



# Evaluation of IL-17, IL-18 and IL-22 as Vital indicators of Iraqi Patients with Psoriasis

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**Abstract:** Psoriasis is a chronic inflammatory disease characterized by a number of immune response abnormalities. Cytokines are small, biologically active proteins that regulate cell growth, function, and differentiation and aid in the direction of the immune response and inflammation in psoriasis. This study was conducted to evaluate serum IL-17A, IL-18, and IL-22, levels by the enzyme-linked immunosorbent assay (ELISA) for detection the importance and effects these cytokines in psoriasis. Seventy-five patients with psoriasis (38 females and 37 males) were recruited from the Al Kindi General Teaching Hospital during the period between the 1st of December 2019 until December 2020, with mean age (35.30 ±8.64) years old, and 75 apparently healthy volunteers (40 females and 35 males), with mean age (33.40 ±6.25) years old, with no symptoms or history of psoriasis or other allergic or skin disorders (control group), In this study 3 ml sera samples from each individual of both groups were collected. The results demonstrated significant elevation of Serum IL-17A, IL-18, and IL-22 in the patient's group compared to healthy controls ( $P \leq 0.01$ ) in patients with psoriasis compared to healthy control. These data support the view that serum IL-17A, IL-18, and IL-22 are involved in the pathogenesis of psoriasis, possibly by induction and maintenance of psoriatic lesions. It recommends the use of cytokine (IL-17A, IL-18, and IL-22) as a useful follow-up marker for monitoring psoriatic patients and optimizing therapeutic strategies.

**Keywords :** Psoriasis, Cytokines, IL-17A, IL-18, IL-22.

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## Introduction

Psoriasis is a chronic, non-communicable, agonizing, disfiguring, and debilitating disease that is untreated until now and has a major adverse effect on the quality of life of patients, with a worldwide prevalence of approximately 1 to 3% (1), which is not explained simply by Mendelian inheritance. Genetic factors play a role in psoriasis development, although the exact causal mechanism of psoriasis is still unknown (2). After that significance of cytokines in psoriasis has been more understood. T helper 1 (Th1) cells and cytokines

released by these cells were the only ones studied at first. tumor necrosis factor (TNF), interferons (IFN), and other proteins found in cells interleukin-2 (IL-2), are linked to the emergence of and the maintenance of chronic inflammatory disorders such as Psoriatic rheumatoid arthritis which is a type of psoriasis (3). T cell activation causes psoriasis, which is associated by the secretion of proinflammatory cytokines such as (TNF-), (IL)-17A, IL-22, and interferon IFN- (5). The T helper inflammatory cytokine interleukin-17 (IL-17) was discovered to be positively linked with the severity

of disease (6). In psoriasis and psoriatic arthritis, IL17A and IL17AR have a significant function in promoting inflammation and as a marker for follow-up following treatment (7). Psoriatic individuals had significantly greater levels of IL22, and its concentrations were found to have a strong, positive relationship with the severity of the disease (8). IL-18 levels were found to be higher in early active and progressing plaque-type psoriatic lesions, and serum or plasma levels of IL-18 were linked to the Psoriasis Area and Severity Index in investigations. The mechanism through which IL-18 influences illness severity, however, is uncertain (9). so, this study was aimed to evaluate the role of IL-17, IL-18, IL-22 in the serum of Iraqi psoriatic patients and compare them to healthy controls. Also, investigate the association with disease severity to determine the use of these cytokines as markers of disease severity in patients with psoriasis.

### Materials and Methods

Blood samples (3 ml) were collected from 75 psoriatic patients and 75 healthy individuals. All patients enrolled in this study underwent no systemic treatment including glucocorticoids, immunosuppressive

drugs, or phototherapy at least 1 month before the cytokine's evaluation and sample collection period. Informed consent was obtained from all the patients and healthy controls. Blood samples from psoriatic patients and controls were taken under sterile conditions and centrifuged at 1000 g/15minutes. Then, the serum samples were subdivided into small aliquots to be stored at  $-20^{\circ}\text{C}$  until analysis for cytokines levels. Using a commercially available kit ELISA kits (AL-shkairate-Jordan) were used to determine serum IL- 17, IL- 18, and IL- 22 levels, according to the manufacturer's instructions.

### Statistical Analysis

The Statistical Analysis System-SAS (2012) ANOVA was used to show the effect of different groups in study parameters. The results were expressed as mean  $\pm$  standard error (SE). P-values  $< 0.05$  were considered significant and P-values  $< 0.01$  were considered highly significant in this study.

### Result and Discussion

The level of the three cytokines was elevated in patients compared with the control group as shown in Figure (1).

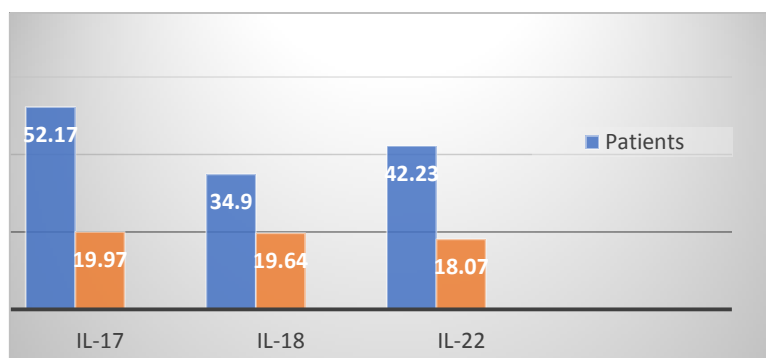


Figure (1): Comparison between Control and Patients groups in IL-17, IL-18, IL-22.

The results of cytokines presented in Table -1 the outcome revealed that there was highly significant ( $P \leq 0.01$ )

and difference between psoriatic patients and control groups.

**Table (1): Comparison between Control and Patients groups Interleukins.**

Group	Mean $\pm$ SE pg/ml		
	IL-17	IL-18	IL-22
Control	19.97 $\pm$ 0.65	19.64 $\pm$ 0.38	18.07 $\pm$ 0.32
Patients	52.17 $\pm$ 1.24	34.90 $\pm$ 0.79	42.23 $\pm$ 0.95
T-test	2.780 **	1.750 **	1.992 **
P-value	0.0001	0.0001	0.0001
** ( $P \leq 0.01$ )			

The results revealed that IL-17 levels were higher in patients with psoriasis than in the controls with mean levels of (52.17  $\pm$  1.24) pg/ml, (19.97  $\pm$  0.65) pg/ml, respectively with significant high differences ( $P \leq 0.01$ ). This finding is consistent with that of Razzaq *et al.* (2015), who discovered a substantial increase in the IL-17 serum mean concentration in psoriasis patients compared to controls in Karbala Province, other remarkable results by Al-Janabi (2018) indicate that IL-17A sera were estimated higher in psoriasis patients than healthy control. also, Abd Al Khaliq (2020) indicated that levels of Interleukin 17A were high before treatment These levels were reduced significantly after treatment with Etanercept injection in the patient's shoulder to give a lower level (13;14;7), IL-17 produced by (Th17) cell induces

the differentiation of naïve CD4+ T cells into helper T cells (Th17) (15). From the present results, in some patients with severe psoriasis, (Almost all of their bodies) as shown in figure (2), a significant increase in the level of IL-17 (78.275-72.676-71.784) pg/ml compared with patients with mild-to-moderate ones (Different parts of their body) as shown in figure (3) which are (55.528-39.443-27.342) pg/ml. And that agreement with (16), who indicated the increasing level of IL-17 in psoriatic patients. According to the severity of psoriasis, and supports the search that referred for the severity of the disease was associated with high levels of interleukin-17 compared to patients with moderate or mild severity with statistically significant high difference ( $p \leq 0.01$ )(17).



**Figure (2): Patient with sever psoriasis.**



Figure (3): Patient with mild psoriasis.

Estimation of IL-18 concentration had shown an elevation in its mean value among psoriasis patients ( $34.90 \pm 0.79$ ) pg/ml, in comparison with the healthy control group ( $19.64 \pm 0.38$ ) pg/ml, ( $P \leq 0.01$ ).

The current results indicate the significantly higher concentrations of pro-inflammatory cytokine IL-18, in psoriatic groups, compare with the control group. Niu *et al.* (13) indicated that this cytokine is implicated in the pathogenesis of psoriatic skin lesions (18), this result agreement with several results previous studies of the presence of an increase in the concentrations of IL-18 in psoriatic patients compared to the control group (19; 20; 21).

The current investigation also discovered a significant correlation between illness severity and psoriasis and serum IL-18 levels. The relation between IL-18 levels and psoriasis can be used as an objective measure of psoriasis activity and severity, this was consistent with the previous study implicating IL-18 with increased severity of psoriasis (22).

At the same time, the results of IL-22 indicated a significant elevation of serum in patients when compared with healthy controls. In which statistical analysis revealed that patients with psoriasis presented significantly higher

( $P \leq 0.01$ ) concentrations of IL-22 than healthy individuals. The mean concentration of IL-22 in psoriatic patients was  $42.23 \pm 0.95$  pg/ml, and the mean concentration of this cytokine in the controls amounted to  $18.07 \pm 0.32$  pg/ml, many of the previous studies were supported present results, where previous studies indicated a significant increase in the level of IL-22 of patients compared to healthy subjects (8). Wawrzycki *et al.* (2019) examined a relation between the plasma concentration of IL-22 and the severity of psoriasis (PASI score) and the statistical analysis revealed a significant positive correlation between PASI scores and plasma concentrations of IL-22 ( $p = 0.000042$ ) (23), this reinforces the current study. It was observed that Interleukin-22 was significantly overexpressed, most likely due to increased IL-23, its expression was also elevated in psoriatic skin, and in psoriasis, IL22 is responsible for altered keratinocyte proliferation and differentiation, and the production of inflammatory molecules.

## Conclusions

The present study has demonstrated that It was found that the level of serum IL17, IL-18, and IL-22 which was

elevated in all Psoriasis patients associated with disease severity. Therefore, Serum levels of IL- 17, IL- 18, and IL- 22 which correlated with the clinical severity of psoriasis may be an objective parameter for successful treatment and may be used for the follow- up of patients.

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