriatic disease. Therefore, these biomarkers might be clinically useful for the following purposes: disease monitoring, assessment of severity and follow-up of therapeutic effects (Zoroddu et al., 2026).

While several important findings were derived, the study does have some limitations. The small size of the study, in particular regarding the subgroup of patients with severe psoriasis, limited some analyses statistically. Moreover, the levels of antioxidant enzymes and inflammatory cytokines could not be assessed, which would have provided a comprehensive view of oxidative and pro-inflammatory interactions. Larger studies with additional molecular biomarkers will needed to better understand the mechanistic link between neopterin and oxidative stress in psoriasis.

### Conclusion

This study showed elevated level of neopterin, and other oxidative stress markers (LDH, MDA, TBARS) among patients with psoriasis, indicating their role in inflammatory process and the course of pathophysiology of psoriasis. The correlation analysis showed that there was a strong positive correlation between serum levels of neopterin and each of LDH, MDA.

### Disclaimer (Artificial intelligence)

The author hereby declares that NO generative AI technologies such as Large

Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators

have been used during the writing or editing of this manuscript.

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