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Original Research Article

Elevated TNF-alpha and its metabolic implications in psoriasis patients

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Abstract

Background: Psoriasis is a chronic inflammatory skin disease linked to excessive production of tumor necrosis factor-alpha (TNF-α), a cytokine that plays a crucial role in disease development. TNF-α stimulates inflammation and accelerates skin cell proliferation, leading to psoriatic plaque formation. Additionally, elevated TNF-α levels are associated with disruption of glucose regulation and lipid metabolism. Thus, elevated TNF-α is a key factor linking inflammation and metabolic dysregulation in these individuals. This study aimed to investigate the effect of high TNF-α levels in patients with psoriasis.

Materials and Methods: The study included 90 patients with psoriasis (46 males and 44 females) aged 18 – 64 years. Consultant Dermatologists diagnosed the patients at the Dermatology Clinic, Al-Nasiriyah Teaching Hospital, Thiqar, Iraq. The study also included 90 control subjects, 46 males and 44 females, aged 18-65 years, who appeared to be in good health and were under the supervision of a qualified physician. The patient and control attended Al-Nasiriyah Teaching Hospital, the study took place in Thiqar, Iraq from January 2024 to the end of June 2024, specifically in Southern Iraq. TNF-α was measured using an (ELISA). FBG, S.TG, and HDL-C levels were also measured using Cobas Integra 400 Plus.

Results: The mean TNF-α level in the patients group was found to be 120.66 ± 24.08, compared to 99.76 ± 13.86 in the control group ($P < 0.001$). The study found no significant difference in S. TNF-α levels among patients with psoriasis based on disease severity.

Conclusion: The study revealed that individuals with psoriasis have higher levels of metabolic and inflammatory biomarkers than healthy individuals, but these markers do not necessarily indicate disease severity.

Keywords: Psoriasis, TNF- α, PASI score.

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1. Introduction

Psoriasis is a chronic inflammatory skin disease characterized by an overactive immune response, primarily involving Th17 cells and cytokines.[1] About 2-3% of adults worldwide suffer from psoriasis, an inflammatory skin disease often related to systemic manifestations. Psoriasis often presents as scaly erythematous plaques that can be locally or widely distributed. There are significant regional, racial, and environmental variations in the worldwide prevalence of psoriasis worldwide.[2,3] Psoriasis is a complex hereditary condition activated by several risk factors including inflammation, antigen presentation, cell communication, and transcriptional control. Psoriasis is characterized by persistent inflammation resulting in unchecked keratinocyte proliferation and impaired differentiation.[4] Psoriasis primarily affects the skin; however, it may also adversely affect the joints and is associated with several other diseases. Inflammation has been demonstrated to affect several organ systems and is not restricted to the psoriatic skin. Therefore, psoriasis is a systemic condition, with patients exhibiting higher levels of hyperlipidemia, hypertension, coronary artery disease, type 2 diabetes, and body mass index.[5] Clinical diagnosis of psoriasis based on visual symptoms is usually sufficient in most cases, and skin samples are not usually required for confirmation. Psoriasis is characterized by well-defined red and scaly plaques. These plaques may be oval, round, or irregular in appearance and frequently appear symmetrically on the body. Points of slight bleeding (known as the "Auspitz sign") may appear when the dry scale is scraped away.[6]

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The Koebner phenomenon refers to the development of lesions at trauma or injury sites.[7] The Psoriasis Area and Severity Index (PASI), which integrates lesion severity and the size of afflicted areas into a singular index value, is the definitive standard for assessing psoriasis severity.[8] This scale is one of the most popular tools for determining psoriasis severity and was created by Fredrikson and Pettersson in 1978. It computes the intensity of psoriatic plaques and affected body surface area.[9] Physicians divide the body into four sections: head, trunk, upper extremities, and lower extremities, scoring each part based on erythema, induration, and desquamation.(**Figure 1**)[10]

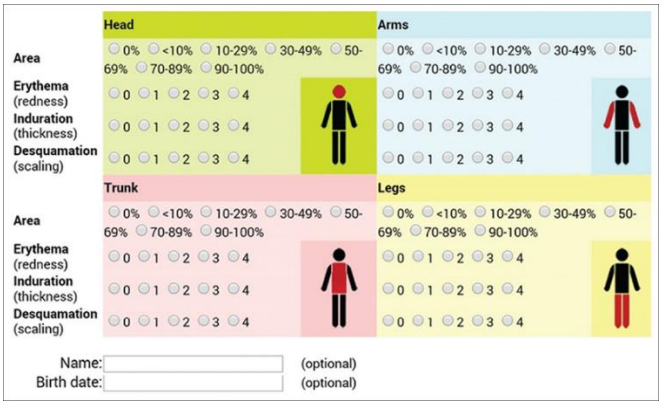

Figure 1: Showing PASI score calculation [9]

The PASI score ranges from 0 to 72, where 0 indicates no disease activity, and 72 represents the most severe form of psoriasis. The score was categorized as follows: a PASI score < 8 was considered mild, 8-12 moderate, and >12 severe.[11]

TNF-α is crucial for the development of insulin resistance (IR). TNF-α is pivotal in several clinical processes such as inflammation, allergies, and congestive heart failure. TNF-α inhibits insulin signaling, affects lipid metabolism, and modifies several other variables associated with the development of IR.[12] TNF-α and IL-6 are pivotal inflammatory mediators, illustrating the relationship between visceral fat and systemic inflammation. Both substances possess a documented history of promoting lipolysis and facilitating the release of free fatty acids, which subsequently elevates IR and hepatic production of glucose, while also inhibiting adipocyte differentiation and inducing inflammation.[13] The serum concentration of adiponectin in individuals with psoriasis is inversely correlated with the levels of IL-6 and TNF-α. TNF-α can impede the multimerization of adiponectin, consequently resulting in a reduction in adiponectin secretion.[14] This may offer a plausible rationale for the observed reduction in adiponectin levels among patients with psoriasis compared with control subjects.[15] This study aimed to meticulously examine the impact of elevated TNF-α levels on the metabolic parameters of patients diagnosed with psoriasis.

2. Materials and Methods

2.1. Subjects

The study included patients with psoriasis (90), 46 males and 44 females, ranging in age from 18 to 64 years. Consultant Dermatologists diagnosed the patients at the Dermatology Clinic, Al-Nasiriyah Teaching Hospital, Thiqar, Iraq. The study also included 90 control subjects, 46 males and 44 females, aged 18-65 years, who appeared to be in good health and were under the supervision of a qualified physician. The patient and control groups visited the Al-Nasiriyah Teaching Hospital in Thiqar, Iraq, from January 2024 until the end of June 2024. We excluded those younger than 18 years of age and pregnant women.

2.2. Biochemical measurements

Serum TNF-α, fasting blood glucose, serum triglycerides, and serum HDL cholesterol were assessed using blood samples. Blood samples were obtained from patients and controls, and centrifugation was used to extract serum from the obtained whole blood for three minutes at 5000 rpm. The serum was isolated and preserved at -20°C until required. Prior to use, all the reagents were allowed to reach room temperature (25°C) for half an hour. TNF-α was quantified using ELISA in accordance with the operational automation protocols of Sunlong, China. FBG, S.TG, and HDL-C levels were measured using Cobas Integra 400 Plus.

2.3. Statistical analysis

The study used SPSS version 26 for statistical evaluation, employing descriptive and inferential techniques. Categorical data are presented using frequencies and percentages, whereas continuous numerical data are described using means and SD. Associations between categorical variables were evaluated using independent samples t-tests and chi-squared tests, with a P-value of ≤ 0.05 demonstrating statistical value.

3. Results

Table 1 Exhibits the socio-demographic and anthropometric characteristics of the research cohorts. The BMI of individuals with psoriasis was considerably elevated compared to control participants ($P < 0.001$). No substantial variations were seen in age, sex, education, and waist circumference between patients and the control group. $P > 0.05$.

Table 1: Comparative analysis of demographic and clinical parameters between control and psoriasis groups.

Parameters		Control group (n=90) Mean ± SD	Psoriasis group (n=90) Mean ± SD	P. value
Age (years)		33.42 ± 11.31	33.09 ± 12.31	0.85^{NS}
BMI (Kg/m^2)		22.55 ± 2.06	24.33 ± 3.53	<0.001***
WC (cm)		78.80 ± 7.26	81.00 ± 9.17	0.07^{NS}
Sex	Male	46 (51.1%)	47 (52.2%)	0.88^{NS}
	Female	44 (48.9%)	43 (47.8%)	
Education	Illiterate	11 (12.2%)	9 (10.0%)	0.72^{NS}
	Primary	6 (6.7%)	5 (5.6%)	
	Intermediate	16 (17.8%)	10 (11.1%)	
	Secondary	28 (31.1%)	30 (33.3%)	
	Higher education	29 (32.2%)	36 (40.0%)	
Smoking Status	Smoker	43 (47.8%)	38 (42.2%)	0.81^{NS}
	Non-smoker	47 (52.2%)	52 (57.8%)	

Independent samples t-test, chi-square test; NS: Non-significant at P>0.05. Statistical significance is indicated by ***p<0.001.

Table 2: Comparative analysis of metabolic and inflammatory markers between control and psoriasis groups

Parameters	Control group (n=90) Mean ± SD	Psoriasis group (n=90) Mean ± SD	P. value
Fasting blood glucose	91.42 ± 11.93	112.43 ± 33.08	<0.001 I***
S. Triglyceride	124.93 ± 2.52	189.67 ± 74.97	<0.001 I***
High density lipoprotein	50.48 ± 8.59	39.00 ± 12.53	<0.001 I***
Tumor necrosis factor -alpha	99.76 ± 13.86	120.66 ± 24.08	<0.001 I***

n: number of cases; SD: standard deviation; I: independent samples t-test; statistical significance is indicated by ***p<0.001.

Table 3: Comparison of metabolic and inflammatory parameters across different severity levels of disease

Parameters	Mild (n=22) Mean ± SD	Moderate (n=19) Mean ± SD	Severe (n=49) Mean ± SD	P. value
FBG	103.86 ± 28.16	112.11 ± 26.26	116.41 ± 37.06	0.33
S. TG	194.18 ± 80.67	213.11 ± 85.21	178.55 ± 67.06	0.22
HDL	39.27 ± 13.06	37.68 ± 19.56	39.39 ± 8.48	0.87
TNF-α	129.55 ± 27.50	114.89 ± 23.13	118.90 ± 22.15	0.11

n-number of cases; SD-standard deviation; I-independent samples t-test; NS-not significant ($p \geq 0.05$).

Table 2 The results indicate significant differences ($p < 0.001$) between the two groups across all measured parameters. Specifically, the psoriasis group exhibited higher mean levels of fasting blood glucose (112.43 ± 33.08 mg/dL), serum triglycerides (189.67 ± 74.97 mg/dL), and TNF-α (120.66 ± 24.08 pg/mL) compared to the control group (91.42 ± 11.93 mg/dL, 124.93 ± 2.52 mg/dL, and 99.76 ± 13.86 pg/mL, respectively). Conversely, the psoriasis group had lower mean HDL levels (39.00 ± 12.53 mg/dL) compared to the control group (50.48 ± 8.59 mg/dL).

Table 3 Examines S.TNF-alpha, FBG, S.TG, and S.HDL-C levels patients with psoriasis, categorized by disease severity. The findings of this study indicated non-significant differences ($p > 0.05$) in the level of TNF-α relative to disease severity. In addition, non-significant differences ($p > 0.05$) in the levels of FBG, S.TG, S.HDL-C among controls and patients with psoriasis.

4. Discussion

Psoriasis, a chronic inflammatory skin condition influenced by hereditary factors and immune responses, has diverse clinical manifestations. While its global incidence is around 2%, the prevalence varies across geographical regions and ethnicities (Carrillo et al.[16] Psoriasis has a multifactorial etiology, including genetic predisposition, environmental factors, and vascular and immune system disturbances Ovcina-Kurtovic et al.[17] Tumor necrosis factor-alpha (TNF-α) is thought to play a key role in the pathogenesis of psoriasis due to its immunomodulatory properties. In psoriasis, TNF-α promotes innate immune cell activation and trafficking to the skin, resulting in accelerated keratinocyte proliferation Ayala-Fontánez N et al.[18]

The present study found that psoriatic patients had a significantly higher BMI than the control group. Bavoso et al[19] and Wei et al.[20] also showed similar results. Researchers have suggested several factors that link obesity and psoriasis, including stress, chronic inflammation, unhealthy eating habits, a lack of exercise, and depression.[21] Obesity may play a significant role in the progression from psoriasis to psoriatic arthritis (PsA). Multiple studies have proposed that obesity is a common risk factor for the development of psoriasis and PsA. In a cohort study utilizing an electronic medical records database that accurately represented the broader UK population spanning a 15-year period, it was observed that the occurrence rates of PsA increased in correlation with BMI. This trend was evident not only within the group of 75,395 individuals with psoriasis but also within nearly 2 million individuals from the general population.[22]

Lipid metabolism in patients with psoriasis has been the subject of study for more than 50 years, and numerous studies have shown decreased levels of HDL and/or increased levels of low-density lipoproteins (LDL), very-low-density lipoproteins (VLDL), and triglycerides (TG) at al.[23] Pro-inflammatory cytokines, such as TNF-α and IL-6, may affect lipid metabolism and result in lipid abnormalities in psoriasis, potentially by the following mechanism: first, TNF-α changes the gene expression profile of hepatocytes and adipocytes, which increases the production and release of VLDL-C, cholesterol, and free fatty acids (FFAs), Secondly, elevated interleukin-6 (IL-6) levels in patients with psoriasis are associated with decreased HDL-C content; and psoriasis is a chronic inflammatory disease that induces a decrease in HDL-C and impairs reverse cholesterol transport by inducing changes in HDL composition and metabolism Alrubaye et al.[24] Mallbris L et.al al. suggested that genetic alterations in HDL-C and/or apolipoprotein A-I may be linked to psoriasis. This genetic hypothesis is supported by a study on lipid and lipoprotein profiles among Swedish patients with psoriasis, which revealed significant lipid abnormalities and supported the notion that this might be genetically determined rather than acquired.[25] The relationship between psoriasis and dyslipidemia is controversial, and no definitive conclusion can be drawn regarding whether they are caused by a common genetic abnormality or if both are caused by psoriasis. However, psoriasis may also induce secondary hyperlipidemia. Future studies are needed to clarify this issue.[23,24,25]

In a study by Sultana et al. (2022), serum TNF-α levels were significantly elevated in individuals with psoriasis compared to those in healthy controls. These levels were particularly high in patients with mild psoriasis, suggesting a critical pathogenic role of TNF-α in the early stages of disease progression. This finding not only reinforces previous research, but also highlights the potential of TNF-α as a biomarker for monitoring disease activity in psoriatic patients.26 Further exploration by Kyriakou et al. (2014) identified a significant difference in serum TNF-α levels between patients with psoriasis with and without nail lesions. Patients with nail involvement exhibited higher levels of TNF-α, indicating its significant role in nail psoriasis pathogenesis. This suggests that treatments targeting TNF-α might be particularly effective for psoriatic nail disease, more so than therapies focusing on other cytokines such as IL-12/23 or IL-17.[27] Tampa et al. (2024) discussed the therapeutic implications of targeting TNF-α in moderate-to-severe psoriasis cases. They pointed out that biological agents targeting TNF-α and other cytokines, such as IL-12, IL-13, IL-17, and IL-23, are designed to manage chronic inflammation by modulating the immune response. These therapies are noted for their efficacy and general tolerability, making them valuable tools for controlling the inflammatory pathways that underpin psoriasis.[28] Abdel-Hamid et al. reported significantly elevated serum levels of TNF-α in patients with chronic plaque psoriasis (CPP) and active skin lesions, as well as the correlation between serum TNF-α levels and disease severity according to the PASI test.[29] The present study also found increased serum TNF-α levels in patients with psoriasis, but there was no statistically significant correlation between the mean serum levels of TNF-α and PASI score. Similar to the results of the present study, Arican et al. demonstrated that the levels of TNF-α in the serum are significantly elevated in patients with active psoriatic lesions than in healthy control.[30]

5. Conclusion

The study results revealed that patients with psoriasis had elevated levels of metabolic and inflammatory indicators compared with healthy control participants. Nevertheless, research findings indicate that while psoriasis patients may have heightened metabolic and inflammatory indicators relative to healthy controls, these markers do not correspond with disease severity.

6. Ethical Committee Approval

Prior to conducting the study and collecting data, we obtained approval from Basrah University/College of Medicine/Basra / Post-Graduate Studies Section in December 2023. Additionally, according to official letter no. 901, dated December 31, 2023, permission was obtained from the Thi-qar Health Directorate/Training and Human Development Center to legally access the Al-Nasiriyah Teaching Hospital to carry out the research.

7. List of Abbreviations

TNF-α, tumor necrosis factor-alpha; FBG, fasting blood glucose; WC, waist circumference; PASI score, psoriasis area and severity index score; IL-6, interleukin 6; CVS, cardiovascular system

8. Conflict of Interest

The author declare that they have no competing interests

9. Source of Funding

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