

Serum interleukin-30 level in patients with psoriasis and its correlation with psoriasis severity: a case-control study

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Abstract

Objectives: To examine the serum levels of interleukin (IL)-30 in patients with psoriasis and evaluate the correlations with the Psoriasis Area and Severity Index (PASI).

Methods: Serum was collected from 26 patients with psoriasis and 26 healthy controls in a case–control setting, and the level of IL-30 was determined using an enzyme-linked immunosorbent assay. Statistical analysis of the IL-30 levels among groups and further correlation analyses of IL-30 levels with PASI scores were performed.

Results: A significant increase in the level of IL-30 in patients with psoriasis compared with healthy controls was observed. In addition, a positive correlation between the IL-30 concentration and PASI scores was found in patients with psoriasis.

Conclusion: IL-30 is presumably involved in the proliferation of epidermal cells during the development of psoriasis. Further studies with a larger number of participants are required to comprehensively elucidate the biological roles of IL-30 in the pathogenesis of psoriasis.

Keywords

Psoriasis, interleukin-30, cytokine, psoriasis pathogenesis, Psoriasis Area and Severity Index, inflammation

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Introduction

Psoriasis is a common chronic autoimmune and skin inflammatory condition characterized by erythematous-round lesions that occur due to rapid skin cell production and the presence of immature skin cells.^{1,2} Psoriasis causes the skin to regenerate at faster than normal rates, resulting in the build-up of skin cells.^{3,4}

Psoriasis scales are commonly observed on large joints, such as elbows and knees. They may also develop on the back, hands, feet, neck, scalp, and face but rarely occur on the nails, mouth, and inguinal genitals.^{1,5} Psoriasis is generally associated with several other conditions that lead to reduced immunity, such as type 2 diabetes, inflammatory bowel disease, heart disease, psoriatic arthritis, anxiety, and depression.^{6,7} Psoriasis affects 2% of the population globally, of which 6.7 million are Americans.⁸

Cytokines are small molecular weight proteins that activate immune cells. Therefore, cytokine evaluation is important for monitoring immune system responses to chronic inflammation and autoimmune diseases, such as psoriasis.⁹⁻¹¹ Interleukin-30 (IL-30) is a 28 kDa protein belonging to the IL-6 cytokine family.¹²⁻¹⁴ IL-30 is mainly produced by immune cells of a myeloid origin, including macrophages, monocytes, microglia, and dendritic cells, activated by diverse microbial and immune stimuli. It is also produced by neutrophils, plasma cells, endothelial cells, and epithelial cells.^{13,15} IL-30 is involved in initiating both classic and trans-signaling pathways, suggesting that it may have various effects on different cell types.^{16,17}

IL-30 independently plays a significant role in the development and progression of autoimmune diseases, such as psoriasis, by regulating both T helper (Th)1 and Th17 cells.¹⁸ Moreover, a previous study reported that the measurement of serum cytokines in

patients with psoriasis allows for a better understanding and prediction of the disease pathology.¹⁹ Therefore, the evaluation of serum IL-30 levels in patients with psoriasis might be useful for monitoring the pathology and prognosis of psoriasis. This study aimed to examine the IL-30 level in the serum of patients with psoriasis and evaluate its correlations with the severity of the disease.

Materials and methods

Patients

Patients with a previously confirmed diagnosis of various degrees of plaque-type psoriasis were enrolled in this case-control study. Additionally, age- and sex-matched healthy, non-psoriatic volunteers with no family history of psoriasis were included as controls. All participants had been admitted to the dermatology inpatient and outpatient departments of Nanfang Hospital, Guangzhou, China, between 2018 and 2019.

Patients on systemic immunosuppressant therapy, such as methotrexate, systemic steroids, and other drugs, and patients with any type of cancer, systemic, or dermatological disease with a potentially compromised immune system were not included in the study. The patients with psoriasis were divided into three groups according to their psoriasis area severity index (PASI) score: mild (PASI < 10), moderate (PASI 10–29), and severe (PASI > 30). The study was approved by the Human Specimens Collection and Use Ethics Committee of the Southern Medical University, Guangzhou, China (Approval. No. NFEC-2018-01-6) and carried out following relevant rules and approved protocols. Signed informed consent was obtained from all patients and volunteers. This study was conducted according to the declaration of Helsinki principles²⁰ and reported

following the STROBE guidelines for case-control studies.²¹

IL-30 measurements. Whole venous blood was obtained from all participants in the study. Their serum was separated by centrifugation for 20 minutes at $1000 \times g$ and stored at -80°C until examination. The serum IL-30 level was examined using an enzyme-linked immunosorbent assay kit for human IL-30 purchased from Elabscience (Wuhan, China), and all steps were performed in accordance with the manufacturer's manual.

Statistical analysis. Data were analyzed using IBM SPSS Statistics for Windows, Version 22 (IBM Corp., Armonk, NY, USA) and Prism software (GraphPad 8 software, San Diego, CA, USA) and expressed as the mean \pm standard deviation (SD). The comparison between two means was performed by student's t-test, and more than two means were compared by one-way analysis of variance. Not normally distributed data were analyzed by Mann–Whitney U and Kruskal–Wallis tests. Spearman's correlation analysis was performed to evaluate the relationship between IL-30 levels and PASI scores. A p -value of <0.05 was regarded as statistically significant.

Results

Twenty-six patients with psoriasis and 26 healthy controls were included in this study (Figure 1a). The mean age \pm SD was 45.5 ± 12.8 years for patients with psoriasis and 40.1 ± 16.2 years for the healthy controls. Additionally, patients aged less than 40 years accounted for the highest proportion of participants (44.2%) (Table 1). No significant difference was observed between the two groups regarding the age distribution. More than two-thirds (69.2%) of the psoriasis cases were men compared with 46.2% for the control group. The statistical

analysis of IL-30 levels in patients with psoriasis (111.96 pg/mL) and controls (33.76 pg/mL) revealed a significant difference in the mean IL-30 concentration between the groups (Table 1 and Figure 1b) ($p < 0.001$). Moreover, the results of the Mann–Whitney test showed that the mean rank of IL-30 in the serum of patients with psoriasis (890) was significantly higher than that of controls (488) ($p < 0.001$). However, no significant differences in the mean rank of IL-30 were found among the age groups (Table 2) of the psoriasis cases or controls. Additionally, a comparison of the mean rank of IL-30 among sexes revealed no significant differences in either the psoriasis or control groups (Table 2).

Regarding Spearman's correlation analysis between IL-30 levels and PASI scores, a weak non-significant positive correlation was found in psoriasis cases ($\rho = 0.174$) (Figure 1c). Moreover, no significant differences were observed in the mean rank of IL-30 among the three categories of psoriasis (mild, moderate, and severe) (Table 3). Our results showed a predominance of male patients with psoriasis (Figure 2a). Among patients with psoriasis, there was no significant association between the mean rank of IL-30 and the duration of their disease (Figure 2b) or their age at diagnosis (Figure 2c and Table 3).

Discussion

Psoriasis is a common chronic immune-mediated inflammatory skin disorder characterized by erythematous silvery scaling of the skin and severe itching. Reports indicate that psoriasis affects about 2% of the global population and reduces the quality of life for patients, limiting their activity and productivity in a community.^{8,22} With the advancement of knowledge regarding this condition, studying the possible contribution of cytokines to the pathogenesis of psoriasis has received increasing attention.

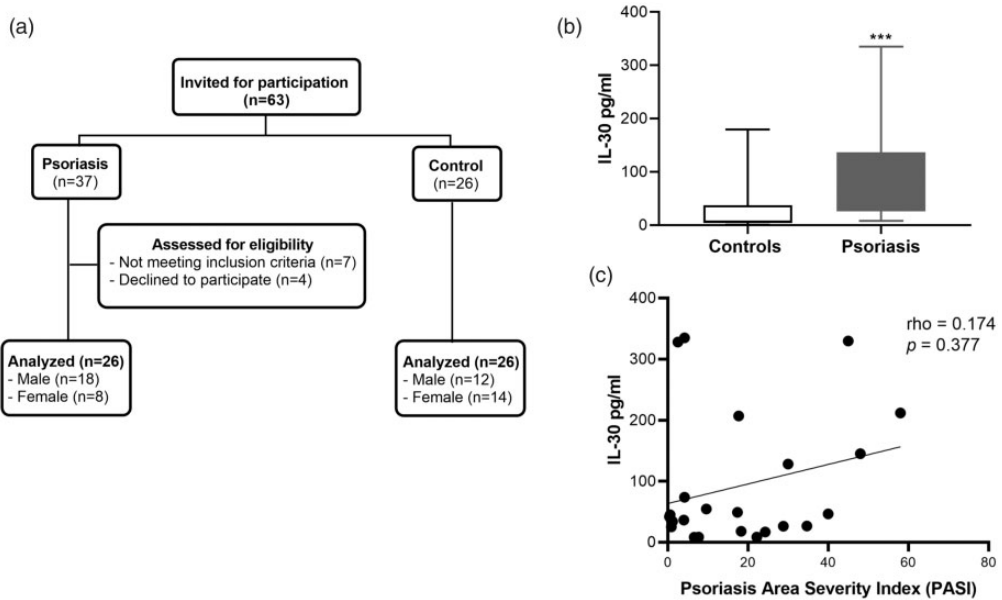


Figure 1. IL-30 levels in patients with psoriasis and healthy controls. (a) Flow diagram of the study. (b) A comparison of the serum IL-30 levels in the psoriatic (N=26) and control groups (N=26) determined using an enzyme-linked immunosorbent assay kit. The results are shown as the mean \pm standard deviation. *** $p < 0.001$ by Student's t-test. (c) Spearman's correlation analysis of IL-30 levels and PASI scores in patients with psoriasis IL-30, interleukin-30; PASI, Psoriasis Severity and Area Index.

Table 1. The age, sex distributions, and IL-30 level in the psoriatic and control groups.

	Psoriasis		Control		Total		p
	No.	(%)	No.	(%)	No.	(%)	
Age (years)							
<40	10	(38.5)	13	(50.0)	23	(44.2)	
40–49	6	(23.1)	4	(15.4)	10	(19.2)	
≥ 50	10	(38.5)	9	(34.6)	19	(36.5)	0.656 [#]
Mean (\pm SD)	45.5	(± 12.8)	40.1	(± 16.2)			0.188 [†]
Sex							
Male	18	(69.2)	12	(46.2)	30	(57.7)	
Female	8	(30.8)	14	(53.8)	22	(42.3)	0.092 [#]
Total	26	(100.0)	26	(100.0)	52	(100.0)	
IL-30							
Mean (\pm SD)	111.96	(± 149.66)	33.76	(± 56.48)			<0.001 [‡]

IL-30, interleukin-30; SD, standard deviation. [†]By t-test for two independent samples. [#]By chi-square test. [‡]By Mann-Whitney test.

To this end, several studies have reported that various cytokines are associated with psoriasis as their levels are increased in the serum of patients. These include IL-6, IL-8,

IL-12, IL-17, IL-18, and IL-23.^{19,23–25} However, as evidenced via a PubMed search, no study has reported the serum levels of IL-30 in patients with psoriasis to

Table 2. Mean IL-30 level by age and sex in the psoriatic and control groups.

	N	Mean IL-30	(±SD)	Mean rank	p†
Psoriasis					
Age (years)					
<40	10	72.94	(±97.41)	12.40	0.467
40–49	6	104.73	(±135.19)	11.50	
≥50	10	155.32	(±196.87)	15.80	
Sex					
Male	18	106.65	(±159.96)	12.72	0.437
Female	8	123.90	(±132.70)	15.25	
Control					
Age (years)					
<40	13	40.77	(±63.93)	14.54	0.720
40–49	4	6.06	(±3.72)	11.13	
≥50	9	35.95	(±57.99)	13.06	
Sex					
Male	12	29.30	(±51.95)	13.75	0.877
Female	14	37.59	(±61.78)	13.29	

IL-30, interleukin-30; SD, standard deviation. †By Kruskal–Wallis test.

Table 3. Comparison of the mean and mean rank of IL-30 with the severity, duration, and age at diagnosis of patients with psoriasis.

Psoriasis characteristics	N	Mean IL-30	(±SD)	Mean rank	p
Severity‡					
Mild	14	121.23	(±183.87)	13.43	0.993#
Moderate	3	91.27	(±101.24)	14.00	
Severe	9	104.43	(±110.07)	13.44	
Duration (years)					
<10	14	86.96	(±113.82)	12.07	0.304†
≥10	12	141.12	(±184.03)	15.17	
Age at diagnosis					
<40	17	106.74	(±170.96)	12.00	0.169†
≥40	9	121.80	(±106.55)	16.33	
Total	26	111.96	(±149.66)		

IL-30, interleukin-30; SD, standard deviation. ‡Assessed by the Psoriasis Area and Severity Index. #By Kruskal–Wallis test. †By Mann–Whitney test.

date. To address this knowledge gap, the current study assessed the demographic and clinical laboratory characteristics of patients with psoriasis and controls, which interestingly revealed the possible contribution of IL-30 to psoriasis.

IL-30 is an independent cytokine produced by immune cells of a myeloid origin that mediates antineoplastic effects in

several tumor models,^{26,27} presumably including psoriasis. This study determined that the serum IL-30 level in patients with psoriasis was significantly higher compared with that of controls. Moreover, our findings suggest a positive correlation between the serum levels of IL-30 and the severity of psoriasis indicated by the PASI score, although this result was not statistically

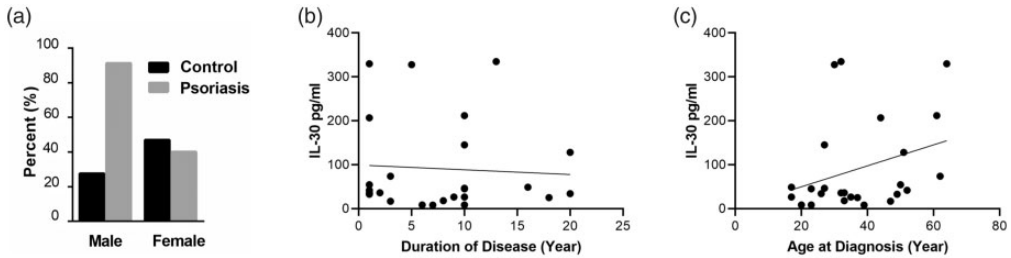


Figure 2. Association of sex, age at diagnosis, and duration of the disease to serum IL-30 levels in patients with psoriasis. (a) Predominance of male patients with psoriasis to female patients with psoriasis. The results are shown as the mean. No significant association was observed by Spearman's correlation analysis between the mean rank of serum IL-30 and the duration of disease (b) or the age at diagnosis (c) in patients with psoriasis.

IL-30, interleukin-30.

significant. Despite the limitations of the PASI score, including its non-linear scale^{28,29} and lack of sensitivity,³⁰ the PASI score has been the most commonly recommended clinical index of psoriasis severity.³⁰ Of note, consistent with the results of previously reported studies on cytokines in psoriasis,^{23,25} the present study showed that the serum level of IL-30 was not associated with age or sex. Similarly, the age at diagnosis and duration of the disease in patients with psoriasis were not significantly associated with the mean rank of the serum IL-30 level. These results are consistent with the findings of previously reported studies on the association of related cytokines with psoriasis.^{25,31}

Several studies have reported a similar incidence of psoriasis in men and women.³² However, the current study showed a predominance of male patients with psoriasis (Figure 2a), consistent with the findings of Fernandez et al.,³³ whereas others reported a higher prevalence of women.³⁴ The reported studies on psoriasis with an increased proportion of women suggest a possible contribution of sex to the quality of life based on the idea that women are more concerned about their health and treatment than men.³⁵ Nevertheless, the limited available data

and the population awareness of psoriasis may have contributed to selection bias. Additionally, in contrast to the findings of several previous studies that have reported age and sex among the most contributing factors to the severity of psoriasis,^{36,37} the current study found no significant differences in the mean rank of serum IL-30 among the age or sex groups of patients with psoriasis.

Recent studies on cytokines have enabled a better understanding of the pathophysiology of psoriasis.³⁸ However, the mechanisms underlying the development of psoriasis are particularly complex.³⁹ Notably, the hyper-proliferation and abnormal differentiation of keratinocytes in psoriasis have been associated with impaired T-lymphocytes.⁴⁰ Consistently, several inflammatory cytokines found to be elevated in serum samples during psoriasis have been shown to be correlated with disease severity. Thus, determining the specific or combined cytokines that play a main role in the pathogenesis of psoriasis can revolutionize the diagnosis and treatment of psoriasis. The function of IL-30 in psoriasis lesions has not yet been fully elucidated and requires further *in vitro* and *in vivo* studies. However, the current study demonstrated a significant increase in the

serum IL-30 level in patients with psoriasis compared with the controls and a positive correlation of the IL-30 level with PASI scores. These findings indicate that the downregulation of IL-30 expression may attenuate the abnormal keratinocyte proliferation and other related features during the pathogenesis of psoriasis.

Overall, consistent with the theoretical features of psoriasis, the current results demonstrate the involvement of IL-30 in the proliferation of epidermal cells in psoriasis, which further confirms that psoriasis represents an immune-mediated systemic disease. However, the origin of IL-30 in the serum and whether the changes in the serum IL-30 level in patients with psoriasis are a cause or a consequence of the disease remain unclear. The limitations of the study include a small number of participants, which may have affected the statistical significance of the results, and the absence of *in vivo* investigations in an animal model. Further *in vitro* and *in vivo* studies would be beneficial to fully elucidate the contributions of IL-30 to the pathogenesis of psoriasis.

Conclusion

The findings of the current study substantiate previously reported studies on the involvement of different cytokines in the pathogenesis of psoriasis.^{19,23–25} These cytokines involved in the interactions between keratinocytes and T-lymphocytes may contribute to the pathogenesis of psoriasis. However, the production and biological properties of these cytokines in psoriasis remain unknown. This study is the first to report on the serum levels of IL-30 in patients with psoriasis, which may improve the early diagnosis and comprehensive management of patients with this disease.


Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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Supplemental Material

Supplemental material for this article is available online.

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