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Original article

Role of serum IL-26 in Pathogenesis of Psoriasis vulgaris

Soha Mahmoud Abd El-Salam[1] , Shimaa Taha Osman[2], Naglaa Abd Elmoniem Radi[3] Yasser Mostafa Gohary[2]

[1] *microbiology and immunology department, Faculty of Medicine, Suez University, Suez, Egypt*

[2]*Dermatology department, Faculty of Medicine, Beni-Suef University, Beni-Suef, Egypt*

[3]*microbiology and immunology department, Faculty of Medicine, Beni-Suef University, Beni-Suef, Egypt*

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Corresponding Author:

Soha Mahmoud Abd El-Salam

soha86484@gmail.com

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Abstract :

Background: Systemic inflammation and thick, red, scaly plaques on the skin characterize psoriasis vulgaris, which is a common and varied chronic inflammatory dermatological disorder. IL-26 has been categorized as both an IL-10 family member and an IL-20 subfamily member. This cytokine was first found in T cells that had been modified by the herpesvirus saimiri. **Aim of the work**: We want to learn more about the relationship between IL-26 levels and the severity of psoriasis by comparing the serum and tissue IL-26 levels of people with psoriasis to those of a healthy control group. **Patients and Methods**: This study was a case-control research that took place between March 2021 and September 2021 at the Beni-Suef University Hospital Dermatology

outpatient clinic. Twenty men and ten females with psoriasis participated in the research, which was approved by the Research Ethics Committee (REC). Patients' ages varied widely, from 28 to 50, with a mean (standard deviation) of (42.50 ±6.5) years. Thirty people who did not have psoriasis (healthy controls) participated in the research. In terms of age and sex, these controls were excellent analogs for the psoriasis patients. Every individual who took part in the study had their whole medical and personal history compiled. The IL-26 Human ELISA kit was used to analyze the concentration of IL-26 in the blood and their expression in tissues. **Results:** In contrast to the control group of healthy people, those with a psoriasis diagnosis were shown to have significantly higher levels of serum IL-26 and tissue expression. Clinical psoriasis severity, as measured by the Psoriasis Area and Severity Index (PASI) score, was shown to be positively correlated with both the blood level and tissue expression of IL-26. Serum IL-26 concentration was positively and statistically significantly related to Psoriasis disease severity and duration. Serum and tissue levels were not associated with age, gender, family history, onset, or progression of illness in patients. **Conclusion:** IL-26 may be related to the severity of psoriasis and plays a crucial part in the disease's development .Our research looks at how Interleukin-26 (IL-26) plays a part in the development of psoriasis by analyzing its expression in both tissue and serum samples.

1. Introduction:

About 2% of people in Europe and North America are affected with psoriasis (1), a chronic inflammatory skin illness that has significant physical and psychological consequences. Psoriasis is more common in men than in women, and its frequency among Japanese dermatology patients is estimated to be 4.43 percent, whereas in the United States it is between 2 and 3 percent. Plaque psoriasis (or psoriasis vulgaris) is one of the subtypes of psoriasis; others include guttate psoriasis, inverse psoriasis, palmoplantar pustulosis, generalized pustular psoriasis, and erythrodermic psoriasis. Many people with plaque psoriasis, which accounts for around 85% of cases, notice erythematous, sharply demarcated plaques on their skin. Usually seen on the extensor surfaces, trunk, and scalp, these plaques are pruritic and coated in silvery scales. Plaques arise when skin lesions join together and multiply, eventually covering large areas of skin (6). Moderate psoriasis is defined by a small number of localized inflammatory skin lesions, whereas severe psoriasis is characterized by widespread plaques that cover more than 10% of the body's surface area (7). Psoriasis is characterized by changes in histopathology caused by keratinocytes secreting cytokines that recruit neutrophils and macrophages to areas of inflammation and activate dendritic cells (1).

Dendritic cells' cytokine release, including interferon-alpha (IFN-a) secretion, contributes to the onset of psoriatic manifestations (8). The epidermis grows too quickly due to the pro-inflammatory cascade (9). Th1, Th17, and natural killer cells (10). all produce significant amounts of interleukin-26 (IL-26). Human and mouse fibroblasts have the IL-26 receptor, and upon stimulation, these cells produce more collagen (11).

Psoriasis and allergic contact dermatitis are only two of the many chronic inflammatory disorders that interleukin-26 (IL-26) plays a crucial role in. Angiogenesis in psoriatic skin is triggered by interleukin-26 (IL-26), which does so by inducing keratinocytes to produce fibroblast growth factors (FGFs). Increased levels of FGF1, FGF2, and FGF7 in the blood of people with psoriasis lead

to increased proliferation, tube formation, increased vascularization, and immune cell infiltration (13). By encouraging angiogenesis and fibroblast growth factor synthesis, IL26 has been hypothesized to contribute to the pathophysiology of psoriasis vulgaris.

1. Patients and methods:

Study population:

Between March and September 2021, Beni-Suef University Hospital's Dermatology outpatient clinic data was collected for the current Case-Control study. Two groups were formed from the participants. Thirty people with psoriasis made up Group 1, whereas the same number of people in perfect health made up Group 2. Specific inclusion and exclusion criteria were used to identify patients and controls. Patients of any age or gender who had been diagnosed with psoriasis met the study's inclusion criteria, The age and gender of the healthy controls is similar to that of the patients. In research, "exclusion criteria" People getting phototherapy were included . Patients who are given medicines (such immunosuppressants) that affect the measured variable sufferers with systemic diseases including diabetes and hypertension, those with impaired immune systems, those with skin cancers, long-term illness sufferers, and those in need of immediate medical attention.

Clinical data:

Procedures performed on patients and controls alike in this investigation included: A detailed history of everything that has happened. Age, sex, start, course, longevity, family history, and triggering causes of psoriasis are among the study's characteristics of interest. The clinical evaluation's stated goal was to use the Psoriasis Area and Severity Index (PASI) to determine the extent, kind, and location of the patient's psoriasis .

Laboratory work out:

Blood samples were collected from people with a psoriasis diagnosis, and 4-mm punch biopsies were taken from the skin of both affected and unaffected regions (matched samples) of both those people and a set of healthy people who served as controls. The buttock area that was not exposed to UV light was used to collect the samples. After that, an IL-26 Human Enzyme-Linked Immunosorbent Assay (ELISA) kit from Sino Gene Clon Biotech Co., Ltd. was used to

determine the IL-26 levels in the blood and tissue samples.

Statistical analysis:

SPSS (Statistical Package for the Social Sciences) version 25 for Windows 10 was used to conduct the statistical analysis. In this investigation, we used the Chi-square test, the Student t-test, and the One-way analysis of variance (ANOVA). In addition, Pearson's correlation analysis was used to check for a linear connection between IL-26 expression and the other variables. P-values less than 0.05 were taken into account to establish statistical significance.

Ethical statement:

The medical school's ethics board at Beni-Suef University has given its stamp of approval to this study. All participants were given a thorough explanation of the study's goals and given the opportunity to provide their written permission before they were enrolled. The database is managed in a way that ensures its security and privacy.

2. Results:

The current study included 30 patients from both sexes with psoriasis. They all presented to dermatology clinic at Beni-Suef University hospital. The psoriatic patients included in these paper were 20 males and 10 females, their age ranged from 28 to 50 years, the average of age was; 42.50 ±6.5. Also 30 healthy controls were taken, their age and sex matched to the psoriasis cases. 66.7% of participants were males and 33.3% were females, the average of age for patients was 42.50 ±6.5 years which is not statistically significant **(Table-1).**

Table (1): Age and Sex Distribution of the Studied Population; (N= 60):

		N (%)		TOTAL	p-value
		Psoriasis Cases N= 30	**Negative Controls N= 30**		
Sex	**Male**	20 (66.7)	24 (80.0)	44 (73.3)	0.283
	Female	10 (33.3)	6 (20.0)	16 (26.7)	
Age		42.50 ±6.5	43.07 ±7.03	60(100%)	0.730

** P-value ≤ 0.05 is significant with (Chi-Square test).*

In psoriasis cases; cold was the highest predisposing factor of psoriasis (53.3%), the majority of cases were with gradual onset of (93.3%), 56.7% were in remission & exacerbation of psoriasis course. 13.3% of cases had positive family history of psoriasis, the average of disease duration was 116.70 ±77.97 months. the Psoriasis Areas and Severity Index (PASI) average was 7.7 ±6.2 points **(Table-2).**

Table (2): Clinical history of Psoriasis Disease among studied patients; (N= 30):

		N	%
Precipitating Factors	Sun	3	10
	Cold	16	53.3
	Stress	8	26.7
	Stress +Cold	3	10
Onset	Sudden	2	6.7
	Gradual	28	93.3
Course	Stationary	4	13.3
	Regressive	7	23.3
	Progressive	2	6.7
	Remission & Exacerbation	17	56.7
Family History	Yes	4	13.3
	No	26	86.7

Table (3): represent a positive significant linear correlation between Psoriasis Area Severity Index (PASI) score and serum level of interleukin-26 (IL-26) was (r=0.734, p<0.001), and between Psoriasis Area Severity Index (PASI) score and tissue expression of interleukin-26 (IL-26) was (r=0.714, p<0.001) among studied cases of psoriasis patients.

Table (3): Correlation between Expression of interleukin-26 (IL-26) (serum and tissue) with Psoriasis Area Severity Index (PASI) score in psoriasis cases; (N= 30):

		Psoriasis Area Severity Index (PASI) score
Level in serum (ng/ml)	r	0.734
	p-value	<0.001*
Level in tissue (ng/ml)	r	0.714
	p-value	<0.001*

r Pearson correlation coefficient analysis

Table (4); demonstrates a moderate positive significant linear correlation between serum level of IL-16 with Psoriasis disease duration (r=0.464, p=0.010), and between tissue expression of IL-26 with Psoriasis disease duration (r=0.471, p=0.000) among studied psoriasis patients.

Table (4): Correlation between Expression of interleukin-26 (IL-26) (serum and tissue) with Disease Duration in studied psoriasis patients; (N= 30):

		Duration of the disease (months)
Level in serum (ng/ml)	r	0.464
	p-value	0.010*
Level in tissue (ng/ml)	r	0.471
	p-value	0.009*

r Pearson correlation coefficient analysis

As shown in **Table (5);** receiver operating characteristic (ROC) curve analysis was used to consider the clinical diagnostic accuracy of IL-26 serum and tissue expression in psoriasis patients and the normal individuals; the results of IL- 26 (ROC) curve analysis showed p-value <0.05 so; the serum and tissue IL-26 levels could help in diagnosis the psoriasis disease state at a statistically significant level. For serum level, with a 48% Sensitivity (true positive cases) and 99.2% Specificity (true negative cases) at a cutoff point level ≥3.89 (ng/ml), while for tissue sample expression, with 56.7% Sensitivity (true positive cases) and 99.8% Specificity (true negative cases) at a cutoff point level ≥3.16 (ng/ml).

Table (5): The ROC curve analysis of interleukin-26 results (IL-26) (serum and tissue) expression in the studied Psoriasis cases and healthy control:

	AUC	**SE**	**95% CI**	**Sensitivity**	**Specificity**	**Cutoff value**	**p-value**
IL-26 (serum)	0.783	<0.001	0.653 – 0.913	48%	99.2%	≥ 3.89 (ng/ml)	<0.001
IL-26 (Tissue)	0.785	<0.001	0.671 – 0.899	56.7%	99.8%	≥ 3.16 (ng/ml)	<0.001

AUC= Area under the curve, SE= Standard Error, CI= Confidence interval of AUC.

3. Discussion:

Over 125 million individuals worldwide are affected by psoriasis, a chronic inflammatory skin disease with immune-mediated features (14). Psoriasis is a skin disorder characterized by persistent inflammation, with inflammatory cells such macrophages, neutrophils, and activated dendritic cells being recruited and defined by the production of cytokines. Through the release of cytokines that excite keratinocytes and associated components (15), Th17 cells are known to play critical roles in the development of this illness.

The expression of IL-26 has been linked to localized inflammation, according to recent studies. In addition, patients with chronic inflammatory disorders like psoriasis have been discovered to have higher IL-26 expression in their blood, sputum, synovial fluid, bronchoalveolar lavage fluid, and cerebral fluid (16).

Using an IMQ-induced model of psoriasis, the authors (15) show that IL-26 contributes to the worsening of skin inflammation. Vascular invasion and immune cell infiltration are thought to be responsible for this worsening .

The major purpose of this research was to examine the expression of IL-26 in psoriasis patients' tissues and blood in relation to a healthy control group. The research also attempted to determine whether or not there was a connection between IL-26 levels and the severity of psoriasis.

Human interleukin 17 generating helper T cells have their cytokine profile and activity analyzed by Wilson and his colleagues , Psoriasis patients' lesional and nonlesional skin had considerably greater levels of the TH-17-derived cytokine IL-26 compared to normal skin (17). In line with this finding, we found that IL-26 expression in psoriatic patients' tissues and serum was much higher than that in the unaffected skin of healthy control participants .

Blood vessel invasion in the dermis is a hallmark histological feature of psoriatic skin lesions (18). Previous studies have shown that IL-26 significantly affects both angiogenesis and leukocyte recruitment. Psoriasis and T cell-mediated contact hypersensitivity responses are inflammatory skin disorders where controlling IL-26 may be of major importance in regulating excessive

angiogenesis. Based on these results, it seems that IL-26 manipulation may have practical implications (13).

There was a moderate positive significant linear correlation between serum level of IL-26 with psoriasis area severity index (PASI) score and with psoriasis disease duration among studied psoriasis patients. It had been reported that increasing concentrations of IL-26 significantly correlated with disease severity ($r = 0{\cdot}6$, $P = 0{\cdot}02$), as assessed by PASI score, even if there is a limit in number of patients **(19)**. According to these observations, the significance of IL-26 had been increased as an inducer of proinflammatory and antimicrobial mediators **(20)**.

Psoriasis is an inflammatory skin disorder, and the search for neutralizing anti-IL-26 monoclonal antibodies has led to the development of a unique therapeutic method for treating this illness (21). Our study's results may pave the way for future studies that aim to determine whether or not IL-26 inhibition can reduce cutaneous production of proinflammatory mediators important for T-cell development and psoriasis treatment.

4. Conclusions:

Our results suggest that IL-26 may play a crucial role in the progression of psoriasis and may affect the severity of the illness. The current study shows that psoriasis is linked to increased IL-26 levels in both blood and tissue. More research with a bigger sample size is needed to confirm or disprove a role for IL-26 in the etiology of psoriasis .

Limitations:

Several problems were encountered over the course of this investigation. First, there was a limited number of patients included in the analysis. Second, the study didn't look at how IL-26 is expressed in the deeper layers of skin. Furthermore, non-lesional skin from the same psoriatic individuals was not compared to lesional skin in the research. In addition, there was no evaluation of the molecular pathways IL-26 uses in the pathogenesis of psoriasis sickness.

Conflict of interest:

None

5. References:

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