AL-KUFA JOURNAL FOR BIOLOGY
ISSN (Print): 2073-8854 **ISSN (online):** 2311-6544

Original Research

Evaluation of levels of IL-2 and TNF- α in the serum of psoriasis patients and their role in inflammatory activity

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Article history
Received: 29/12/2025
Revised: 16/3/2026
Accepted: 3/5/2026

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Abstract: Psoriasis is a chronic, inflammatory, immune-mediated skin disorder, which is characterized by hyperplasia of keratinocytes and long-term cellular immunity. Pro-inflammatory cytokines, especially interleukin-2 (IL-2) and tumor necrosis factor-alpha (TNF-α), are the basis of the pathogenesis and progression of the disease.**Aim:** The study was intended to determine the serum levels of IL-2 and TNF-α in psoriasis patients and to determine the correlation of these variables with clinical severity and other variables of clinical concern.**Materials and Methods:** Fifty clinically diagnosed patients with psoriasis and fifty age- and sex-matched controls (apparently healthy subjects) were involved in the study. The serum levels of IL-2 and TNF-α were determined using enzyme-linked immunosorbent assay (ELISA). The Psoriasis Area and Severity Index (PASI) was used to determine the severity of the disease. **Result:** The serum levels of IL-2 and TNF-α in patients with psoriasis were significantly greater than those of the controls ($P < 0.01$). It was found that the two cytokines were significantly elevated with increasing PASI score ($P < 0.05$). There was a positive correlation between cytokine levels and disease duration. There was a significant increase in the level of TNF-α in the group of smokers compared with non-smokers, with no significant increase in the level of IL-2. There was no significant sex-related difference. **Conclusion:** The serum IL-2 and TNF-α levels were identified to be elevated relative to the severity and duration of psoriasis and, therefore, have been established as effective inflammatory mediators in disease activity. The findings support the use of IL-2 and TNF-α as immunological biomarkers to track disease progression.

Keywords: Psoriasis, interleukin-2, tumor necrosis factor alpha, cytokines, ELISA technique

1. Introduction

Psoriasis is a persistent, immune-mediated inflammatory dermatologic disease that manifests itself in disordered proliferation of keratinocytes, unremitting production of pro-inflammatory cytokines in the dermis, and the constant stimulation of immune cells [1,2]. Even though in the past psoriasis was considered a localized dermatological disorder, nowadays it is a well-established fact that psoriasis is a systemic inflammatory condition that is linked with several comorbid diseases that involve the joints, cardiovascular system, and nervous system [3,4]. The primary role in the development and progression of the disease is a significant disruption in the cellular and humoral immunity [5]. T lymphocytes, especially T cells, which

are the $CD4^+$ and the $CD8^+$ type, play a significant role in the immunopathogenesis of psoriasis [5,7]. These cells release a wide range of inflammatory mediators that sustain keratinocyte hyperproliferation and persist with the chronic inflammatory process involving the presence of inflammatory mediators in psoriatic lesions [6,7]. Two of the most vital of these intermediates include tumor necrosis factor-alpha (TNF-alpha) and interleukin-2 (IL-2) that are major mediators in local tissue inflammation and also in systemic immune dysregulation [8–10]. One of the first groups of cytokines that are released in the process of inflammation is TNF-alpha, which is mainly produced by activated macrophages and T cells [8,9]. It increases the expression of endothelial adhesion molecules, thus promoting leukocyte recruitment into the psoriatic lesions on the skin [9]. Moreover, TNF-alpha enhances inflammatory and cascades, facilitates the production of other cytokines and chemokines, as well as the proliferation of keratinocytes- an activity which leads to epidermal thickening and development of the classic psoriatic plaques directly [10,11]. On the contrary, IL-2 is a growth and survival factor of T lymphocytes. T-cell activation, clonal expansion, memory formation, and maintenance of natural killer (NK) cell activity require its presence [12,13]. The production of IL-2 starts after the presentation of antigens and engagement of the T-cell receptor. The high level of IL-2 promotes the Th1- and Th17-mediated immune responses that are both highly involved in maintaining chronic psoriatic inflammation [14,15]. TNF-alpha and IL-2 circulating levels are affected by a variety of clinical and behavioral factors such as the severity and duration of the disease, psychological stress, and lifestyle habits such as smoking [16]. Especially smoking has been proven to cause oxidative stress and immune dysregulation, resulting in augmented TNF-alpha discharge and aggravation of the inflammatory condition [16,17]. Smoking individuals with psoriasis are often reported to have worse clinical features and worse responses to treatment than non-smokers [17]. TNF-alpha has a specific therapeutic value, with biologic TNF-alpha therapies (infliximab, adalimumab, and etanercept) proving to be of significant efficacy in moderate-to-severe psoriasis patients [18–20]. On the same note, IL-2 receptor signaling has become a promising immunotherapeutic interactant in autoimmune conditions, such as psoriasis [21–23]. Although much progress has been made in the elucidation of the molecular basis of psoriasis, serum cytokine profiling is a viable technique that can be used to evaluate immune activation and disease activity in normal clinical practice [24]. The measurement of circulating IL-2 and TNF-alpha can help to obtain meaningful information on the level of systemic inflammation and the overall burden of psoriasis in a specific patient [24,25]. In order to better understand the role of these cytokines in the chronic inflammatory pathway that characterizes psoriasis, this study compares serum IL-2 and TNF-alpha levels in psoriasis patients and healthy controls. It also investigates correlations between cytokine levels and significant clinical and demographic variables, such as disease severity and duration.

2. Methodology

Samples collection

In collaboration with the Clinical Analyses Laboratory, the Dermatology Department at Imam Sadiq Teaching Hospital in Babylon Governorate, Iraq, conducted this descriptive analytical case-control study between January and June of 2025. In order to better understand the role of these cytokines in the inflammatory activity of the disease, the study sought to assess changes in the serum levels of interleukin-2 (IL-2) and tumor necrosis factor-alpha (TNF-α) in psoriasis patients and compare them with those who appeared to be healthy.

Study population

The study included fifty (50) patients clinically diagnosed with psoriasis by a specialist dermatologist based on typical clinical manifestations such as erythematous plaques covered with silvery scales and their characteristic distribution. Patients were aged between 18 and 60 years and included both males and females. Disease severity was classified using the Psoriasis Area and Severity Index (PASI) into mild, moderate, and severe categories. Clinical data regarding disease duration and lifestyle habits, including smoking status, were recorded.

The control group consisted of fifty (50) apparently healthy individuals matched for age and sex, with no history of psoriasis, other autoimmune, inflammatory, or chronic systemic diseases.

DOI: 10.36320/ajb/v18.i2.22802

Inclusion and exclusion criteria

Patients were included if they had clinically confirmed psoriasis and were within the age range of 18–60 years. Patients with other autoimmune diseases, acute or chronic infectious diseases, malignancies, or those who had received systemic immunosuppressive therapy during the previous three months were excluded. Pregnant women and individuals with severe systemic illness were also excluded from the study.

Blood sample collection

Venous blood samples (5 mL) were obtained from each participant after an overnight fast of at least 8 hours. Samples were collected into plain tubes without anticoagulant, allowed to clot at room temperature, and then centrifuged at 3000 rpm for 10 minutes to separate the serum. The separated serum was transferred into sterile Eppendorf tubes and stored at −20°C until laboratory analysis.

Measurement of serum cytokines

Serum concentrations of interleukin-2 (IL-2) and tumor necrosis factor-alpha (TNF-α) were determined using the enzyme-linked immunosorbent assay (ELISA) technique according to the manufacturer's instructions (Elabscience Biotechnology Co., Ltd., Wuhan, China). The ELISA kits used were Human IL-2 ELISA Kit (Cat. No. E-EL-H0102) and Human TNF-α ELISA Kit (Cat. No. E-EL-H0109).

The detection ranges of the kits were 7.81–500 pg/mL for IL-2 and 15.6–1000 pg/mL for TNF-α, with analytical sensitivities of <4.69 pg/mL and <9.38 pg/mL, respectively. Serum samples and standards were run in duplicate, and the absorbance was recorded at 450 nm. Cytokine levels (pg/mL) were then calculated based on standard calibration curves.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25. Mean and standard deviation (SD) were used as measures of quantitative variables. Student's t-test was used to compare the means of the patient and the control groups. One-way analysis of variance (ANOVA) was used to compare the levels of cytokines based on categories of disease severity based on PASI. The Pearson correlation coefficient was employed to evaluate the correlation of cytokine levels and clinical parameters like disease duration and PASI score. The statistically significant P value was taken as less than 0.05.

3. Results and discussion

Comparison between psoriasis patients and healthy controls

A significant elevation in IL-2 and TNF-α serum markers was observed in the psoriasis group versus the control group. Specifically, the mean serum IL-2 for patients reached 48.6 ± 12.9 pg/ml, whereas it was 25.4 ± 8.4 pg/ml in the control group ($P < 0.01$). Similarly, the mean TNF-α level was significantly higher in patients (71.0 ± 25.0 pg/ml) than in controls (33.2 ± 9.8 pg/ml) ($P < 0.01$) (Figure 1).

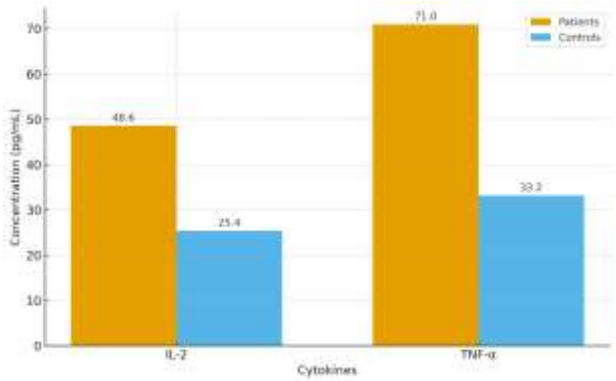

Fig 1. Comparison of mean serum concentrations of interleukin-2 (IL-2) and tumor necrosis factor-alpha (TNF-α) between psoriasis patients and healthy controls. A significant increase was observed in both cytokines among patients ($P < 0.01$).

Cytokine levels according to disease severity

A gradual and statistically significant increase in serum IL-2 and TNF-α levels was observed with increasing disease severity based on PASI scores. In mild cases, the mean IL-2 and TNF-α levels were 34.1 pg/ml and 49.8 pg/ml, respectively. These values increased to 42.5 pg/ml for IL-2 and 65.7 pg/ml for TNF-α in moderate cases and reached the highest levels in severe cases (56.8 pg/ml for IL-2 and 82.3 pg/ml for TNF-α). This stepwise increase was statistically significant ($P < 0.05$) (Figure 2).

DOI: 10.36320/ajb/v18.i2.22802

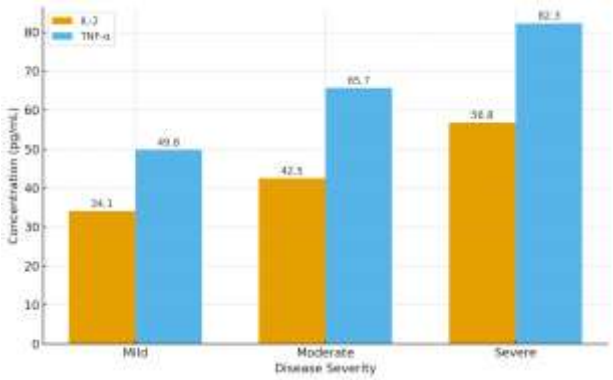

Fig 2. Gradual increase in serum IL-2 and TNF-α concentrations according to psoriasis severity based on PASI scores. Both cytokines showed a stepwise rise from mild to severe cases ($P < 0.05$).

Correlation between cytokine levels and disease duration

A positive correlation was detected between serum cytokine levels and disease duration. Patients with longer disease duration showed higher levels of both IL-2 and TNF-α. The correlation coefficient for IL-2 was $r = 0.62$, while for TNF-α it was $r = 0.58$, indicating a moderate positive correlation ($P < 0.01$) (Figure 3).

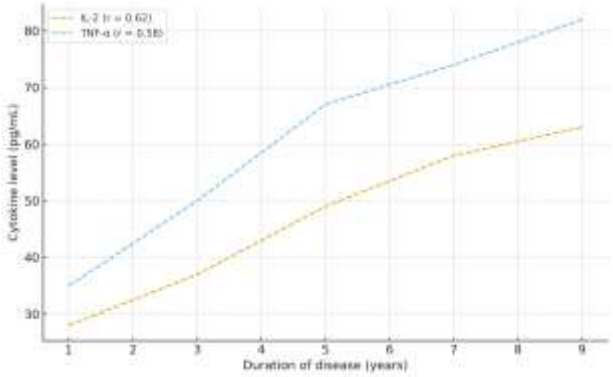

Fig 3. Correlation between cytokine levels and disease duration.

Effect of smoking on cytokine levels

The effect of smoking on cytokine levels was also evaluated. The mean serum TNF-α level was significantly higher in smokers (76.3 ± 22.4 pg/ml) compared with non-smokers (64.1 ± 19.7 pg/ml) ($P < 0.05$). However, no statistically significant difference was observed in IL-2 levels between smokers and non-smokers ($P > 0.05$) (Figure 4).

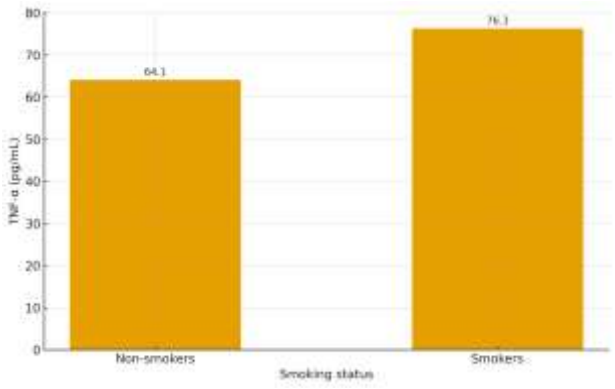

Fig 4. Comparison of mean serum TNF-α concentrations between smoking and non-smoking psoriasis patients. A significant increase was observed among smokers ($P < 0.05$), while IL-2 showed no significant difference.

Individuals with psoriasis in the study at hand demonstrated that the serum concentration of interleukin-2 (IL-2) and tumor necrosis factor-alpha (TNF-α) rose significantly amongst healthy individuals, which signifies that the cellular immune system is intensively activated [26,27]. This observation supports the idea that psoriasis is not a localized skin disease, but it is a long-term autoimmune disease where cellular immune imbalance is strongly linked to unremitting systemic inflammation [28]. Such findings are in line with those reported in the past that show a similar increase in the levels of IL-2 in the psoriasis patients which are also due to hyper activation of T lymphocytes and increased systemic inflammatory reactions [26]. Similarly, TNF-α has been noted as a pivotal mediator in psoriatic inflammatory cascade and its suppression by biological therapy has been termed with a great clinical response in the psoriatic lesions [27,29].

On the contrary, other studies have indicated partial contradiction to these results since they did not record an intensive rise in the levels of the cytokines at the chronic stages of the disease. Differences in the analytical methods, sample size or population characteristics might be attributed to such discrepancies among studies [28,29]. However, it is becoming increasingly evident that IL-2 and TNF-α can also be viewed as functioning in a feedback loop where one protein promotes the other protein and vice versa [30,31].

The current paper also revealed a direct correlation between the levels of IL-2 and TNF-α and the severity of the disease estimated using the PASI index. This is in line with reports that TNF-α stimulates IL-2 production by T cells by activating the NF-κB signal transduction pathway and that IL-2, conversely, increases the action of TNF-α producing cells leading to a self-perpetuating cycle of inflammation that proves challenging to break without specific pharmacological intervention [30,31]. The interaction of these two synergistically results in a mechanistic explanation of how inflammation persists and psoriatic lesions recur frequently in the absence of acute clinical remission [32].

It was also assumed that there was a close relation between high levels of cytokines and disease duration whereby the higher levels were found in patients whose disease duration was over five years. This result is in line with the reports that long period of disease development is linked to an expression of TNF-α in psoriatic skin tissue to continue over the time, which is related to a gradual aggravation of the chronic inflammation process with time [31].

On the demographic variables, the cytokine levels were no different between the male and female patients with statistical significance. This finding corresponds with the prior findings that sex has no significant effect on the behavior of cytokines and that it is disease-associated processes that cause immune activation instead of hormonal or age-related ones [32].

The effect of smoking on TNF-α levels was found to be significant, as the levels of smokers were significantly greater than those of the non-smokers; however, smoking had no effect on the levels of IL-2. This observation is in line with the findings of other studies that attribute oxidative stress brought by smoking to hyperirritation of macrophages and increased output of TNF-α which worsens inflammation and diminishes treatment response [33].

Physiologically, the observed relationship between IL-2 and TNF-α is not the parallel upsurge of two independent cytokines, but a more sophisticated network of interactions between Th1 and Th17 T-lymphocytic subsets that facilitates sustained discharge of inflammation in the psoriatic skin. This is the interaction that elucidates the clinical efficacy of TNF-α-blocking biological agents like infliximab and adalimumab in the treatment of severe psoriasis because the inhibition of one inflammatory pathway indirectly suppresses the other [34].

In general, the current work supports the primary role of IL-2 and TNF-α in the sustenance of the chronic inflammatory response in psoriasis and presents the objective data in the correlation between the levels of cytokines and the severity and the course of the disease. The application of direct serological evaluation in the present study has increased the clinical relevance and applicability of the results in practice as compared to the other earlier studies that used complicated molecular methods.

Conclusion

This study confirms that psoriasis is not a simple skin disease as is traditionally thought, but rather a complex inflammatory immune disorder in which a number of cytokines interfere that contribute to the continuation of inflammatory activity. The outcomes revealed that interleukin-2 (IL-2) and tumor necrosis factor alpha (TNF-α) are much higher in serum patients than in healthy persons, and that such an increase is directly associated with the severity of psoriasis and the duration of the damage. These data suggest that hypersecretion of these cytokines is a manifestation of a persistent state of immune response, since both elements participate in the stimulation of T cells of the Th1 and Th17 types, which causes the increase of inflammation and skin lesion renovation. It was also demonstrated that smoking could exacerbate the inflammatory state, elevating the concentrations of TNF-α, and therefore smoking cessation is a supportive factor in enhancing the therapeutic effect, particularly modern immunotherapy. To sum up, the trend of managing the IL-2/TNF-α axis as a promising treatment option that helps to achieve the desired result without causing the adverse effect on the overall functioning of the immune system is supported in the examined study and promotes the creation of more precisely focused treatment options and reduced side effects that would help increase the quality of life of patients and mitigate the chronic burden of the disease.

Acknowledgement

The authors would like to express their sincere gratitude to the staff of the laboratory and all participants who contributed to this study.

Funding Information

This research received no external funding.

Author's Contributions

The author solely contributed to the conception, design, data collection, analysis, and writing of the manuscript.

Ethics

The protocol of the study was discussed and accepted by the Ethics Committee of DNA Research Center, University of Babylon, Iraq (Approval No. Ref: M776325), in compliance with the principles of the Declaration of Helsinki. All the participants were informed by writing before they gave informed consent before sample collection. Anonymity and confidentiality were strongly observed during the study.

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