

Association of HLA class I and class II alleles with psoriasis vulgaris in Turkish population

Influence of type I and II psoriasis

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ABSTRACT

Objective: To investigate the role of human leukocyte antigen (HLA) in susceptibility to psoriasis vulgaris in the Northeast region of Turkey and to contribute to the data related to HLA and psoriasis.

Methods: The study included 72 unrelated psoriatic patients (43 men and 29 women; aged 11-76 years) admitted to the Dermatology Department, University Research Hospital, Erzurum, Turkey between April 2002 and November 2003. We studied the distribution of HLA class I and II antigens in patients with psoriasis: 72 patients were divided into 2 groups according to the onset of psoriasis before age 40 years with family history (type I) and onset after age 40 without family history (type II). The HLA class I and II antigens were analyzed using the PCR-SSP method in 72 patients and in 104 controls.

Results: We found an increase in HLA-A*30 and A*68, B*7, B*13, B*57, Cw6, and DRB1*07 antigens in psoriatic patients compared with controls. As we compared type I and type II psoriasis with control group, B*57, Cw6 and DRB1*07 alleles were more significant in patients with type I psoriasis. Our patients with type II psoriasis represented a significant association with the HLA-B*13.

Conclusion: Our findings along with previous HLA studies on psoriasis vulgaris patients from different racial groups showed that HLA-B*57 and DRB1*07 alleles are associated with the disease.

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Psoriasis is a chronic, inflammatory, hyperproliferative disease of the skin, scalp, nails and joints.¹ Accumulating evidence suggests that genetic factors, including human leukocyte antigens (HLA) association, are strongly involved in the pathogenesis of psoriasis.² Gene products of the major histocompatibility complex located on the short arm of chromosome 6 are HLA molecules. The

genes most distant from the centromere are those that encode the classic HLA class I antigens A, C and B.³ The association of several HLA class I antigens with susceptibility for development of psoriasis has been reported in the different populations, showing the increased frequencies of the occurrence of HLA-A1, A2, B13, B37, B39, B57, Cw1, Cw6, and others in patients with psoriasis.⁴⁻⁶ Additionally, psoriasis is the

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well-known disease linked to HLA-C genes. Certain HLA antigens act as strong modifiers of disease expression, decreasing the threshold for developing psoriasis in susceptible individuals. The development of psoriasis has been implicated to be triggered by some environmental factors in susceptible individuals with a particular genetic background. Some studies have demonstrated that susceptibility to psoriasis is associated with HLA class I and II alleles specificity in different ethnic groups.¹ In terms of HLA associations, Henseler and Christophers⁷ have defined 2 types of psoriasis. The early onset form, type I, is inherited and associated with Cw6, B*13, B*57 and DRB1*07, while type II occurs sporadically later in life. The role of the Cw6 gene in the development of psoriasis is very well documented.⁸⁻¹⁰

The aim of this study was to investigate the role of HLA in susceptibility to psoriasis vulgaris in the Northeast region of Turkey and to contribute to the data related to HLA and psoriasis.

Methods. Seventy-two unrelated psoriatic patients (43 men and 29 women; aged 11-76 years) attending to the Dermatology Department, Faculty of Medicine, Ataturk University, Erzurum, Turkey were included in this study. Fifty patients with a positive family history and disease onset before 40 years old were assessed as type I, while 22 patients with no family history and onset of disease after 40 year old were classified as having type II psoriasis. The diagnosis of all patients was made by a dermatologist and confirmed by histopathological analysis. The control group consisted of 104 healthy renal transplant and bone marrow transplant donors (62 men and 42 women; aged 9-59 years). All patient subjects were asked for blood examinations and signed consent form. Patient with psoriasis vulgaris was informed about the study and HLA tissue typing report was given for each patient.

To prepare DNA from peripheral blood cells, EDTA blood was used applying the Sigma Gen Elute Kit as to the manufacturer's instructions.

Low-resolution typing for the HLA-A, B, C and HLA-DR/DQ were performed by means of the PCR-SSP method using SSP HLA class I generic DNA Typing Tray, Lot 002 and using SSP HLA class II generic DNA Typing Tray, Lot 004 (One Lambda, Canoga Park, CA, USA) according to the manufacturer's instructions.

Chi-square with Yates' correction was performed and then both standard p value and the significance of an association were evaluated. The degree of association was calculated by odds ratio (OR). All statistical calculations were performed using the

Statistical Package for Social Sciences version 11.5 program for windows software.

Results. The frequencies for significantly elevated HLA-A, HLA-B, HLA-Cw and HLA-DR antigens identified by PCR-SSP in 72 patients with psoriasis vulgaris compared to controls are given in **Table 1**. **Table 1** shows a significant increase in the frequency in patients compared with controls, representing that these alleles were positively associated with psoriasis, of which the HLA-Cw6 and B*57 were the most strongly associated with this dermatosis. Depending on familial history and age, 50 patients were assigned to the type I psoriasis group and 22 patients to the type II psoriasis group. The frequencies for significantly increased HLA-B and -DR antigens in type I patient group are given in **Table 2**, and the frequencies for significantly increased HLA-B antigen in type II group of patient is given in **Table 3**. In **Table 2**, the frequencies of B*57, Cw6 and DRB1*07 were significantly increased in early-onset psoriasis compared with controls. However in **Table 3**, the frequencies of B*13 was significantly increased in late onset psoriasis compared to controls.

Discussion. Although the pathogenesis of psoriasis is not clear there is evidence to suggest that psoriasis is a T cell mediated autoimmune disease.¹¹⁻¹² Studies in 1990s focused on a disease gene in the HLA region depending on HLA association studies. The precise genetic basis of HLA relation in psoriasis remained elusive. This was possibly due to little or no evidence found linking to the HLA region. Knowledge regarding expression of HLA molecules may, therefore, help to understand the disease process. Many studies reported that several HLA antigens were shown to be increased frequencies among patients with psoriasis vulgaris in different ethnic groups: HLA A*2, A*30, B*13, B*17, B*37, B*39, B*57, Cw6, Cw7, Cw11 and DRB1*07.^{1,8,9,12-14} The possible role of HLA association with the age at onset of psoriasis presented by various studies and HLA Cw6 antigen was indicated as a marker of the type I psoriasis.^{2,8,12,13,17,18} HLA B*13, B*17 and B*57 were also described an increased odds ratio in early onset psoriasis.^{8,12-18} This study provides analysis of HLA-A, -B, -C and -DR polymorphisms in control and psoriasis groups. Allelic distributions or allele carrier frequency was compared between control and psoriasis subjects.

The results of our study showed that there is strong association with HLA-B*57, Cw6 and DRB1*07 in patient with psoriasis as compared to controls. The importance of HLA A*30, Cw3, Cw6,

Table 1 - Comparison of statistical significant HLA antigens frequencies between control and patients.

HLA Alleles	Controls N=104		Patients N=72		χ^2_{ν}	P	OR	CI (95%)
A*30	8	(7.6%)	16	(22.2%)	6.443	0.011*	3.429	1.379 - 8.521
A*68	15	(14.4%)	20	(27.7%)	3.961	0.047*	2.282	1.076 - 4.84
B*7	11	(10.5%)	24	(33.3%)	12.438	0.000**	4.227	1.191 - 9.353
B*13	4	(3.8%)	16	(22.2%)	12.498	0.000**	7.143	2.277 - 22.411
B*57	4	(3.8%)	32	(44.4%)	40.64	0.000**	20	6.643 - 60.216
Cw6	9	(8.6%)	48	(66%)	62.767	0.000**	21.111	9.104 - 48.952
DRB1*07	8	(7.6%)	33	(45.8%)	32.536	0.000**	10.154	4.308 - 23.932

*Significant at the level $p < 0.05$, ** Significant at the level $p < 0.01$
OR - odds ratio, CI - confidence interval

Table 2 - Frequencies of statistical significant HLA antigens in type I psoriasis compared to controls.

HLA Alleles	Controls N=104		Type I N=50		χ^2_{ν}	P	OR	CI (95%)
B*57	4	(3.8%)	30	(60%)	58.669	0.000*	37.5	11.892 - 118.247
Cw6	9	(8.6%)	45	(90%)	94.59	0.000*	95	30.101 - 299.823
DRB1*07	8	(7.6%)	31	(62%)	49.828	0.000*	19.579	7.803 - 49.127

*Significant at the level $p < 0.01$
OR - odds ratio, CI - confidence interval

Table 3 - Frequencies of statistical significant HLA antigens in type II psoriasis compared to controls.

HLA Alleles	Controls N=104		Type II N=22		χ^2_{ν}	P	OR	CI (95%)
B*13	4	(3.8%)	15	(68.1%)	53.577	0.000**	53.571	13.985 - 205.207

**Significant at the level $p < 0.01$
OR - odds ratio, CI - confidence interval

DRB1*07 and DRB1*14 antigens were reported by other studies performed on Turkish patients with psoriasis vulgaris.^{13,16} In our study, despite the fact that HLA-A*30, A*68, B*7 and B*13 alleles were also significantly increased in patients with psoriasis, when we compared type I and type II psoriasis with controls, B*57, Cw6 and DRB1*07 alleles were more significant in patients with type I than type II. In our patients, type II psoriasis represented a significant association with the HLA-B*13 allele.

In conclusion, our findings along with other previous HLA studies on psoriasis vulgaris patients from different racial groups, showed that HLA-B*57,

Cw6 and DRB1*07 alleles are associated with the disease. Type I psoriasis is strongly related to HLA-B*57, Cw6 and DRB1*07 alleles, and type II with the HLA-B*13 allele in our study group. Our results were not only similar to other studies, but also contributes information for the association of HLA with types I and II psoriasis vulgaris.

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