Kufa Medical Journal | Vol. 21, No.2, 2025

Original article | DOI: https://doi.org/10.36330/kmj.v21i2.19978

p-ISSN: 1993-517X
e-ISSN: 2709-4464

The Assessment of Serum Interleukin-18 (IL-18) Level and Its Role as a Biomarker for Psoriasis in Najaf Province

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ABSTRACT

***Background**: Psoriasis is a common and chronic autoimmune disorder that predominantly impacts the skin. Its development involves genetic susceptibility and immune system activation. The disease affects roughly 2–3% of the world's population. **Objective:** This study aims to evaluate the IL-18 levels in serum of Iraqi patients suffering from psoriasis and compare it to control groups as a diagnostic biomarker. **Material and Methods:** A total of 130 people were included in this study. Of these, 65 had psoriasis (43 males and 22 females) and 65 were controls (apparently healthy individuals); 42 were males and 23 were females. The age range of both the psoriasis patient group and the control group was 18 to 70 years. The sandwich Enzyme-Linked Immunosorbent Assay test (ELISA) was used to determine the serum levels of IL-18 in both (patients and controls). **Results:** Serum concentration of IL-18 was significantly markedly elevated in the patients group compared to controls ($P < 0.001$). ROC analysis indicated that IL-18 has an acceptable diagnostic accuracy in distinguishing psoriasis patients from healthy individuals. There was no significant difference in IL-18 levels between patients with a family history of psoriasis and those without. Additionally, IL-18 levels showed no significant variation between patients with moderate and severe psoriasis. **Conclusion:** Serum IL-18 levels were significantly higher in psoriasis patients, indicating its potential as a diagnostic marker.*

Keywords: Psoriasis, Interleukin-18 (IL-18), Biomarker, Diagnostic accuracy, Autoimmune, Skin disease.

Article Information

Received: June 03, 2025; Revised: December 11, 2025; Online December, 2025

INTRODUCTION

Psoriasis is a prevalent autoimmune disorder that can occur in individuals of any age group. It is non-infectious, and causes physical damage [(1)] . It also has a complex, multifactorial nature triggered by (genetic, environmental, immunological variables, and immunological factors) with a worldwide prevalence of about 1-3% [(2)]. Psoriasis induces an immune response in the skin, activating a pro inflammatory system. Recent investigations showed a clear association between psoriasis and systemic inflammatory disorders [(3),(4)] . Psoriasis is associated with an elevated inflammatory burden, which plays a role in the development of several immunoinflammatory conditions such as cardiovascular disease and metabolic syndrome [(5),(6)]. Therefore, psoriasis should be regarded as an immune-mediated systemic disorder rather than merely a localized skin condition [(7)] .

Interleukin-18 (IL-18) is a pro-inflammatory cytokine belonging to the IL-1 family, primarily produced by monocytes, macrophages, dendritic cells, and keratinocytes. It plays a key role in both innate and adaptive immune responses, mainly by inducing the production of interferon-gamma (IFN-γ) and promoting the activation of Th1 cells. Through these mechanisms, IL-18 contributes to the amplification of inflammatory cascades in various autoimmune inflammatory diseases such as psoriasis [(8),(9).] Previous studies have demonstrated a significant correlation between serum IL-18 levels and the Psoriasis Area and

Severity Index (PASI) [10]. In addition, increased IL-18 mRNA and protein expression have been reported in both the skin lesions and serum of patients with psoriasis compared with healthy individuals [11],[12]. Therefore, this study aims to evaluate the serum concentration of IL-18 in Iraqi patients with psoriasis and compare it with that of healthy controls to assess its potential usefulness as a diagnostic biomarker.

METHODS

Study design and setting

This is a case-control that study was conducted between November 2024 and February 2025. Participants were recruited from the Dermatology unit of Al-Najaf teaching Hospital. The study included a total of 130 participants, comprising 65 patients clinically diagnosed with psoriasis by dermatologists (43 males and 22 females), and 65 apparently healthy individuals serving as the control group (42 males and 23 females), matched in age and gender. The age range for both groups was between 18 and 70 years.

Sample collection and processing

A 5 ml syringe were used to collect venous blood from both the patients and controls into a gel tube. Next, the serum samples were left standing for 5 minutes to coagulate. After that, the centrifugation process was applied at 2000-3000 rpm for 10 minutes; the serum was stored in a 2 ml Eppendorf tube at -80 °C until all serological markers were determined.

Inclusion and Exclusion Criteria

A) Inclusion Criteria

For Psoriasis patients (Case Group):

1. Age between 18 and 70 years.
2. Patients must be clinically diagnosed with Moderate and severe psoriasis by a dermatologist

For Controls (Control Group):

1. Age between 18 and 70 years.
2. No personal or family history of psoriasis.
3. Free from other chronic inflammatory skin diseases

B) Exclusion Criteria for patients

1. Women who are pregnant
2. Persons with long-term diseases (e.g., autoimmune disorders).
3. Persons with any systemic infections or inflammatory diseases.
4. Patient less than 18 years of age.
5. Patients who took systemic treatment at the last month.
6. Patients with mile psoriasis

Ethical and Scientific Approval

Before collecting the sample, Verbal consent was obtained from both physicians and participants after clearly explaining the objectives of the study.

Laboratory tests

The levels of IL-18 were measured using a sandwich Enzyme-Linked Immunosorbent Assay (ELISA), based on a standard calibration curve, according to the manufacturer's protocol (BT LAB).

Statistical Analysis

Data were analyzed using SPSS version 26 and Excel 2010. Normality was assessed with the Kolmogorov-Smirnov test. Parametric tests (independent t-test, one-way ANOVA) were used for normally distributed data, while non-parametric tests (Mann-Whitney) were applied for non-normal data. Chi-square tested associations between categorical variables. ROC curve analysis determined diagnostic cut-off values. Pearson correlation assessed relationships between numeric variables. Significance was set at $P < 0.05$, with $P \leq 0.01$ considered highly significant [13].

RESULTS

The comparison of serum Interleukin-18 (IL-18) levels between psoriatic patients and healthy control subjects is presented in Table (1). The mean ± standard deviation of serum IL-18 levels was 7.60 ± 2.6 in psoriatic patients and 4.01 ± 0.99 in controls. The difference was highly statistically significant ($P<0.001$), with IL-18 levels being markedly higher in the patient group compared to the control group.

Receiver Operating Characteristic (ROC) analysis, as illustrated in Figure 1, was conducted to evaluate the prognostic accuracy of serum Interleukin-18 (IL-18) levels in distinguishing psoriatic patients from healthy control subjects. An optimal IL-18 cut-off value greater than 2.71 yielded an AUC of 0.714 (95% confidence interval [CI]: 0.639–0.819, P = 0.001), with a sensitivity of 70.8%, specificity of 72.3%, positive predictive value (PPV) of 71.9%, and negative predictive value (NPV) of 71.2%. These findings suggest that IL-18 may serve as an acceptable prognostic biomarker for differentiating psoriasis patients from healthy individuals.

Table (1): comparison of serum Interleukin-18 (IL-18) level in psoriatic patients and controls.

Interleukin-18 (IL-18) level	*n* = 65		*P*
	Patients	Healthy control	
Mean ± SD	7.60 ± 2.6	4.01 ± 0.99	< 0.001 † HS
Range	0.87 – 22.00	1.11 – 10.17	

n: number of cases; SD: standard deviation; †: independent samples t-test; HS: Highly significant at P ≤ 0.001.

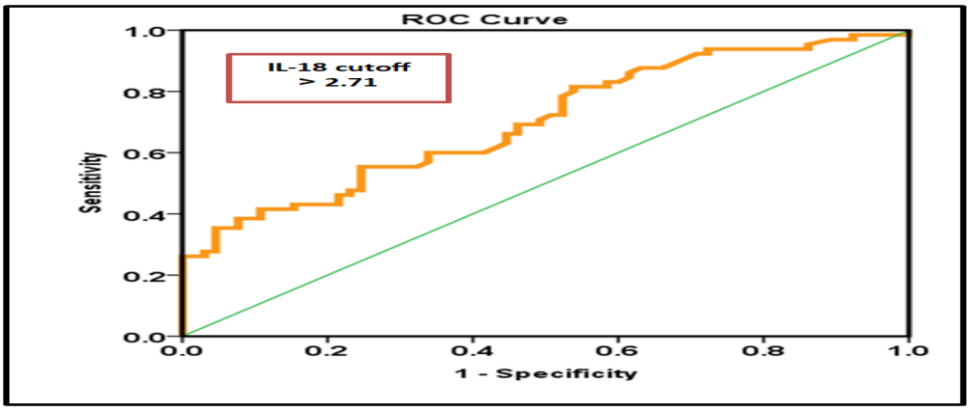

Figure (1): Receiver operator characteristic curve analysis of IL- calculation of possible diagnostic cutoff value.

n Table 2, the comparison of the immunological parameter according to family history. The mean of patients with family history (6.34 ± 1.6), and the mean of those without a family history (8.12 ± 1.9).The current results a show non-significant difference between patients with positive family history and patients with negative family history according to IL18 (p>0.05).

Table (2): Frequency distribution of IL-18 levels according to some characteristics

Characteristics		*N*	Mean ± SD	*P*
Sex	Male	43	6.88 ± 1.28	0.380 † NS
	Female	22	8.24 ± 1.61	
Family history	Positive	19	6.34 ± 1.6	0.328 † NS
	Negative	46	8.12 ± 1.9	

n: number of cases; SD: standard deviation; †: independent samples t-test; NS: not significant at P < 0.05

In Table 3, results showed a non-significant difference in IL-18 levels between patients with severe and moderate psoriasis (p > 0.05).

Table (3): Frequency distribution of immunological parameter according to severity of disease

Severity of disease	IL-18
Severe	9.07 ± 1.2
Moderate	6.58 ± 1.8
p-value	0.119 †

In table 4, the frequency distribution of patients according to chronic disease was as following: 17 (26.2%) of patients have cardiovascular disease, 9 (13.8 %) have diabetes mellitus, while 18 (27.7 %) of psoriatic patients have hypertension. The frequency distribution of patients according to obesity are shown in table (4)

Table (4): The frequency distribution psoriatic patients according to comorbidities.

Characteristic	**Patients** *n* (%)
Cardiovascular disease	
Present, *n* (%)	17 (26.2 %)
Absent, *n* (%)	48 (73.8 %)
Diabetes mellitus	
Present, *n* (%)	9 (13.8 %)
Absent, *n* (%)	56 (86.2 %)
Hypertension	
Present, *n* (%)	18 (27.7 %)
Absent, *n* (%)	47 (72.3%)
Obesity	
Obese	19 (29.2%)
Non-obese	46 (70.8 %)

DISCUSSION

The study demonstrated a highly significant difference in serum interleukin-18 (IL-18) levels in patients compared to controls ($P < 0.001$). As shown in Table 1. These findings are consistent with previous studies by Arican[14] , Takahashi [15], and Forouzandeh [16] all of which reported significantly elevated IL-18 levels in patients with psoriasis compared to controls. Moreover, previous studies have demonstrated a positive association between serum IL-18 levels and both the severity and activity of psoriasis, highlighting its potential utility as an objective biomarker for evaluating disease status. [17]. This is consistent with the pathogenesis of psoriasis, as IL-18 plays a role in promoting Th1 and Th17 immune responses, leading to keratinocyte proliferation and sustained inflammation in psoriatic lesions [18] .

The current study, the findings have demonstrated a moderate diagnostic performance of serum IL-18 in psoriasis patients (AUC = 0.714). This is consistent with a previous study by (Forouzandeh et al. 2020)[16], who also reported elevated IL-18 levels in psoriatic patients and a relatively high AUC of 0.7818, suggesting that IL-18 may serve as a potential diagnostic biomarker in psoriasis, although results may vary depending on population characteristics and methodologies.

The present study showed no statistically significant difference in serum IL-18 levels between male and female psoriasis patients ($p > 0.05$), a mean 6.88 ± 1.28 and 8.24 ± 1.61 respectively as shown in Table (2). The lack of a significant difference in IL-18 levels between sexes may be due to the fact that Interleukin-18, a potent proinflammatory cytokine, regulates both Th1 and Th2 responses and is produced by various immune and non-immune cells [19]. IL-18 expression is primarily regulated by innate immune mechanisms and local inflammatory stimuli, rather than by sex hormones.

However, this result contrasts with the findings reported by (Wang et al. 2022)[20], who investigated the relationship between clinical characteristics and cytokine levels in psoriasis patients and found that male patients had significantly higher serum IL-18 levels compared to female patients ($p = 0.015$).

This study is consistent with the findings (Arican et al. 2005)[14], who reported that serum levels of IL-18—along with IFN-γ, IL-12, and IL-17—were significantly correlated with disease severity but showed no correlation with sex. This further supports the notion that IL-18 is more closely related to disease activity rather than sex-based biological differences

The discrepancy between these studies may arise due to differences in sample size, demographic characteristics, disease severity (PASI scores). These variations underscore the complex nature of IL-18 regulation in psoriasis.

Regarding the relationship between family history and IL-18 levels in psoriasis patients, as shown in Table(2) the study reported that individuals with a positive family history exhibited lower serum IL-18 levels (6.34 ± 1.6 pg/mL) compared to those with a negative family history (8.12 ± 1.9 pg/mL). However, this difference was not statistically significant ($p = 0.328$). This indicates that familial predisposition may not have a direct or consistent influence on circulating IL-18 concentrations in psoriatic patients.

These findings are in agreement with the study (Wang et al. 2022)[20], which also reported no significant association between IL-18 levels and family history. That study suggested that the elevation of IL-18 in psoriasis patients is more closely linked to disease activity and systemic inflammation rather than hereditary factors.

In contrast, some studies have suggested that genetic predisposition may influence cytokine expression [21].

The lack of statistical significance in our results may be attributed to interindividual variability, or differences in disease duration and severity, which were not controlled for in this sub-analysis. Moreover, since IL-18 expression can be affected by various systemic factors such as obesity, infections, and metabolic comorbidities [29]. It is possible that these confounding variables may have diluted any potential association with hereditary predisposition. The current study shows that IL-18 levels were higher in patients with severe psoriasis (9.07 ± 1.2) compared to those with moderate disease (6.58 ± 1.8) as shown in Table (3), although the difference did not reach statistical significance ($p = 0.119$). Despite the non-significance, this trend suggests association between IL-18 and disease severity.

These findings are consistent with those reported by (Jasim 2017)[17], who observed elevated IL-18 levels in Iraqi patients with moderate and severe psoriasis. Their study

demonstrated a significant linear correlation between serum IL-18 concentrations and PASI (Psoriasis Area and Severity Index) scores, indicating a strong association between IL-18 and disease severity. Similarly, the current study revealed a comparable upward trend in IL-18 levels among patients with increasing disease severity.

According to the prevalence of comorbid conditions among individuals with psoriasis, including cardiovascular disease, diabetes mellitus, hypertension, and obesity. These findings align with previous research showing that psoriasis is not merely a skin disorder, but a systemic inflammatory disease associated with multiple comorbidities. [22], Among the participants, 26.2% were reported to have cardiovascular disease (CVD). This aligns with studies showing that chronic systemic inflammation in psoriasis patients contributes to endothelial dysfunction and atherosclerosis, thereby increasing the risk of CVD. Mehta et al. 2010 [23] found that severe psoriasis is linked to a higher risk of major adverse cardiovascular events, including myocardial infarction and stroke.

Diabetes mellitus was present in 13.8% of the sample. Psoriasis has been linked with insulin resistance, likely due to the inflammatory milieu shared by both conditions [24]. A meta-analysis by Armstrong et al. [25], reported that psoriasis patients have a significantly higher risk of developing type 2 diabetes mellitus. Regarding to hypertension was observation 27.7% of patients have hypertension this study align with (Armstrong, et al.)[25] who reported observational studies demonstrated that patients with psoriasis, particularly those with severe forms, have a significantly higher risk of developing hypertension compared to individuals without psoriasis.

On other hand several studies did not demonstrate an association between psoriasis and hypertension [26],[27], In the current study, 29.2% of psoriasis patients were obese, which aligns with findings from study by [28], showing a significant association between psoriasis and obesity. This reinforces the growing evidence that metabolic factors may play an important role in the pathophysiology and clinical burden of psoriasis.

CONCLUSION

Serum IL-18 levels were significantly higher in psoriasis patients, indicating its potential as a diagnostic marker. While not influenced by sex or family history, IL-18 levels tended to rise with disease severity. The moderate diagnostic accuracy (AUC = 0.714) supports its clinical value. Psoriasis was also associated with common comorbidities, confirming its systemic inflammatory nature.

ACKNOWLEDGMENT

I am especially grateful & indebted to all the staff of Al-Najaf Teaching Hospital, especially the Dermatology Consulting Staff. Financial and funding were personal.

Ethical approval

The present study which is conducted by authors (Noor saeed abd) was approved by the local Department of Medical Microbiology, Faculty of Medicine, University of Kufa, Najaf, Iraq committee.

Statement of Permission and Conflict of Interests

The others declare that there is no conflict of interest associated with the manuscript.

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