

Study of Serum Level of Interleukin 2, Interleukin 10 and Tumor necrosis factor- α in sample of Iraqi psoriasis patients

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Abstract :

The aim of this study was to determine the Th1 and Th2 serum cytokines, in patients with psoriasis and to compare their cytokine levels with those of normal control subjects. where study included 55 Iraqi patients with psoriasis:30 (15 females ,15 males) were untreated with any drugs. The other patient group consist of 25 (9 female and 16 male) treated with a biological treatment (infliximab) ,and 30 healthy control group were withdrawn (5) ml of venous blood for both patients and members of the control ,to conduct Immunological tests to determine the quantitative for each of level of IL-2,IL-10 and TNF- α in a manner (ELISA). The results showed significant increase in the level of probability ($P < 0.05$) in the rate of level of IL-10 and TNF- α in patients compared to the control (healthy) .As well as the result also show no significant increases of IL-2.From this we can deduce that pro inflammatory and anti-inflammatory cytokines have an important role in the pathogenesis of psoriasis, the increase of IL-10 and TNF- α indicated the balance between the proinflammatory and the anti-inflammatory cytokine .

Introduction:

Psoriasis is a chronic inflammatory skin disease, affecting approximately (2-3%) of the world's population, it is more common in Caucasians , it can affect any race and can occur at any age and recognized by change proliferation and differentiation keratinocytes. (1,2). Psoriasis is a related with inflammation and scaling of skin. in psoriasis, cells of the skin come on surface quickly before their complete maturation (3).

It is characterized by sharply demarcated erythematous plaques with silvery scales, They most often occur on the elbows, knees, other parts of

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legs, scalp, lower back, face, palms, and soles of the feet, but they can occur in skin anywhere on the body, Its ranges in severity from a few scattered red, scaly plaques to involvement of almost the entire body surface. It may progressively worsen with age, and wane in its severity, the degree of severity depends on inheritance and environmental factors (4). Clinically a spectrum of different subtypes may be observed: psoriasis vulgaris, guttate psoriasis, erythrodermic psoriasis, pustular psoriasis, inverse psoriasis, and arthritis (5).

Evidence indicating that Genetic, environmental, and immunological factors contribute to the pathogenesis of psoriasis and play important roles in its development. Many external factors including infections, stress, Smoking, Alcohol and medications may exacerbate psoriasis. Some of the most common medications know to trigger or worsen existing psoriasis include lithium, gold salts, beta blockers and anti-malarial (6).

The molecular pathogenesis of psoriasis ,its central importance to an interaction between acquired and innate immunity ,Psoriasis characterized by increased activation of CD4+ T lymphocytes, systemic and local overexpression of pro-inflammatory cytokines such as interleukin 2 (IL-2), gamma interferon (IFN- γ), IL-6 and tumour necrosis factor alpha(TNF- α), indicating immunopathogenesis of the disease is T helper 1 (Th1) mediated,At the onset of the disease, special dendritic cells (DCs) in the epidermis and dermis are activated; among other effects, these cells produce the messenger substances tumor necrosis factor (TNF)- α and interleukin (IL)-23, which, in turn, promot development of Th1, and Th17 cells. These T cells secrete mediators that contribute to the vascular and epidermal changes of psoriasis (7).

Materials and Methods:-

• Samples Study

This study was carried out at the Department of Dermatology and Venereology in Baghdad Teaching Hospital Clinic during the period from November 2013 to April 2014. The study included 60 patients with psoriasis; their ages ranged from (6-70) years.The diagnosis by the medical staff at the clinic based on international criteria. Patients were distributed in two groups; the first group was the untreated group. It consist of 30 patients of both sexes (15 males and 15 females). The second group was the group that had a biological treatment (influximab). It consist of 25 patients of both sexes (16 males and 9 females). The study also included

25 apparently healthy people of both sexes(13males and 12 females) .Who were matched patients by age.

• **Collection of Blood Samples and Methods:-**

The blood sample was collected (5) ml from the venous blood of the patients of both groups and control groups .Each model was deal with as flows: 5 ml of blood was transferred to a plain tube and was left to clot at temperature laboratory for 30 minutes. Then, the sample were discarded using the device Centrifuge at speed 2500 RPM for 10 minutes. Then, the serum was collected by using Micropipte to be later distributed in the three of the Eppendrof tubes, and kept at a temperature -20 ° C to be later used in the testing immune mode. Later, the level of IL-2, IL-10 and TNF- α (PeproTECH ,USA) kit by Enzyme Linked Immunoasorbent Assay (ELISA) technique, were measured. The results were calculated using the SAS program (2010) in the statistical analysis of the data for the study of the effect of the studied factors in different qualities, and compared the moral differences between the test averages less significant difference LSD (8).

Results:-

The present study include patients suffered from different types of psoriatic disease [plaque (vulgaris), guttate, pustular, erythrodermic and arthritis]. Most of them suffered from plaque psoriasis,figuer (1,2).



Figure (1) :Psoriasis Vulgaris in the Leg



Figure (2): Psoriasis Vulgaris in the Abdominal

The patient treated with a biological treatment (Infliximab) were asked to give blood sample through the period of taking the treatment. Most of them took about (4-6 dosages) through the period of study was monitored to find out the extent of the effect of the treatment figurer (3;A,B)



**Figure (3):A-psoriasis patient before treatment
B-psoriasis patient after treatment**

Serum Level of Interleukin-2(IL-2):

Untreated psoriasis patients showed an elevated mean serum level of IL-2 (43.90 ± 1.22 pg/ml).Then come the healthy control group mean serum level of IL-2 (43.27 ± 1.57 pg/ml). The lowest rate recorded by the patients treated with the biological treatment (Infliximab) was with a mean serum

level of IL-2 (41.82 ± 1.24 pg/ml). There was no significant ($P > 0.05$) difference between the patients group .There was no significant ($P > 0.05$) difference between the untreated psoriasis patient groups and the healthy control group. There was also no significant ($P > 0.05$) difference between the treated psoriasis patient group and healthy control , Table(1).

Serum Level of the Interleukin10 (IL-10):

The untreated psoriasis patient showed an elevated mean serum level of IL-10 (17.71 ± 2.70 pg/ml).The patients treated with biological treatment (Infliximab) had a mean serum level of IL-10 that was equal to (13.40 ± 1.31 pg/ml). The lowest rate recorded in the healthy control group the mean serum level of IL-10 (11.70 ± 2.01 pg/ ml).

The results showed no significant difference in the sera of IL-10 mean level between patient groups ,the untreated psoriasis patients and the patients treated with a biological treatment (Infliximab), (17.71 ± 2.70 pg/ml, 13.40 ± 1.31 pg/ml ,respectively $P > 0.05$). There was also no significant difference in the sera of IL-10 mean level between the patients treated with a biological treatment (Infliximab) and the healthy control group ,(13.40 ± 1.31 pg/ml, 11.7 ± 2.01 pg/ml , respectively $P > 0.05$).There were significant difference in the sera of IL-10 mean level between the untreated psoriasis patients and the healthy control group (17.71 ± 2.70 pg/ml , 11.7 ± 2.01 pg/ml, respectively $P < 0.05$), Table (2) .

Serum Level of Tumor Necrosis Factor- α (TNF- α):

Untreated psoriasis patients showed an elevated mean serum level of TNF- α (18.63 ± 1.69 pg/ml).This was Followed by the healthy control group, whose mean serum level of TNF- α was (13.57 ± 0.76 pg/ml). The lowest rate recorded in the patient treated with a biological treatment (Infliximab) was the (12.85 ± 0.41 pg/ml) of TNF- α .

The results showed a significant difference in the sera of TNF- α mean level between the patient groups, the untreated psoriasis patients and the patients treated with a biological treatment (Infliximab) (18.63 ± 1.69 pg/ml, 12.85 ± 0.41 pg/ml ,respectively $P < 0.05$).Result also showed, significant difference in the sera of TNF- α mean level between the untreated psoriasis patients and the healthy control group (18.63 ± 2.70 pg/ml, 13.57 ± 0.76 pg/ml respectively $P < 0.05$).Moreover, no significant difference in the sera of TNF- α mean level was found between the patients treated with a biological treatment (Infliximab) and the healthy control group (12.85 ± 0.41 pg/ml, 13.57 ± 0.76 pg/ml ,respectively $P > 0.05$), Table(3) .

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Table(1): Serum Level of IL-2 pg/ml in Patient with Psoriasis and Healthy Subject

Groups		Number	Mean \pm S.E. IL-2 pg/ml	LSD value
Patients	Group1	30	43.90 \pm 1.22a	3.80
	Group2	25	41.82 \pm 1.24a	
Control		25	43.27 \pm 1.57a	
NS No Significant				

Table(2) : Serum Level of IL-10 pg/ml in Patient with Psoriasis and Healthy Subject

Groups		Number	Mean \pm S.E. Of IL-10 Pg/ml	LSD value
Patients	Group1	30	17.71 \pm 2.70* a	5.187
	Group2	25	13.40 \pm 1.31 ab	
Control		25	11.70 \pm 2.01 b	
* (P \leq 0.05)				

Table(3): Serum Level of TNF- α pg/ml in Patient with Psoriasis and Healthy Subject

Groups		Number	Mean \pm SE of TNF- α pg/ml	LSD value
Patient	Group1	30	18.63 \pm 2.70*	3.386
	Group2	25	12.85 \pm 0.41	
Control		25	13.57 \pm 0.76	
P \leq 0.05				

Discussion:

Psoriasis is a common skin disease characterized by various immunological alterations. In the present study, serum of IL-2, IL-10, TNF- α were demonstrated in psoriasis patients compared to control group.

The recent data suggest that psoriasis patients which are associated with similar level of IL-2 in the untreated psoriasis patients and the healthy control group. Psoriasis patients in the early stage of disease were recognized by significantly increased expression of the pro-inflammatory cytokine such as IL-2 and shift towards IL-10 secretion (Th2 response) was observed with increased the duration of the disease. These observations suggest a possible shift from a Th1 to a Th2 cytokine response (9). The subjected in the study were not identification to mild, moderate and sever

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psoriasis patients. Therefore the IL-2 in our result show the no significant increases, its appear normally.

The current mentioned data suggests that the psoriasis patients have increases in the mean serum level of IL-10 in patients 17.70 while 11.7 is in the control group . previous studies are extremely varied and the result appear to be contradictory ,for example IL-10 has been reported to be increases such a result of (10),who observed that mild-to-moderate psoriasis vulgaris patients have higher level of IL-10, above result compatible with present study. IL-10 has been reported to be decreases in the study of (11) who reported mean value of IL-10 in the control group was higher as compared to cases, but the difference in the serum values of IL-10 was not significant. The result above in compatible with current study. This difference in the result was attributed to the study that indicated in psoriatic lesions, expression of IL-10 is weak or absent in the early stage of diseases .Low level of IL-10 in the cutaneous lesions of psoriatic patients ,after progressive diseases high level of IL-10 can be found in peripheral blood mononuclear cells (12,13).The result of present study may be due to the status of the patients ,since the decreases level of IL-10 in early stage of disease ,whereas the subjected in the study were not identification to mild ,moderate and sever psoriasis patients.

The results indicated that significant increases of TNF- α in psoriasis patient as compare with healthy control. Many studies have dealt with measuring the serum level of TNF- α and some of them came in agreement with the present results, like the study of (14,15) ,whose stated that were an elevated mean serum level of TNF- α in the sera of the untreated patients compared with the healthy control group.

The current study refer to significant decreases of TNF- α in patients treated with a biological treatment (Infliximab) as compare with untreated patients ,this result support by the result stated by (16) has reported a significant decrease in the TNF- α level only after infliximab and etanercept therapies.

These results indicate the importance of TNF- α in the incidence of psoriasis, TNF- α which is a kind of the proinflammatory cytokines .It is a key cytokines in psoriasis diseases. TNF- α may be a marker of the psoriasis disease severity. That increase the expression of (ICAM-1), enhance the skin infiltration of T cells and other inflammatory cells, such as monocytes during pathogenesis of psoriasis (17).

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TNF- α -converting enzyme from the peripheral blood mononuclear cells may contribute to the regulation of TNF-R1 in the psoriasis. The TNF-R1 elevated concentrations in psoriasis were correlated with PASI. The foundation of some psoriasis therapies strengthens the great role of this cytokine in the psoriasis disease (18).

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دراسة المستوى المصلي للبين الابيضاضي ٢ (IL-2) والبين الابيضاضي ١٠ (IL-10) وعامل

التنخر الورمي الفا (TNF- α) في عينة مرضى داء الصدفية العراقيين

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الخلاصة :

صممت الدراسة الحالية بهدف تقييم مستوى سايتوكينات Th-2, Th-1 في مصل المرضى الذين يعانون من الصدفية ومقارنتها مع مجموعة السيطرة , حيث شملت الدراسة ٥٥ مريض (ذكر وأنثى) تتراوح أعمارهم ما بين ٦-٧٠ سنة وكان ٣٠ منهم غير معالجين و ٢٥ معالجين بعلاج بايولوجي ومجاميع سيطرة بأجناس وفئات عمرية مماثلة لأغراض المقارنة مكونة من ٢٥ فردا أصحاء ظاهريا . تم سحب (5) مل من الدم الوريدي لكل من المرضى وافراد السيطرة . لإجراء الفحوصات المناعية لتحديد الكمي لكل من IL-2, IL-10, TNF- α بطريقة (الأليزا) ELISA , أظهرت نتائج ارتفاع معنوي عند مستوى احتمالية ($P < 0.05$) لكن من مستوى البين الابيضاضي ١٠ (IL-10) وعامل التنخر الورمي الفا TNF- α عند المرضى مقارنة بسيطرة (الأصحاء) وعدم وجود ارتفاع معنوي في مستوى البين الابيضاضي ٢ (IL-2) . ومن هنا نستنتج ان السيتوكينات الالتهابية والمضادة للالتهابات لها دور في إمراضيه الصدفية .