Evaluation of CARD14(PSORS2) Gene Expression and IL-17 Serum Levels in Iraqi Patients with Psoriasis

Aqeel Razak. Abdel Abbas[1], Heyam Mohammed Al-Kenan[2]

[1]*Department of Medical Microbiology College of Medicine, University of Qadisiya, Diwaniya, Iraq. Email: med.post24.38@qu.edu.iq*
[2]*Clinical Immunology Professor, Department of Medical Microbiology, University of Al-Qadisiya, College of Medicine, Diwaniya, Iraq*

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ABSTRACT
Background: Psoriasis is an inflammatory skin condition influenced by CARD14 gene dysregulation and polymorphisms, affecting NF-kB activation and cytokine production, with IL-17 playing a key role in its pathogenesis. Objective: To estimate serum IL-17 level and andCARD14(PSORS2) gene expression in Iraqi patients with Psoriasis. **Materials and methods:** the study involved 60 Psoriasis patients, and 60 healthy individuals admitted to a hospital between October 2023 and April 2024. Blood samples were collected, frozen for RT-PCR detection of CARD14 gene expression, and used for IL-17 serum levels by ELISA assay. **Results:** The study reveals a significant increase in IL-17 levels in psoriasis patients compared to healthy controls and a significant increase in PSORS-2 gene expression in psoriasis patients. Conclusion The study reveals a significant rise in IL-17 levels and PSORS-2 gene expression in psoriasis patients, suggesting that inflammation may be exacerbated by increased IL-17 production.

1. Introduction

Psoriasis is a prevalent inflammatory dermatological illness affecting around 3% of the worldwide population[1][2] [3]. Plaque psoriasis, which accounts for around 90% of cases, presents as red plaques on certain body parts.[4] [5]. Psoriasis is distinguished by the excessive synthesis of antimicrobial peptides, which could be used as diagnostic indicators and targets for treating inflammatory disorders[6] [7]. Undefined Psoriasis is a multifactorial condition that includes gene susceptibility elements, environmental triggers, and immune system imbalance, where plaque psoriasis is the most common Psoriasis[8]. Undefined IL-17A, IL-17F, and IL-17 receptor A are the main cytokines that act in psoriatic disease situations [9][10]. The cause of proinflammatory cytokines and chemokines produced by keratinocytes is cytokines. These chemokines cause epidermal hyperplasia, resulting in the proinflammatory feed-forward cycle linked to plaque psoriasis[11] [12]. According to clinical studies, patients with Psoriasis may enjoy the advantages of IL-17A inhibition, which relates to improving hepatic and metabolic markers[13][14]

The CARD14 gene is found to be critical in the course of Psoriasis because it regulates NF-kB signalling, one crucial pathway in this disease[15][16]. Psoriasis, which has many paperwork consisting of common plaque kind, Psoriasis of scaly ache, palms and soles Psoriasis, and pityriasis rubra pilaris, is connected to mutations found inside the gene CARD14[17]. Inactivating mutations of the NF-κB pathway are key elements of immune sign transduction in the skin, severely concerned modulation of inflammatory responses and the law of cutaneous mobile viability [18].undefined A additionally that mutations of the gene autosomal dominant CARD14 are related to an expanded chance of Psoriasis, which further confirms the important function of the gene inside the physiology of this disorder[19].

Aim of study

The aim of this study was to assess the serum IL-17 concentration and evaluate the expression of the CARD14 (PSORS2) gene in psoriasis patients from Iraq.

2. Methodology

The current study involved a cohort of 60 participants, 32 males and 28 females. The participants' ages spanned from 10 to 68 years, and they were enrolled in the experiment from October 2023 to April 2024. As a control group, this study included another group of 60 people who seemed healthy

(34 women and 26 men) and had no history of systemic disease. These people were deemed clinically healthy. Patients with DM, autoimmune disorders, atopic dermatitis, patients with inflammatory skin conditions, and pregnant women were not included in our sample. Five millilitres of blood were drawn via vein puncture with an aseptic technique and disposable syringes. 2 ml of every sample was moved into an EDTA tube and promptly frozen at -20 degrees Celsius until it was needed again. This prevented repetitive thawing and freezing during the polymerase chain reaction amplification and card14 (PSORS2) gene expression procedure. The remaining (3 ml) was transferred to sterile test tubes (Plain tube), allowed to clot at ambient temperature for a few minutes, and then centrifuged for ten minutes at 2500 rpm to extract the serum. After that, the sample was kept cold for the ELISA assay procedure. Every subject gave their oral informed agreement, and the research complies with the ethical guidelines of Marjan Teaching Hospital.

Measurement of serum IL-17 by ELISA

The Sandwich Enzyme-Linked Immunosorbent Assay (ELISA) kit was used to measure the amount of IL-17 in accordance with the manufacturer's instructions (Elabscience, USA).

RNA extraction

Blood samples were extracted with RNA using the TRIzolTM reagent procedure (Thermo Scientific, USA).

Calculating Gene Expression (Gene Fold)

Results from qPCR can be interpreted using two methods: absolute and relative quantification. Relative quantification measures changes in gene expression in relation to a reference gene sample, whereas absolute quantification employs a standard curve to measure the amount of input gene. When relative gene abundance between treatment groups is more relevant than exact DNA/RNA molecular counts, relative quantification is frequently used. To ensure accuracy when creating standard curves, the Pfaffl equation is utilized to determine gene expression, gene fold, and R.Q. values.[20]:

$RQ = 2\text{-}(\Delta\Delta CT)$

By gathering the C.T.e. C.T. average value for every sample that was triple-counted, the gene fold was computed. To normalize the gene to a gene unaffected by the experiment, the ΔCT value—the difference in iC.T.CT values for the reference gene and the interest gene—was computed for each sample.

$\Delta\Delta$ CT = Δ CT (treated sample) – Δ CT (untreated sample (Control))

Statistical analysis

The study used SPSS 26 and Excel 2010 to gather, analyze, and present quantitative data. The Kolmogorov-Smirnov normality test was used to assess the normal distribution of variables. Independent sample t-tests were used to compare means between groups. ANOVA tests were used to compare group means. The chi-square test was used to analyze associations between categorical variables. The risk was evaluated using an odds ratio and 95% confidence interval. The Pearson correlation coefficient was used to assess numerical variables. The receiver operator characteristic (ROC) curve was used to determine the significance level [21].

3. Results and Discussion

In this study, sixty participants with a diagnosis of Psoriasis and sixty healthy persons who served as control subjects were enlisted. The patient and control groups' demographic characteristics are shown in Table (1). The patient's average age was 30.11 ± 8.07 years, whereas the control group's average age was 32.86 ± 8.32 years. There is no statistically significant difference in the mean age between the two groups, according to the statistical analysis (P=0.321). The frequency distribution of ill and control individuals is shown in Table (1), with age group classifications. There was no statistically

significant difference (P=0.149) in the age group frequency distribution of the patients and control group, which is consistent with findings from other studies. The group of patients.

Table (1): The healthy control groups and Psoriasis sufferers' demographics

Characteristic	Patients with Psoriasis *n* = 60	Healthy control *n* = 60	P
Age (years)			
Mean ±SD	30.11 ± 8.07	32.86 ± 8.32	0.321 ŧ
Range	10–68 years	11– 70 years	NS
< 20, *n* (%)	21 (35.0%)	12 (20.0%)	0.149 ¥ NS
20-29, *n* (%)	12 (20.0%)	18 (30.0%)	
≥ 30, *n* (%)	27 (45.0%)	30 (50.0%)	
Gender			
Male, *n* (%)	32 (53.3 %)	26 (43.3 %)	0.273 ¥ NS
Female, *n* (%)	28 (46.7%)	34 (56.7%)	
Smoking			
Positive, *n* (%)	16 (26.7%)	13 (21.7 %)	0.522 ¥ NS
Negative, *n* (%)	44 (73.3%)	47 (78.3%)	

n stands for the number of instances; SD for standard deviation; t-test for independent samples; The symbol ¥ represents the Chi-square test, whereas NS is an abbreviation indicating insignificant at a significance level of P > 0.05.

Family History of Psoriasis.

Distribution according to Treatment Intake

According to treatment intake, the frequency distribution of psoriasis patients was as follows in Table (2): 34 (56.7 %) of psoriasis patients without treatment and 26 (43.3 %) of patients with therapy.

Table (2): Frequency distribution of psoriasis patients according to Treatment Intake

Characteristic	**Patients** *n* (%)
Treatment Intake	
Treating, *n* (%)	26 (43.3 %)
Without treating, *n* (%)	34 (56.7 %)

Subjects Immunological Analysis Results

Interleukin-17 level in patients with Psoriasis and healthy control.

Table (3) and Figure (1) present the results of comparing the levels of interleukin-17 (IL-17) in individuals with Psoriasis with healthy control subjects. Comparing psoriasis patients to healthy controls, the average IL-17 concentration was statistically significantly higher in the former group (19.68 ± 5.31 versus 13.23 ± 3.23; P<0.001).

Table (3): Interleukin-17 level in patients with Psoriasis and healthy control.

Parameters	Patients with Psoriasis *n* = 60	Healthy control *n* = 60	*P*
Interleukin-17 (IL-17) levels			
Mean± SD	**19.68 ± 5.31**	**13.23 ± 3.23**	**< 0.001 † HS**
Range	6.46 – 58.09	7.57-20.25	

SD stands for standard deviation, n for number of instances, t-test for independent samples, and HS for highly significant at P < 0.001.

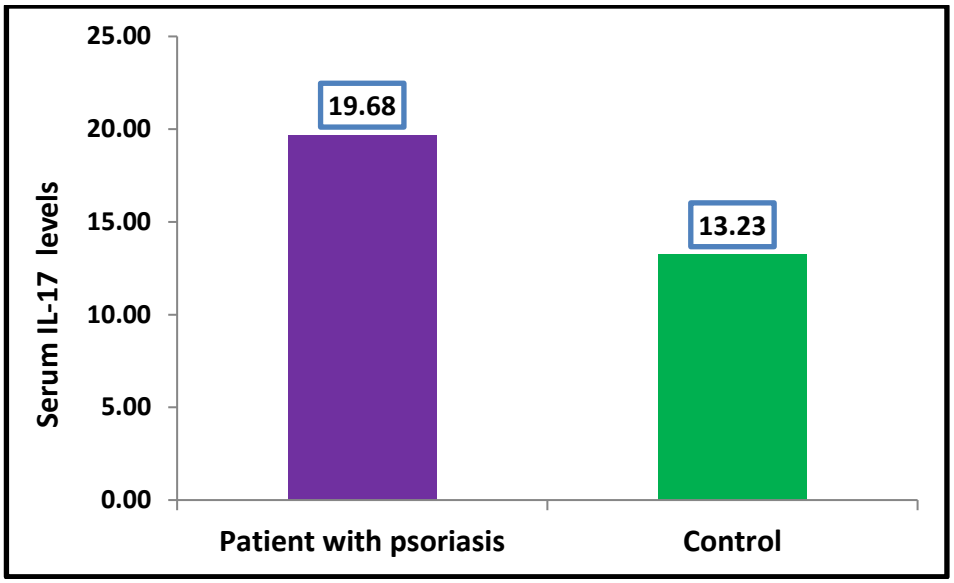

Figure (1): Mean Interleukin-17 (IL-17) levels of patients and healthy controls

Frequency distribution of IL-17 levels according to some characteristics.

A comparison of IL-17 levels based on specific attributes has been done, and the outcomes are shown in Table (4). The findings indicate no significant difference in IL-17 levels between the two examined characteristics (P<0.05).

Table (4): Distribution of serum IL-17 level according to some characteristic

Characteristics		N	IL-17 Mean ± SD	*P*
Family History	**Positive**	**32**	**19.84 ± 6.19**	**0.889 † NS**
	Negative	**28**	**19.54 ± 5.54**	
Treatment Intake	Treating	**26**	**18.52 ± 5.41**	**0.119 † NS**
	Without treating	**34**	**21.20 ± 3.94**	

SD stands for standard deviation; n for number of instances; and t-test for independent samples P < 0.05 indicates not significant (NS); P ≤ 0.05 indicates very substantial (S).

Gene expression results

***PSORS-2 gene expression* in patients with HT and healthy control.**

The gene expression levels of the PSORS-2 gene were compared between psoriasis patients and

healthy control subjects. The results may be found in Table (5) and Figure (2). The mean PSORS-2 gene expression levels in individuals with Psoriasis and those without the condition were 17.73 ± 4.20 and 1.15 ± 0.61, respectively. The gene expression in psoriasis patients exhibited a statistically significant elevation compared to the healthy control group (P< 0.001).

Table (5): *PSORS-2 gene* expression in patients with Psoriasis and healthy control.

Parameters	**Patients with Psoriasis** ***n* = 60**	**Healthy control** ***n* = 60**	***P***
PSORS-2 gene expression			
Mean± SD	**17.73 ± 4.20**	**1.15 ± 0.61**	**< 0.001 † HS**
Range	9.75– 26.45	0.13-4.49	

SD stands for standard deviation, n for number of instances, t-test for independent samples, and HS for highly significant at P < 0.001.

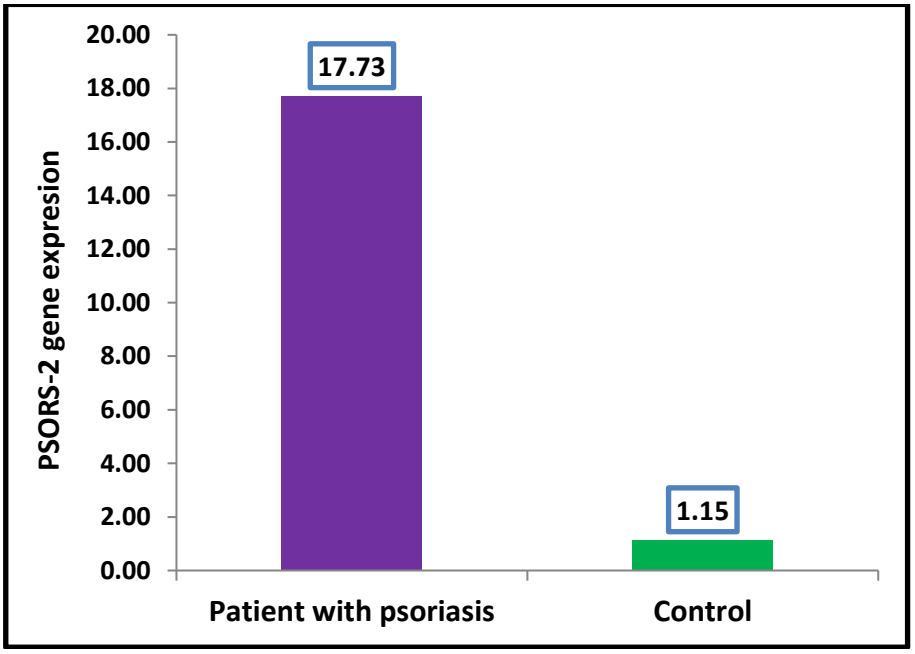

Figure (2): *PSORS-2 gene* expression in patients with Psoriasis and healthy controls

PSORS-2 gene expression frequency distribution is based on several attributes.

PSORS-2 gene expression has been compared based on several factors, and the findings are shown in Table (6). Compared to patients with an adverse family history, the current results demonstrate a significant increase in PSORS-2 gene expression in patients with a positive family history (P>0.05). However, based on Treatment Intake, the current results do not indicate a significant difference (P>0.05).

Table (6): Distribution of PSORS-*2 gene expression* according to some characteristic

Characteristics		**N**	**PSORS-2 gene expression Mean ± SD**	***P***
Family History	**Positive**	**32**	**19.07 ± 3.24**	**0.001 † S**
	Negative	**28**	**15.45 ±4.08**	
Treatment Intake	Treating	**26**	**17.15 ± 3.82**	**0.358 †**
	Without treating	**34**	**18.17 ± 4.67**	

				NS

SD stands for standard deviation; n for number of instances; and t-test for independent samples P < 0.05 indicates not significant (NS); P ≤ 0.05 indicates very substantial (S).

PSORS-2 gene expression connections with other factors using logistic regression analysis.

According to Figure (3), the logistic regression model demonstrates that the expression of specific genes, such as PSORS-2, directly correlates with IL-17 in psoriasis patients. This finding may indicate that psoriasis conditions increase the production of IL-17 about PSORS-2 gene expression.

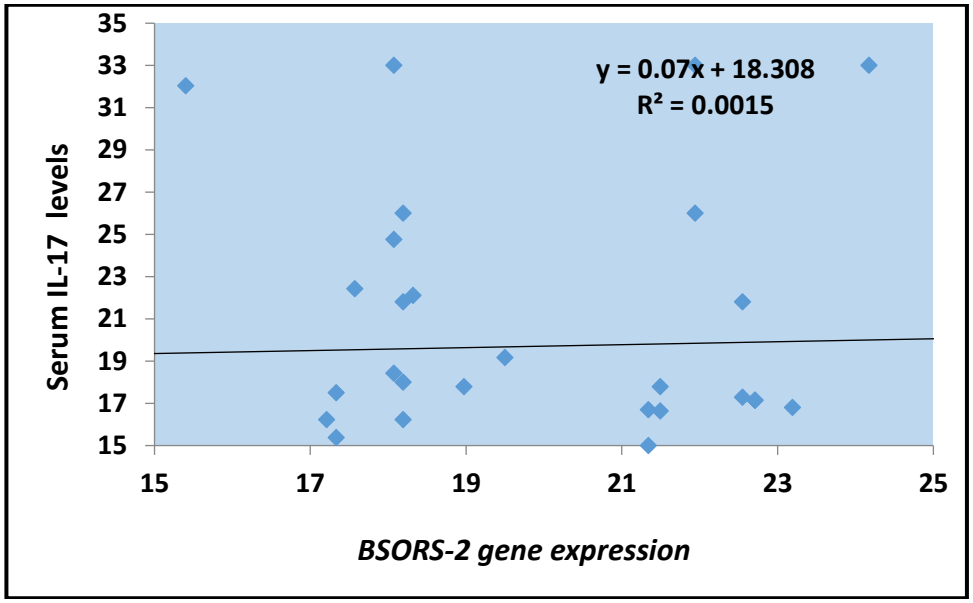

Figure (3): The Logistic Scatter Blot revealed the patients' IL-17 and PSORS-2 gene expression.

Psoriasis is a prevalent, long-lasting skin condition characterized by inflammation, genetic background, environmental triggers, and immune dysregulation. Genetic components play a significant role in psoriasis onset, with studies identifying specific gene variants associated with the disease [22]

The present study highlights the growing need to comprehend gender differences in Psoriasis and co-more Psoriasis in diagnosis and management. In similar studies, the observations comply with the existing literature[23] that reported a distribution of psoriasis severity among females (45.3%) and males (54.7%), with 67.2% classified as mild to moderate and 32.8% as severe. Additionally, the study by[24] highlighted that more females with psoriatic arthritis (PsA) reported a prominent/moderate negative compared to males, emphasizing the importance of considering gender differences in disease impact perceptions as a prevalent 2-3% of the global, with an equal distribution between men and women[25]. Studies have consistently shown an equal impact of Psoriasis on both genders. The psoriasis ratio of females to males is 1:1 or very close to it [26].

Psoriasis (PSO) is a complex disease with a heritability estimate of 68%, where about 53% of patients have an affected family member[27]. Studies in various populations like Dutch, Singaporean, Australian, and USA show similar findings with minor differences due to genetic background variations[28]. Twin studies suggest that PSO is not purely genetic, emphasizing its complexity [29]. Childhood PSO patients often have a positive family history, with increased risk in siblings and first-degree relatives. The risk decreases with fewer affected family members, highlighting multifactorial inheritance. [30]. Specifically, [31] reported that 35-50% of individuals with Psoriasis have Psoriasis relative to the disease [32], demonstrating a 29.53% association of family history with psoriasis patients. Additionally, [33] found a 26% association of family history with psoriasis patients.

Studies by [34] collectively support the notion of increased IL-17 expression in Psoriasis. Additional

Psoriasis is by [35] all reported elevated IL-17 levels in psoriasis patients. Notably, [36][37] A study by Song et al. supports the concept of high IL-17 exacerbated Psoriasis, revealing a correlation between psoriasis severity and IL-17 levels, indicating medication effectiveness [38]. This correlation is justified by prior studies, which have shown the association between IL-17 levels and the severity of Psoriasis[39][40].In the case of Psoriasis of higher IL-17 levels found in moderate to severe psoriasis patients, it is suggested that the individuals in the study may be seeking treatment to manage their condition [35]. Histopathological analysis of skin samples has also shown enhanced values of IL-17-producing cells, predominantly Th17 T lymphocytes, in the psoriatic skin than normal skin, indicating that IL-17 seems to have a pathogenetic role in Psoriasis[41].

The CARD14 gene has an important responsibility to maintain the inflammatory reactions in the skin, and it operates by activating the NF-κB protein complex that detects the genes getting involved in inflammation as well as cell survival[42][43].CARD14 gain of function mutation is linked with psoriasis vulgaris (PsV) and pityriasis rubra pilaris (PRP) with increased signalling of NF-κB and chemokines[44]. On the other hand, loss-of-function mutations in CARD14 are associated with atopic dermatitis, further demonstrating that the CARD14 gene has two roles: in maintaining skin health and contributing towards disease progression[45].

CARD14-associated papulosquamous eruption (CAPE) was also an inflammatory skin disease with clinical findings of psoriasis and pityriasis rubra pilaris, which resulted from CARD14 gene mutations [46]. CAPE, a youth-onset facial skin condition, presents with pink-red macules, keratoderma palmoplantar, and follicular papules. Treatment complexities and patients' refusal to accept traditional agents are common. [47]. Also, another study revealed that patients with CAPE have a lower QoL and may experience depression, so it can be concluded that this disease reasonably affected the patient's quality of life.

Conclusively, the research also observed higher card 14 gene expression ($P < 0.001$). However, they have not elaborated on the penetrance of these alleles in individuals homozygous for CARD14[45]. Compared to the levels of CARD14 in Pos, the results revealed higher levels of CARD14 in the skin than in non-skin, thus a direct validation of the observation that the CARD14 gene is up-regulated in Psoriasis lesions[48]. The study explores the link between CARD14 gene polymorphisms and enhanced CARD14 protein expression in Psoriasis patients. It confirms the role of CARD14 in the disease's manifestation and progression. The research emphasizes the CARD14 gene's potential for therapeutic intervention in Psoriasis. CARD14 is also implicated in regulating IL-17 levels, a critical cytokine in the disease's development.

[49]. Also, the PSOR assay showed that in psoriatic disease, the IL-17F level was mentioned higher than that of IL-17A, suggesting different inflammatory cell populations that regulated these cytokines [50]. This dysregulation of the secretion and release of IL-17 is associated with excessive inflammation and activation of immune cells, as well as the diagnosis of Psoriasis [51]. Therefore, it is significant for clinicians to uncover the association between CARD14 and the pathways that involve enhancing IL-17 following the determination that enhanced and dysregulated IL-17 is a key issue in managing Psoriasis.

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4. Conclusion

Patients with Psoriasis had greater blood IL-17 levels linked to disease. Thus, IL-17 was the critical mediator of lesion onset. This study found a link between CARD14(PSORS2) gene expression and psoriasis risk. Show how psoriasis patients' IL-17 and CARD14(PSORS-2) gene expression are closely connected. This implies that the CARD14(PSORS-2) gene increases IL-17 production in Psoriasis. Mutations in the CARD14 gene increase Psoriasis risk, especially in severe forms.

Mutations that increase IL-17 production, a critical factor in psoriatic inflammation, may cause inflammation.

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Conflicts of interest

There are no conflicts of interest

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