



SERUM INTERLEUKIN 6 AND 8 LEVELS AS MARKERS OF PSORIASIS: A CROSS-SECTIONAL, SINGLE INSTITUTION BASED STUDY

Dermatology

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ABSTRACT

Background: Psoriasis is a common inflammatory, immune-mediated disorder, characterized by skin lesions and associated with systemic manifestations. Recent progress in the understanding of psoriasis has shown that the regulation of local and systemic cytokines plays an important role in its pathogenesis. The most often used psoriasis score is the psoriasis area and severity index (PASI). A simple laboratory test from a blood sample would be an attractive, patient-independent, and observer-independent marker of disease severity.

Objective: We evaluated the association of serum levels of some pro-inflammatory cytokines in vivo and their correlation with severity of psoriasis. The serum levels of Interleukin (IL-6 & 8) levels were determined with the use of the ELISA method.

Results: Serum IL-6 and IL-8 levels of patients were significantly higher than those of controls. There was a significant correlation between serum levels of IL-6 and IL-8, and severity of the disease.

Conclusion: Psoriasis can be described as a T-cell-mediated disease, with a complex role for a variety of cytokines, which has led to the development of new immune-modulatory therapies. Our study confirms the contribution of IL-6 and IL-8 in the pathogenesis of psoriasis and indicates a possible role in the active phase of the disease.

KEYWORDS

Interleukin (IL-6 & 8); Psoriasis Area and Severity Index (PASI); Psoriasis

Introduction

Psoriasis is a group of chronic inflammatory and proliferative conditions of skin, associated with systemic manifestations. [1] Psoriasis is universal in occurrence, with the prevalence in different population varies from 0.1% to 11.8%. It may begin at any age, but most likely to appear between the age of 15 to 30 years.[2] Considered to be immune-mediated polygenic skin disorder, various environmental triggering factors such as infections, medications, trauma, may induce the disease in a genetically predisposed individual.[3] Clinically psoriasis is characterized by well demarcated erythematous plaques with silvery white, micaceous scales. Histopathology of a psoriatic lesion shows hyperkeratosis, parakeratosis, acanthosis, supra-papillary thinning, neutrophils in epidermis, tortuous and dilated blood vessel and an inflammatory infiltrate mostly composed of lymphocytes. Psoriasis area severity score (PASI), created by Fredriksson and Pettersson in 1978, is a very practical measure of disease severity as well as response to therapy.[4] Historically psoriasis was considered to be a disorder of keratinocytes, but recent investigations showed that T-Helper cell subset and their secreted cytokines are implicated in the pathogenesis of psoriasis.[5] Complex cytokine network is involved with actions and interactions of many cytokines, chemokines, growth factors and their receptors secreted by many cell types.[2] Among T-cell cytokines, interleukin 6 (IL-6) cause keratinocyte proliferation. [1] IL-6 is multifunctional cytokine with over-expression of IL-6 is implicated in psoriasis.[6] In a normal host, during acute inflammation, IL-6 has protective effect by suppressing inflammatory cytokines without affecting anti-inflammatory cytokines, however in chronic inflammation IL-6 has got detrimental effect by favouring mono-nuclear cell accumulation, angio-proliferation and anti-apoptotic effects on T-cells. The complex of IL-6 and its soluble receptors IL-6R also activates endothelial cells to secrete IL-8.[7] Apart from a potent chemokine for neutrophils, Interleukin 8 is also CXC chemokine that is known to be angio-genic by attracting endothelial cells. [2] In this study we measure the levels of serum IL-6 and 8 levels in patients and correlate these parameters with the disease severity.

Material and Methods

Data Collection

This is a cross-sectional study from January 2015 to July 2016. All the patients who were clinically diagnosed with psoriasis were asked for participation in the study. Informed written consent was taken from all

the patients. A pre-structured proforma was used to collect the baseline data. Detailed clinical examination and biochemical tests were done on all patients.

Selection of samples

Blood samples were collected from 40 psoriasis patients without any other associated disease. A patient with all types of psoriasis was included like psoriasis vulgaris, guttate psoriasis inverse psoriasis and pustular psoriasis, palmo-plantar psoriasis, psoriatic arthritis. Patients were clinically diagnosed by grattage test and auspitz sign and histopathologically by skin biopsy. Pregnant women, psoriatic erythroderma, patients on biological therapy and patients on immunosuppressive drugs were exclusion criteria. Age and both sexes matched healthy consenting volunteers were included.

Investigation Details

Venous blood samples (5-10 mL) were taken in vacutainer tubes under sterile conditions from patients and controls. Serum was obtained from freshly drawn, rapidly centrifugated. Serum was quickly frozen at -80°C and stored until processed. Serum IL-6 and IL-8 levels were measured by enzyme-linked immunosorbent assay (ELISA) technique (Diacclone SAS F-25020 Besoncon Cedex, France). The severity of psoriasis was assessed by the psoriasis area and severity index (PASI) for each patient. The control group was comprised of healthy, non-psoriatic volunteers with no family history of psoriasis.

Statistical analyses

All data were analyzed using the statistical package for social science (SPSS) 21.0 for Windows program on the computer. The D'Agostino-Pearson and Mann-Whitney tests were used. Results were expressed as median and interquartile range or mean \pm standard deviation (SD) for variables with normal distribution. Pearson's correlation coefficient was used in correlation analyses. The statistical significance was accepted when $p < 0.05$.

Results

Clinical Parameters of patients with Psoriasis

Mean age of cases was 40.37 ± 13.1 year & for controls was 38.21 ± 12.1 year. Maximum numbers of cases were from 41 to 50 year age group and of controls from 21 to 30 year age group. There were 36 and 31 males in cases and control respectively. There were four and nine females in cases and control respectively. Mean PASI score in males

was 10.57±5.75, in females was 14.42±9.58. Mean PASI of all the patients was 10.95±6.18. Median duration of illness of male was 3 years and for female was around 2.5 years. Total mean age for duration of illness is 3 years.

IL-6 and IL-8 serum levels in patients with psoriasis and healthy controls

The results of serum levels of IL-6 and IL-8 in patients with psoriasis and healthy controls do not follow the normal distribution so, according to the D'Agostino-Pearson test the serum level of IL-6 and IL-8 were expressed by median with interquartile range. The median and range of serum levels of IL-6 was increased in cases than in control (P=0.013).The median and range of serum levels of IL-8 was also increased in cases than in control (P=0.043) (Table 1)

Correlations between IL-6 and IL-8 Serum Levels patients with psoriasis and PASI Score and Age

In our study we observed that serum levels of IL-6 and IL-8 were increased in patients with psoriasis as compared to healthy controls and also the serum levels of IL-6 and IL-8 significantly correlate with PASI as shown in figure 1 and 2. However in our study no correlation was found when we analyze the serum levels of IL-6 and IL-8 in patients with psoriasis and age of patients as shown in Table 2.

Discussion

The present work revealed that psoriasis affects both sexes however higher percentage of males than females with no significant differences. Mean PASI in males was 10.57±5.75 and in females were 14.42±9.58. Mean duration of psoriasis in males was 3 years and in females was 2.5 years.

In our study, increased serum levels of IL-6 were present in patients with psoriasis in comparison to healthy controls. Similar to our study, Alenius GM et al [8] in their in 219 patients with psoriasis and psoriatic arthritis patients found increased serum levels of IL-6. Also Arican et al [9] in their study in 30 patients of psoriasis found increased serum levels of IL-6. However De Oliveir et al in 2015[10], no correlation was observed with disease activity and serum IL-6 levels. Treatment of psoriasis with biological like infliximab and adalimumab also leads to decrease in serum levels of IL-6 [11], however when we treat the psoriatic patients with anti-IL-6 therapy, it is ineffective. Possible explanation of ineffectiveness of anti IL6 in psoriasis is that inhibition of IL-6 led to compensatory pro-inflammatory effects by other cytokines.[12]

In our study, increased serum levels of IL-8 were present in patients with psoriasis in comparison to healthy controls. Other studies also found the serum levels of IL-8 in patients with psoriasis. [13-15] Also Biasi D. et al [16] in their study showed a great increase of IL-8 in the exudate from psoriatic patients compared to controls. Jacob et al [14] in their study of 12 patients with psoriasis found increased IL8 levels and the level correlated with the lesional erythema. In Egyptian study, Abdel et al [17] found serum IL-8 levels were also moderately elevated and correlated with the age of patients with psoriasis. Borska et al [13] in their study used goeckerman regimen for the treatment of psoriasis, they observed increase in serum levels of IL-8, but Chen et al [15] in their study used NBUVB for the treatment of psoriasis, they noticed significant decrease in IL-8.

In our study we found elevated serum IL-6 and IL-8 levels in psoriatic patients in correlation with PASI. In a recent study Cordiali-Fei et al. [18] showed increased IL-6 serum levels, but no correlation with PASI was attempted. However Elango et al in their study reported a positive correlation with only two components of PASI, namely, infiltration and desquamation [19].

Conclusion

In conclusion, our study confirms the contribution of IL-6 and IL-8 in the pathogenesis of psoriasis and indicates a possible role in the active phase of the disease. In the light that these cytokines have been recently introduced as therapeutic targets for psoriasis this knowledge might help in the choice of most appropriate candidates for the treatment of psoriasis. However, larger studies conducted in a prospective manner are required to further confirm our findings.

Declaration of Conflicting Interests

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Table 1: Serum IL-6 and IL-8 levels in cases & controls

	Median	Range	Man-Whitney test
Serum Interleukin 6 levels			
Cases	8.25	0.81-59.60	0.013
Controls	5.1	0.81-32.5	
Serum Interleukin 8 levels			
Cases	28.0	28-1200	0.043
Controls	28.0	28-80	

Values are represented by median with (minimum–maximum). * $p < 0.05$ and **** $p < 0.0001$.

Table 2: Correlation of PASI and Age with Serum IL-6 and IL-8 levels

	Correlation (R)	p-value
PASI		
IL-6	0.823	0.0001***
IL-8	0.425	0.006*
Age		
IL-6	0.065	0.692
IL-8	0.142	0.381

* $p < 0.05$ and **** $p < 0.0001$.

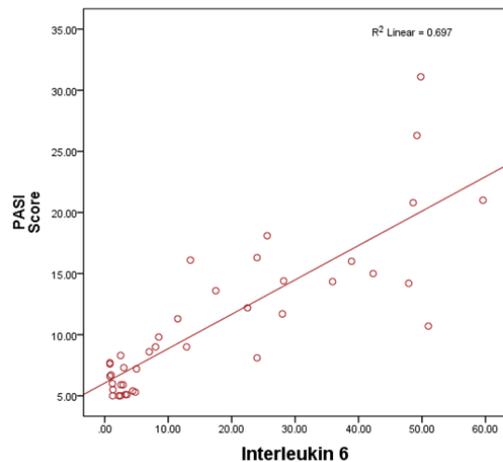


Figure 1: Correlation of PASI and Age with Serum IL-6 levels

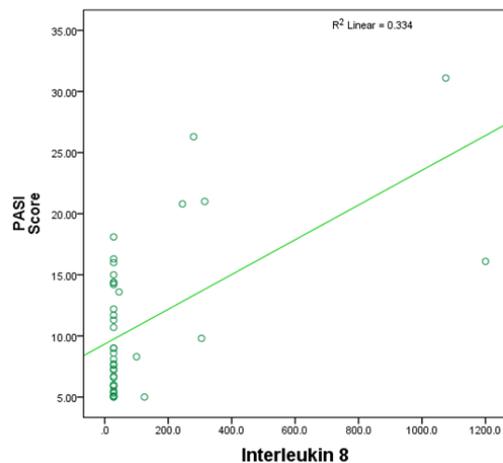


Figure 2: Correlation of PASI and Age with Serum IL-8 levels

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