# Association between Hashimoto's Thyroiditis and human leucocyte antigens

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*HLA-DR and DQ antigens positivity was searched in 27 patients with Hashimoto thyroiditis (HT) in and in 100 healthy control subjects. No significant difference was found at HLA-DR locus between HT patients and controls. However HLA-DQw3 antigen was found less frequent in HT patients when compared with controls that was statistically significiant.(p<0.01). These results suggest that the lack of HLA-DQw3 antigen may leads to HT or at least it may be considered as a contributory factor for the diseases. [Turk J Med Res 1997, 15(1): 29-31]*

**Key Words:** Hashimoto's Thyroiditis, Human Leucocyte Antigen

Autoimmune thyroid disease consist of Grave's disease, Hashimoto's Thyroiditis(HT) and primary myxedema. Atrophic and goitrogenic subtypes of HT were described (1-4). In animal studies an association was reported between autoimmune thyroid disease and HLA system (2,5) particularly with HLA-DR and DQ antigens but not with HLA-A,B,C antigens (6). HLA system which is located on the short arm of 6th chromosome codes different surface Major Histocompatibility Complex(MHC) antigens such as Class I, Class II, and Class 111.(13) Class I MHC antigens exist in the nucleus of all body cells and cytogenetic and supressor T cells as well. Class II MHC antigens exist primarly in immune system cells and also in T helper subgroup. Class III MHC antigens are known as components of complement pathway . Class II MHC antigens were found at the surface of thyroid cells of murine thyroid cells (7). It has been reported that HLA-DR and DQ subgroups were associated with HT (1,2,8-12).

We designed a study to evaluate whether such as an association exists in our population and if it does with which HLA subgroups it is associated.

## MATERIALS AND METHODS

In our study, 27 patients with HT and 100 healthy control subjects were searched. HT diagnosis was made by history, physical examination , TT3, TT4, FT3, FT4, TSH, anti microsomal antibody (anti-M), antithyroglobulin antibody (anti-T), ultrasonography of thyroid gland and scintigrapy. The diagnosis was supported with biopsy if necessary. MHC-Class antigens were studied by lymphocytotoxicity method by using (Biotest) plaque. Four of the patients were male (14.8%) and twentythree were female.(85.2%) The patients mean age was 39.42+11.74. The control group consisted of healthy subjects who were donors for renal transplantation.

HLA Class II MHC was studied in both patients with HT and control group.

Statistical analysis was done by chi-square and Fisher's exact tests.

## RESULTS

The HLA-DR and DQ status of the patients who were diagnosed as HT and healthy control group are are given in the Table 1. As it can be seen in table 1, there was no difference between HLA DR locus of both groups statistically. However in HT group HLA-DQw3 was less frequent than the control group and this diference was significant ($p<0.01$) and HLA-Dqw1 was also seen less frequently but less evident. FT4, FT3, TSH, anti-M antibody and anti-T antibody levels of patients with HT are shown in Table 2. As fine needle aspiration biopsy is unnecessary for most HT patient, in our study we supported the diagnosis of HT only in three patients by biopsy.

The FT3, FT4, TSH levels were found higher than they were expected. This might be attributed to the fact patients were under substition therapy before they entered the study.

## DISCUSSION

HT is an autoimmune thyroid disease (1,2,7,13). It is reported that autoimmune thyroid diseases are developed

**Received:** 16.12.1996 **Accepted:** 01.04.1997

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**Table 1.** DR and DQ Antigen Frequencies, Ratios, Relative Possibility Risk and p Values.

| TEST | Cases n=27 | Case % | Controls n=100 | Control % | QR | (CI 95%) | Chi-square | P |
|---|---|---|---|---|---|---|---|---|
| DR1 | 5 | 18.5 | 11 | 11 | 1.84 | 0.50-6.57 | 1.09 | >0.05 |
| DR2 | 1 | 3.7 | 0 | | - | | - | >0.05 |
| DR4 | 6 | 22.2 | 21 | 21 | 1.07 | 0.34-3.30 | 0.02 | >0.05 |
| DRw5 | 2 | 3.7 | 0 | | - | | | |
| DR7 | 3 | 11.1 | 18 | 18 | 0.57 | 0.12-2.30 | - | >0.05 |
| DR8 | 1 | 3.7 | 3 | 3 | - | | - | >0.05 |
| DR9 | 2 | 7.4 | 1 | 1 | - | | - | >0.05 |
| DR10 | - | | 2 | 2 | - | | - | >0.05 |
| DRw11(5) | 9 | 33.3 | 33 | 33 | 1.17 | 0.43-3.11 | 0.11 | >0.05 |
| DRw12(5) | 1 | 3.7 | 3 | 3 | - | | - | >0.05 |
| DR13 | 1 | 3.7 | - | | - | | - | >0.05 |
| DRw13(6) | 2 | 7.4 | 11 | 11 | 0.65 | 0.09-3.43 | - | >0.05 |
| DRw14(6) | 1 | 3.7 | 5 | 5 | 0.73 | 0.03-6.97 | - | >0.05 |
| DRw15(2) | 5 | 18.5 | 15 | 15 | 1.29 | 0.36-4.36 | - | >0.05 |
| DR16(2) | 1 | 3.7 | 10 | 10 | 0.35 | 0.09-2.86 | - | >0.05 |
| DRw16(2) | 2 | 7.4 | - | | - | | - | >0.05 |
| DR17(3) | 5 | 18.5 | 20 | 20 | 0.91 | 0.26-2.97 | 0.03 | >0.05 |
| DRw51 | 4 | 18.5 | 16 | 16 | 0.91 | 0.23-3.32 | - | >0.05 |
| DRw52 | 17 | 62.9 | 66 | 66 | 0.88 | 0.33-2.32 | 0.09 | >0.05 |
| DRw53 | 9 | 33.3 | 40 | 40 | 0.75 | 0.28-1.99 | 0.40 | >0.05 |
| DQw1 | 9 | 33.3 | 52 | 52 | 0.46 | 1.17-1.22 | 2.97 | <0.10 |
| DQw2 | 9 | 33.3 | 27 | 27 | 1.35 | 0.49-3.68 | 0.42 | >0.05 |
| DQw3 | 3 | 11.1 | 64 | 64 | 0.07 | 0.02-0.27 | 23.86 | <0.01 |
| DQw4 | 1 | 3.7 | 0 | | | | | >0.05 |
| DQw5(1) | 4 | 14.8 | 24 | 24 | 0.55 | 0.14-1.92 | 1.04 | >0.05 |
| DQw6(1) | 5 | 18.5 | 28 | 28 | 0.58 | 0.17-1.85 | 0.99 | >0.05 |

**P<0.05**
**QR=** Relative Possibility Risk
CI = Security Interval

as a result of genetic and enviromental factors (14). One of the genetic factors is HLA antigens (5,6).

Significiant increases in HLA-DR and DQ loci are established, although they change from population to population (5,13). In Japanese seropositive and seronegative cases DRw53 phenotypic character was demonstrated predominantly (1).

It was reported that patients with Grave's disease had much higher HLA-B8 levels than the control subjects, but the difference was not statistically significant (1). In a study which was done in Turkey, it was found that HLA-DR4 antigen was higher in Grave's disease (15).

In a study which was performed on HT patients HLA-B8 seen more frequently than the other HLA subtypes, but the difference was not statistically significiant. In the same study HLA-AW30 level was found higher which was statistically significant (1).

In a study reported from Changai, an increment at frequency of HLA-BW46 in goitrogenic HT was shown (12). In another study which was from Southern China, a strong association between HLA-DRw9 and HT was found (16). The MCH patterns of Eastern Asian imigrants inhabiting in England was evaluated and it was reported that a close correlation between HLA-DR4 and HT was shown (11). In a research by Mones et al in autoimmune atrophic thyroiditis, HLA-DR3 was detected with positive 55% in the patients with autoimmune atrophic thyroiditis where as in the control group it was only 26% (9). Uptill now ther has been only one study performed on HT patients . In this study HLA-DR4 antigen positivity in HT group detected more than as it was in the control subjects (17).

**Table 2.** Thyroid Function Tests

| | | |
|---|---|---|
| **Free T3** | 3.78+12 | *(NR=3.1-5.4pg/ml)* |
| **Free T4** | *1.2±1.49* | *(NR=0.7-1.9ng/ml)* |
| **TS H** | *47.5±37.81* | *(NR=0.3-5.0plu/ml)* |
| **Anti-M** | *467.08±826.69* | *(NR=<25lu/ml)* |
| **Anti**-T | *2661.80* | *(NR=<50lu/ml)* |

NR=Normal Range

In our study there was no significant difference between HLA-DR antigen positivity HT patients and controls. The discrepancy between our study and others may be due to the method used or smaller number of patients.

In Japanese HT patients an increase in HLA-DQw4 and decrease in HLA-DQw1 frequencies was established (2). The frequency HLA-DQw2 was found lower in Eastern Asian imigrate population inhabiting in England. Although no significiant difference between HT patients and controls in a study which was designed to evaluate the frequencies of HLA-DQ subgroups, we demonstrated that HLA-Dqw3 frequency was lower in HT patients than the control subjects.

In conclusion; despite the previous studies that showed a relation between HLA-DR antigens and HT, we were unable to find any correlation of this type in our study. Indeed we consider the prevelance of is much higher in HLA-DQw3 negative subjects.

**Hashimoto Tiroiditi ile human lökosit antijen ilişkisi**

*Hashimoto Tiroidit'i (HT) tanısı alan 27 ve sağlıklı 100 olguda Human lökosit antijen (HLA)-DR ve DQ antijen pozitiflikleri araştırıldı. HLA-DR antijeni bulundurma yönünden, HT bulunan hastalarla, sağlıklı kontrol grubu arasında istatistiki yönden önemli bir fark bulunmadı. HLA-DQ antijen pozitifliği yönünden ise, HLA-DQw3 açısından hasta ve sağlıklı kontrol grubu arasında istatistiksel yönden önemli fark tesbit edildi. HT'li olgularda, sağlıklı kontrol grubuna göre HLA-DQw3 antijeni daha az bulunmakta idi (P<0.01). Sonuç olarak ülkemizde HLA-DQw3'ün negatif olmasının HT'in gelişme olasılığını arttırdığı söylenebilir. [T Klin Araştırma 1997; 15(1):29-31]*

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