ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 12, pp.43793-43797, December, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ROLE OF IL 17 IN THE PATHOGENESIS OF PSORIASIS

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ARTICLE INFO

Article History:
Received 23rd September, 2016
Received in revised form
25th October, 2016
Accepted 18th November, 2016
Published online 30th December, 2016

Key words:

Psoriasis, Pathogenesis, Cytokines,
T helper cells, Interleukin 17.

ABSTRACT

Background: Psoriasis is a common, chronic, inflammatory disease of multiple etiological factors, mainly immunological, affecting skin and joints. Many cytokines produced by T lymphocytes, especially T helper type, have been implicated in its pathogenesis.
Objectives: This study aimed at detecting the role of interleukin 17 in the pathogenesis of psoriasis.
Methodology: This study was a case control study. IL 17 was measured in twenty plaque psoriatic patients in both lesional and non lesional skin and the results were correlated with the disease severity and compared with twenty sex and age matched healthy volunteers that were included as control group.
Results: IL 17 was statistically significant higher in lesional than in non lesional areas and also than the control group.

Citation: Basma Hamada Mohammed, Dr. Talal Ahmed Abd-El-Raheem, Dr. Olfat Gamil Shaker and Dr. Mohammed Hassan Mohammed, 2016. "Role of IL 17 in the pathogenesis of psoriasis", *International Journal of Current Research*, 8, (12), 43793-43797.

INTRODUCTION

Psoriasis is fundamentally an inflammatory skin condition with reactive abnormal epidermal differentiation and hyper proliferation affecting 2-3 % of world's population (Kuchekar *et al*., 2011). Its exact cause is unknown, but a wealth of studies indicate that the disease results from a complex and dynamic interplay between genetic and environmental factors that trigger an excessive inflammatory response in the skin (Monteleone *et al*., 2011). Psoriasis recognize two pathogenetic moments, the first one involving innate immunity triggered by unknown stimuli and the second one involving the adaptive immunity, due to cytokines released from cells of the innate immune system, mainly dendritic cells (Skroza *et al*., 2013). The involvement of T lymphocytes in the pathogenesis of psoriasis can be described in terms of 3 events: the initial activation of T lymphocytes, the migration of T lymphocytes into the skin, and the various roles played by cytokines released from T lymphocytes and other cells (El-Darouti and Abdel Hay, 2010). Both Th1 and Th17 cells have been verified as major T-cell components of psoriasis. It is still not clear which cell type has a predominant role, although a greater number of Th17 and Th22 cells are identified in the circulations of psoriasis patients than Th1 cells (Carrier *et al*., 2011). IL-17 is regarded as a signature cytokine for Th17 cells and is involved in inflammatory responses (Peiser, 2013). Despite its protective effects against certain pathogens, IL-17 can be dysregulated in some individuals and thereby contribute to the pathogenesis and/or maintenance of autoimmune and immune inflammatory disorders (Van den Berg and McInnes, 2013).

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Aim of work

This study aimed at detecting the role of interleukin 17 in the pathogenesis of psoriasis through detecting its tissue gene expression in plaque psoriatic patients in both lesional and non lesional skin and correlating its level with disease severity and comparing those results with its level in control healthy individuals.

Subjects and methods

It was a case control study implemented in Fayoum university hospital. The study included 2 groups: the patients group which included 20 patients of both sexes and of different age groups. They were selected from attendants of Dermatology,

STDs & Andrology outpatient clinic. Twenty age and sex matched healthy volunteers were included as a control group with no family or past history of psoriasis. Diagnosis was made on clinical basis. The psoriasis in all patients was of plaque type. Exclusion criteria were being erythrodermic, pustular, or palmoplantar or having other forms of psoriasis, nail psoriasis, psoriatic arthritis. Full personal, present, past, medical, treatment and family history were taken. Clinical examination included:

- Distribution of lesions and severity graded in mild, moderate and severe degree, according to surface area affected.
- Calculation of severity of psoriasis by PASI scores (psoriatic area and severity index).
- Any kind of treatment except for emollients was stopped for four weeks before taking the skin biopsies. Two skin biopsies were taken from each patient; (one from lesional area and the other from non lesional area), and one skin biopsy from each control.

The selected area was cleaned with alcohol and a local anesthetic (lidocaine 2%) was injected subcutaneously. A 3.5 mm. punch biopsy was used to obtain the specimen. The biopsies were kept directly at -5 without any preservatives at Dermatology, STDs & Andrology outpatient clinic, Fayoum University hospital. Then transported in an ice box to the lab, for detection of the tissue gene expression of Il 17. Each Skin biopsy was used for RNA extraction and RT-PCR of IL-17.

Data entry and Statistical Analysis

Data was collected and coded to facilitate data manipulation and double entered into Microsoft Access and data analysis was performed using SPSS software version 18 under windows 7. Qualitative data were described using numbers, percentages and arithmetic means as central tendency measurement, standard deviations as measure of dispersion for quantitative parametric data. Inferential statistic tests (student t-Test, anova test and Paired t-test for quantitative data and chi square test and bivariate correlation test for qualitative data) were used to detect differences between different categories, with a significant level of less than 0.05.

Ethical considerations

This study was reviewed and approved by the faculty of medicine research ethical committee. The study was conducted after explaining the aim of the study and the exact procedure used and all collected data were kept confidential. All participants had the right not to participate in the study. Treatment was prescribed when indicated and method of use was explained.

RESULTS

The age of patients ranged between 6 and 67 years with a mean ±SD of 33±20.9 years. Sex distribution showed that 55% were females (11 patients) and 45% were males (9 patients). Both age and sex were matched with control group as shown in (Table 1), (Table 2).

Disease severity showed that 20% (4 patients) had mild disease, 55% (11 patients) had moderate degree and 25% (5 patients) had severe degree as shown in (Table 3).

Table 1. Mean age of different study groups

Age (years)	Cases (n=20)		Controls (n=20)		p-value	Sig.
	Mean	SD	Mean	SD		
	33	20.9	32	8.9	0.9	NS

Table 2. Sex distribution among different study groups

Sex	Cases (n=20)		Controls (n=20)		p-value	Sig.
	No.	%	No.	%		
Male	9	45%	13	65%	0.2	NS
Female	11	55%	7	35%		

NS=no significance.

Table 3. Frequencies of disease characters among psoriatic cases

Variables	Number (n=20)	%
Severity of disease		
Mild	4	20%
Moderate	11	55%
Severe	5	25%
Type of previous treatment		
No treatment	3	15%
Topical	11	55%
Systemic	1	5%
Both topical & systemic	5	25%

Duration of disease ranged between 2 months and 30 years with a mean± SD of (4.7±7.1) years, the PASI score ranged between 1.2 and 34.8 with a mean± SD of (9.3 ± 8.9) as illustrated in (Table 4).

Table 4. Description of disease characters among psoriatic cases

Variables	Minimum	Maximum	Mean	SD
Duration of disease (years)	(2 months)	30	4.7	7.1
PASI score	1.2	34.8	9.3	8.9

IL-17 level in lesional area ranged between 1.5 and 14.4 with a mean± SD of (5.8 ± 3.8), and IL-17 level in non-lesional area ranged between1.1 and 3.3 with a mean± SD of (1.8±0.66) as shown in (Table 5).

Table 5. IL-17 level in psoriatic cases

Variables	Minimum	Maximum	Mean	SD
Lesional IL-17	1.5	14.4	5.8	3.8
Non-Lesional IL-17	1.1	3.3	1.8	0.66

There is a statistically significant difference between IL 17 level in lesional and non-lesional area among psoriatic cases with higher level of IL-17 in lesional area with p-value <0.05 as shown in (Table 6).

Table 6. Comparison of IL-17 level among psoriatic cases

Variables	Cases (n=20)		p-value	Sig.
	Mean	SD		
Lesional IL-17	5.8	3.8	<0.001	HS
Non-Lesional IL-17	1.8	0.66		

HS=high significance.

There is a statistically significant difference with p-value <0.05 between case group (lesional area) with a mean ±SD of

5.8±3.8 and control group with a mean ±SD of 1.2±0.15 as shown in (Table 7).

Table 7. Comparison of IL 17 between cases (lesional) and control

Variable	(Lesional) Cases (n=20)		Controls (n=20)		p-value	Sig.
	Mean	SD	Mean	SD		
IL-17	5.8	3.8	1.2	0.15	<0.001	HS

Also, there is statistically significant difference with p-value <0.05 between case group (non-lesional area) with a mean ±SD of 1.8±0.66 and control group with a mean ±SD of 1.2±0.15 (Table 8).

Table 8. Comparison of IL 17 between cases (non lesional) and control

Variable	(Non lesional) Cases (n=20)		Controls (n=20)		p-value	Sig.
	Mean	SD	Mean	SD		
IL-17	1.8	0.66	1.2	0.15	0.001	HS

There is a statistically significant difference with p-value <0.05 between different degrees of disease severity as regards to IL-17 level in lesional and non-lesional area among psoriatic cases with higher level among cases with severe degree of psoriasis (Table 9).

Table 9. Comparison of IL-17 level in lesional and non lesional skin between different degrees of disease severity among psoriatic cases

Variables	Severity of disease			p-value	Sig.
	Mild Mean ± SD	Moderate Mean ± SD	Severe Mean ± SD		
Lesional IL-17	2.2±0.50	4.5±1.7	11.4±2	<0.001	HS
Non-Lesional IL-17	1.3±0.18	1.6±0.60	2.5±0.46	<0.001	HS

There is no statistically significant correlation between disease duration and level of IL-17 in both lesional and non-lesional area among psoriatic patients (p-value > 0.05) as illustrated in (Table 10).

Table 10. Correlation between duration of disease and level of IL-17 among psoriatic cases

IL17 level	Disease duration (years)		
	r	p-value	Sig.
Lesional IL-17	0.02	0.9	NS
Non-Lesional IL-17	-0.05	0.8	NS

This study showed that there is a statistically significant positive strong correlation with p-value <0.05 between PASI score and level of IL-17 in both lesional and non-lesional area among psoriatic patients as illustrated in (Table 11), (Fig. 1, 2).

Table 11. Correlation between PASI score and level of IL-17 among psoriatic cases

IL17 level	PASI score		
	r	p-value	Sig.
Lesional IL-17	0.90	<0.001	HS
Non-Lesional IL-17	0.74	<0.001	HS

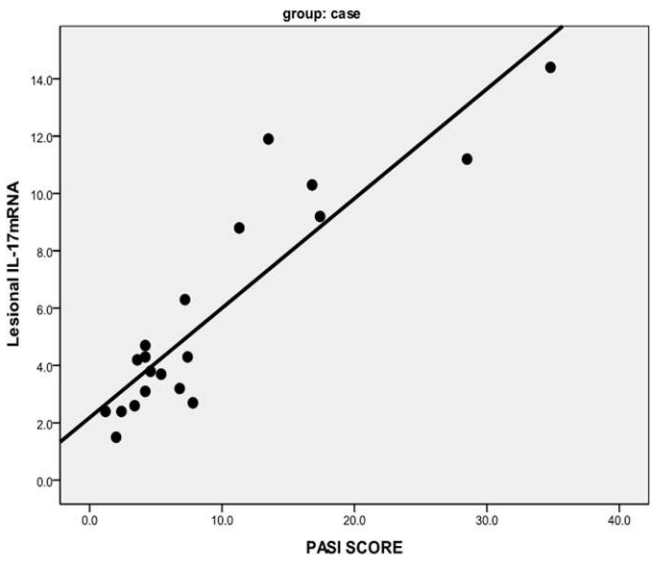

Fig.1. Correlation between PASI and IL-17 in lesional area among psoriatic patients

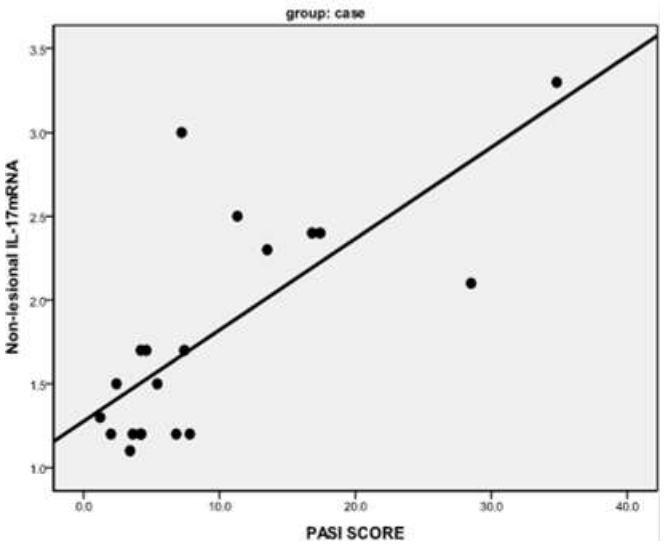

Fig. 2. Correlation between PASI score and level of IL-17 in non lesional area among psoriatic patients

DISCUSSION

In the 1990s, Th17 cells were described as a new T-cell population that produces IL-17, IL-6, IL-21, IL-22, and TNF. Transforming growth factor (TGF)-β1, IL-6, IL-23, and IL-15 stimulated initial Th17 differentiation from naive T cells (Michalak-Stoma *et al*., 2013). Interleukin 17 family of cytokines, a newly emerged cytokine subset, displays broad influence on the pathogenesis of multiple inflammatory disorders (Song and Qian, 2013). The present study was designed to assess role and level of IL 17 by quantitative method using PCR technique in lesional and non lesional skin from psoriatic patients and correlate it with the disease severity expressed clinically and via PASI score and compare it with its level in healthy control individuals. By measuring tissue gene expression of IL 17, our data revealed that IL 17 in lesional skin ranged between 1.5 and 14.4 with a mean± SD of (5.8 ± 3.8), and IL-17 level in non lesional area ranged between1.1 and 3.3 with a mean± SD of (1.8±0.66). IL 17 in the control group ranged between 1 and 1.5 with a mean± SD of (1.2±0.15). IL 17 was higher in lesional than in non lesional

skin and the difference was highly statistically significant with p-value <0.05. Both lesional and non lesional IL 17 was higher than control group and the difference was highly statistically significant with p-value <0.05, which is consistent with Johansen *et al*. (2009), Lowes *et al*. (2008), Zaba *et al*. (2007) whose researches showed increased expression of IL-17 ligands in lesional skin compared with both non lesional and normal skin. This was also in agreement with the results of Harper *et al*. (2009) Russell *et al*. (2011) who measured expression of IL-17A, IL-17C, and IL-17F which was elevated in psoriatic lesional tissue compared with non lesional tissue. The same with Wolk *et al*. in 2006 and Matsushita and Higashi in 2008 who observed increased IL-17A and IL-17F mRNA in psoriatic skin lesion comparing to non lesional or healthy skin. Moreover, many researchers have studied serum level of IL 17, not the tissue level, in psoriasis like Takahashi *et al*. (2010), Yilmaz *et al*. (2012) who detected that it is elevated and also significantly correlated with PASI score. Others have measured IL 17 cells level in both tissue and peripheral circulation of psoriatic patients as Zhang *et al*. (2010), Caproni *et al*. (2009) who found that it was positively correlated with disease severity as measured by PASI score. This is in agreement with our results that documented positive strong correlation between IL 17 level and disease severity together with PASI score with high statistically significance. Kagami *et al*. (2010) found that circulating IL-17A+ cells were elevated in psoriatics compared with healthy individuals but -unlike our results-did not significantly correlate with skin disease severity. On the contrary, Kyriakou *et al*. (2014) documented that median serum levels of IL-17, using ELISA, did not differ significantly between the cases and the control group in his study and no significant correlations were found between PASI and the cytokine serum. In Egypt, to our knowledge, we are the first to study tissue gene expression of IL 17 in lesional and non lesional areas in psoriatic patients in relation to control group and correlating the results with disease severity through PASI score. Almost all studies were conducted on the serum level of IL 17, not the tissue level like our study. Almakhzangy and Gaballa (2009), Abdel Mawla *et al*. (2013), El-Moaty Zaher *et al*. (2013), Abo Elmajd *et al*. (2014) observed a statistically significant higher serum level of IL-17 ($p< 0.05$) in psoriatic patients versus control.

Conclusion and Recommendations

As we gain further insight into the immunopathogenesis of psoriasis, we hope it will provide the basis for the development of safer, more efficacious, and more durable therapeutics in the future. Given its enormous toll on patient health and quality of life, steps should be taken to prevent or decrease the risk of psoriasis associated comorbidities. *In conclusion*, there is no doubt that IL17 has a major role and importance in the orchestra played by the cytokines in order to create the psoriatic plaque in the end, evident by its high tissue gene expression in comparison to control in our study and the high significant correlation with PASI score. We suggest that, a use of an array of this cytokine and others related may be considered as a useful follow-up marker for monitoring of psoriatic patients and optimizing therapeutic strategies.

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