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The Role of Interleukin 12 in Iraqi Patients with Psoriasis

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***Abstract*— Psoriasis is a chronic skin condition with immune-mediated inflammatory etiology. Many** studies **have indicated that Interleukin-12 (IL-12) plays an essential role in the severity of psoriasis.So to elucidate IL-12 role in regulating psoriasis promotion, the sera levels of IL-12 are detected in psoriasis patients and healthy people. The study contains 45 individuals with psoriasis, and the same number of healthy persons are included as controls .The PASI (Psoriasis Area and Severity Index) was used to assess the severity of psoriasis. Patients were divided into three groups depending on severity: mild psoriatic patients (13), moderate psoriatic patients(15), and severe psoriatic patients (17).Five ml of serum was obtained from each individual in per groups to determine IL-12 levels. The data demonstrated that the age range (36-45) has the highest prevalence of psoriatic patients (51.11 %). In addition, the female to male ratio in patients with psoriasis was 1.2:1.IL-12 levels in psoriasis patients were significantly higher than in healthy persons (3.55 pg/ml and 2.79 pg/ml). Furthermore, there was a significant association between blood IL-12 levels and PASI for psoriatic patient groups. The findings suggest that IL-12 has a key role in the psoriasis pathogenesis and that it might be utilized to evaluate psoriasis and as a follow-up indicator for those with it.**

Keywords*— *Psoriasis , Inflammation , IL-12

I. INTRODUCTION

Psoriasis is a widespread chronic inflammatory skin disease characterized by a complex interplay of genetic risk factors, environmental risk factors, and abnormal immune responses. It can occur at any age, although it has a two-mode distribution, with the majority of cases occurring between the ages of 15 - 20 and 55 - 60. The appearance of more severe psoriasis is closely associated with growing older and having a family history that affects several family members(Langley *et al.*, 2005) . Although the actual cause of psoriasis is unknown, genetic factors have a role in its development(Capon, 2017). Psoriasis disorders may be induced by an inappropriate immune response to unknown causative factors, such as "autoantigen" or "bacteria," in which white blood cells are attracted and stimulated at the regions of inflamed tissue, hence exacerbating the condition (Nickoloff and Nestle, 2004) .Interleukins (ILs) are cytokines are released by a various cells and play significant roles in immune cell activation, development, proliferation, maturation, migration, adhesion, and pro-inflammatory actions (Akdis *et al*., 2011; Oleiwi, 2020). Although the cytokine-mediated response is an essential element of the body's defense system, excessive production of pro-inflammatory cytokines or cytokine production in the inappropriate biological system has been related to the development of a number of disorders, such as psoriasis. Psoriasis appears to be associated with increased in T helper 1 (Th1) cell cytokine release and a reduced in Th2 cell cytokine production (Jasim, 2016). IL-12 improves the link between innate and adaptive immune systems.

IL-12 functions primarily as a pro-inflammatory mediator (Guo *et al.*, 2019). Dendritic cells (DCs) and macrophages are major producers of IL-12. IL-12 stimulates CD4 naive T cells to differentiate into T-helper 1 (Th1) cells as well as activating natural killer(NK) cells. These activated cells produce IFN-γ as a result of the IL-12 effect. IFN-γ appears a vital role in psoriasis pathogenesis by promoting T-cell infiltration and keratinocyte proliferation (Torti and Feldman, 2007). Not only does IL-12 stimulate a pro-inflammatory response, but it also exacerbates psoriatic lesions. Furthermore, IL-2 is released from Th1 in response to IL-12. The primary role of IL-2 is to induce the Th1 response, which results in the production of IFN-γ (Cataldi *et al.*, 2019). Several studies have indicated that IL-12 has an important role in the pathogenesis of psoriasis via (Th1/IFN-γ) axis as well as its association with disease severity and can be used as a biomarker on psoriasis and its severity (Arican *et al*., 2005 ; Divyapriya *et al*., 2021).

II. METERALS AND METHODS

A . Design of Study

The study comprised 45 psoriatic patients of both genders who visited AL-Nasiriyah General Hospital's Dermatology and Venereology Section between October 1, 2021 and April 1, 2022. The age group was (16-45 years). Patients with psoriasis had not received any therapy. In addition, 45 healthy people with no family history of psoriasis served as a control group. Dermatologists confirmed the patient's clinical diagnosis. Psoriasis patients were divided into three groups depending on the severity of their psoriasis as measured by PASI: mild, moderate, and severe.

B. Methods

Five milliliters of patient and healthy controls blood were taken , and placed in a clot-activator tube to collect serum.

The collected serum was stored at -20°C after being centrifuged at 3000 rpm for 10 minutes. Serum IL-12 levels in psoriasis patients and controls were evaluated by using the ELISA Kit of the provided company (Elabscience - USA).

C. Statistical Aanalysis

The results have been displayed as a mean ± standard deviation (SD). P-values < 0.01 were interpreted highly significant. Microsoft® Excel 2010 was used to create the graphs

III. Result and Discussion

According to the current results of this study, 48.89 % of the control group were male, while 51.11 % were female. Furthermore, the patient group included 46.67 % men and 53.33 % females, as shown in Figure (1). Several risk factors of Iraqi psoriatic patients were discovered in this study by evaluating questionnaires gathered from personal interviews with psoriatic patients and control people. Risk variables were gender, age, and family history. According to the current study, females outnumber males in the percentage of psoriasis patients, indicating that females predominate in the psoriasis disease. This result corroborated the results of Al-Sariay *et al.* (2021) .

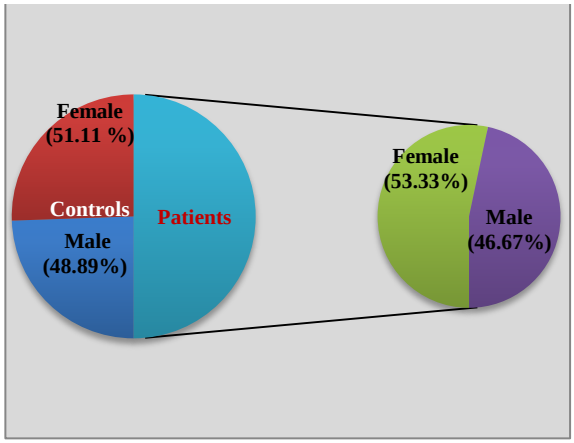

Figure (1): Gender distribution of psoriatic patients and healthy controls.

The age group 36-45 years had the most psoriasis patients, with 23 (51.11 %). The remaining psoriasis and control cases were spread among the age ranges, as demonstrated in (Table 1). This observation is compatible with Mahmood and Saeed (2020).

Table (1): Distribution according to the age of psoriatic patients and healthy controls.

Age groups	Patients		Control	
	No.	%	No.	%
16-25	5	11.11%	4	8.89%
26-35	17	37.78%	19	42.22%
36-45	23	51.11%	22	48.89%
Total	45	100%	45	100%

Twelve (26.70% of 45 psoriatic patients) had a psoriatic family history. This emphasizes the significance of heredity as a cause of psoriasis, especially when sickness begins at a young age.(Ferrándiz *et al,*. 2002).These findings were nearly identical to that of Sharquie *et al.* (2017).

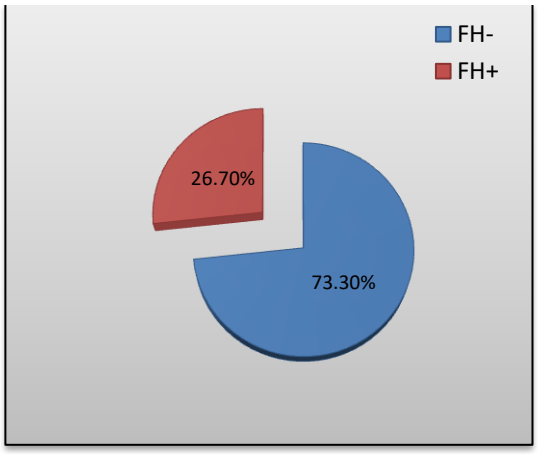

Figure (2): Family history among psoriatic patients.

According to the result shown in table (4-4),serum IL-12 levels in the psoriatic patient group were higher compared with healthy individuals, with mean levels of (3.55 ± 0.28) pg/ml, (2.79 ± 0.30) pg/ml, respectively with significant high differences (P<0.01). This result came in agreement with ESSA *et al.* (2009), who found that serum IL-12 level was significantly higher in psoriatic patients than in healthy controls .The result also was compatible with the results published by other investigators Salama *et al.* (2013), and those which reported by Attallah *et al.* (2016). In parallel, a study by Roussaki-Schulze *et al.* (2005)and Chong and Wong (2007) reported that IL-12 was highly increased in patients with psoriasis than in healthy individual.

Likewise, a data by Takahashi *et al.* (2010) reported that psoriatic patients have high levels of IL-12, as well as this interleukin can be used as marker for psoriasis activity. The results presented by Borska *et al.* (2008) showed that IL-12 has a major pro-inflammatory function on the immunopathogenesis of psoriatic disease.

Table (2): Comparison of Sera mean levels of IL-12 in the Patients group and controls.

Parameter	Groups	Mean ± SD
IL-12	Controls n=45	2.79 ± 0.30
	Mild Psoriasis n=13	3.14 ± 0.14 a*
	Moderate Psoriasis n=15	3.48 ± 0.12 a*
	Sever Psoriasis n=17	3.80 ± 0.09 b*
	Total Psoriasis n=45	3.55 ± 0.28 *

n: number of subjects

* Significant difference as compared with Control group (P<0.01). Results with non-identical superscripts(a,b) within different psoriatic groups were considered as a significant difference (P<0.01).

IL-12 has been associated with numerous of inflammatory disorders in which Th1 cells play a role in pathogenesis. IL-12 has been demonstrated to increase the production of new psoriatic plaques in psoriasis (Brito-Luna et al., 2016).

IL-12 stimulates the differentiation of naïve T lymphocytes toward Th1 cells, inducing a Th1-mediated response. In combination with IL-18, IL-12 increases Th1 cell IFN-γ secretion, which then in turn increasing IL-12 release (Rosmarin and Strober, 2005).

Our findings disagree with Michalak-Stoma et al. (2013), Bai *et al.* (2018) who found that serum IL-12 levels was without differed between individual with psoriasis and controls.

Also, a paper by Jacob *et al.* (2003) reported that IL-12 was not raised but rather decreased was unexpected ,considering IL-12 is an essential cytokine for Th1 differentiation, stimulating proliferation and IFN-γ synthesis by Th1 cells. Despite it is important for optimal IFN-γ secretion, other cytokines including TNF and IL-18, that are also elevated in psoriatic lesions, are have impact role of increase IFN-γ production (Shaker *et al.* , 2006).

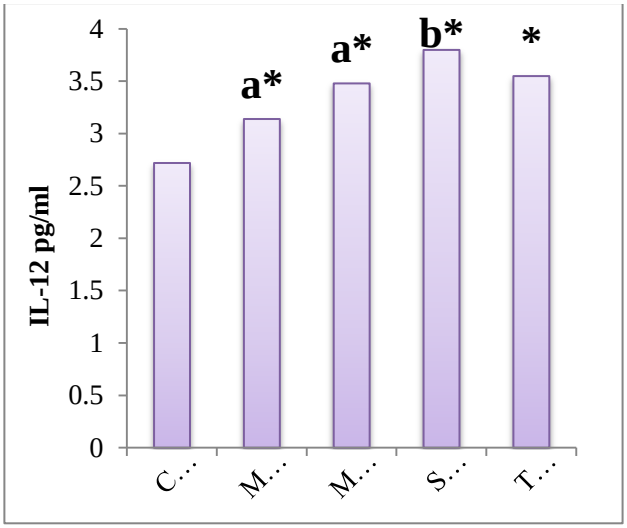

Figure (3): Serum levels of IL-12 for control and psoriatic patient groups.

* Significant difference as compared with Control group (P<0.01).Results with non-identical superscripts(a,b) within different psoriatic groups were considered as a significant difference (P<0.01).

The current findings also found a significant association between serum IL-12 levels and disease severity depending on PASI and these findings are consistent with author Arican *et al*. (2005) and Hwang *et al.* (2014) , who reported that IL-12 might be used as a biomarker for psoriasis activity and clinical severity.

Also, a study by Divyapriya *et al.* (2021) reported a significant correlation between IL-12 levels and PASI and indicated that IL-12 has an important part in the pathogenesis of psoriasis via the (Th1/IFN- γ) axis. IL-12 stimulates Th1 cells to produce IFN-γ. IFN-γ as well as IL-22, in turn, promote keratinocyte proliferation and inhibit apoptosis (Anupam Prakash, 2010)

Conclusion

According to the findings of this study, IL-12 levels are higher in patients with psoriasis and have a significant association with severity. These findings indicate that this marker plays a vital role in psoriasis pathogenesis and can be employed as a marker to assess psoriasis.

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ETHICAL CONSIDERATION

To conduct the research ethical permission was obtained from the hospital and from all participants in this work patients and healthy.

Conflict of interest

The authors declare no conflicts of interest

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