Increased Serum Levels of TNF-α and IL-6 are not Related to HLA-Cw6 in Psoriasis Patients Correlation of Cytokine with HLA Cw6

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Abstract
Psoriasis is a T cell mediated inflammatory skin disease. Complex network of cytokine induces and maintain the psoriatic lesion. Study was performed to evaluate the correlation between the level of TNF- α and IL-6, in the psoriasis patients with HLA-Cw6. Cytokine levels were assayed by sandwich ELISA and HLA-Cw6 typing was done by microcytotoxicity method. Serum TNF-α and IL-6 were significantly (p=<0.001 in both) expressed in psoriasis patients. TNF-α had significant positive correlation with IL-6 (p=0.56, p=<0.001). We can conclude that TNF-α and IL-6 are found elevated in serum in psoriasis patients, compared to the control group. Prolinflammatory cytokine such as TNF-α and IL-6 may cause inflammatory changes in microenvironment of psoriasis lesion. Gender of patient and age on onset of disease does not influence the expression of these cytokine in psoriasis cases. Results suggest that HLA- Cw6 did not influence these cytokine secretion.

Keywords: Psoriasis, TNF-α, IL-6, HLA-Cw6

Introduction
Psoriasis is characterized by two primary events hyper proliferation of keratinocyte and inflammatory dermal infiltration of mononuclear cells [1]. Previous studies had confirmed that altered T cells regulation along with complex network of cytokines are the main factors for induction and maintenance of various pathological stages of psoriasis [2-4]. Studies also demonstrated that proinflammatory cytokines TNF-α and IL-6 were markedly increased in the serum of psoriasis patients [5-9]. HLA antigen positive and negative individual differ in their ability to produce cytokines [10,11] or cytokines induce the expression of HLA antigen [12]. So present study was performed to evaluate correlation between the level of TNF- α and IL-6, in the psoriasis patients with HLA-Cw6.

Methods and Methods
In total of 60 psoriasis patients and 60 healthy controls were enrolled in this study. Neither patients nor control had present or past history of any skin disease or systemic or present history of infectious disease. Psoriasis patients who had not received any prior local or systemic treatment within three months were included in the study and were in active state of their disease.

About 5 ml of venous blood sample were collected from patients and controls in plain sterilized vials and 5 ml in heparinized vial for HLA-Cw6 typing. Serum sample was stored at -70°C until processed. Serum TNF-α and IL-6 were assayed using sandwich ELISA of Beckman Coulter, France. Typing for HLA-Cw6 antigen was performed by microcytotoxicity method of Terasaki and McCleland as described in detail by Mehra [13]. Antisera used for HLA-Cw6 typing was of BAG Company, Germany. The study was approved by ethical committee of the institution and informed consent was taken from all patients enrolled in the study.

Statistical Analysis
All data was analyzed using SPSS 14.0 (SPSS Inc., Chicago, IL, USA) computer statistics programme. Values were given as mean ± Standard deviation (SD). Student t test used to compare mean, Pearson Chi-square used for comparing frequency and Pearson correlation was used to analysis of correlation. p values less than 0.05 were considered significant.

Results
A total of 120 subjects were enrolled in the study comprise of 60 psoriasis patients (median age 35 years) and 60 controls (median age 28 years). In patient group 35 males and 25 females were included and in control group 37 males and 23 females were included. Disease duration ranged from 0.5-30 years with the mean of 6.37 ± 6.35 years and age of onset ranged from 4- 69 years with the mean age of 30.48 ± 9.03 years. HLA-Cw6 was found positive in 20 cases (33.3%) of psoriasis while only six cases (10.0%) in control group. HLA-Cw6 was significantly expressed in patients with psoriasis as compared to control group with p value 0.002.

In controls mean value of serum TNF-α was 7.58±4.19 pg/ml (range 2-15 pg/ml) while in psoriasis TNF-α was markedly increased (29.73 ± 17.31 pg/ml, range 9-74 pg/ml). Rise of TNF-α was highly significant (p<0.001). Similarly serum IL-6 was markedly raised in psoriasis (36.88 ± 26.61 pg/ml, range 5-98 pg/ml) as compared to healthy control (5.56 ± 2.29 pg/ml, range 2-11 pg/ml) which was statically significant (Figures 1 and 2). In patients univariate analysis showed that serum TNF-α correlated significantly with IL-6 (r=0.26, p=0.024). HLA-Cw6 showed positive correlation with family history (r=0.35, p=0.003) suggesting that HLA Cw6 was expressed in patients with positive family history psoriasis. No correlation was found among the cytokines and HLA Cw6 (Tables 1 and 2).

Discussion
Cytokines are essential for various pathological changes in the development of psoriasis. Cytokines form a complex and multidimensional network in psoriasis pathobiology, none of which alone can be considered to involve in disease causative mechanism [2].
They influence keratinocyte proliferation, induce neutrophil and T cell chemotaxis, keep T cells in type 1 differentiation, enhance angiogenesis and upregulate adhesion molecules on endothelial cells, and stimulate the release of other chemokines. We found IL-6 and TNF-α to be elevated in our patient's group than in control group. Elevated serum levels of these cytokines were reported by most of the investigators [14-17]. TNF-α is produced by Langerhans cells, macrophages, monocytes, T cells and keratinocytes [18]. TNF-α is a proinflammatory cytokine and increases proliferation of keratinocytes [19]. TNF-α also induces IL-6 and TNF-α to be elevated in our patient's group than in control group. Elevated serum levels of these cytokines were reported by most of the investigators [14-17]. TNF-α is produced by Langerhans cells, macrophages, monocytes, T cells and keratinocytes [18]. TNF-α is a proinflammatory cytokine and increases proliferation of keratinocytes [19]. TNF-α also induces

**Figure 1:** Showing serum TNF-α level in psoriasis patients and controls. Mean of TNF-α in psoriasis group and mean of TNF-α in control group.

**Figure 2:** Showing serum IL-6 level in psoriasis patients and controls. Mean of TNF-α in psoriasis group and mean of TNF-α in control group.

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Group</th>
<th>Range</th>
<th>Mean ± SD</th>
<th>p</th>
<th>CI (95%)</th>
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* Significant (p < 0.05)

**Table 1:** Serum level of TNF-α and IL-6 in patients of psoriasis.

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**Table 2:** Correlation of cytokines with HLA-Cw6, age of onset, gender and family history.

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**References**