# The distribution of HLA-A, B and C antigens in Turkish population

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*The HLA-A, B and C antigens of 2180 individuals, living in different geographical regions in Turkey have been determined, HLA-A, B and C antigen frequencies were compared with data reported for European Caucasoids and other populations. The most common A and B locus antigens in all geographic regions were A2, A9, A1, B5, B35 and B12. Most similarities in antigen frequencies were seen between Turkish and European Caucasoid populations. Linkage disequilibria between alleles of HLA loci were examined; the most common HLA alleles in linkage disequlibrium in Turkish population B35Cw4, A1B8 and B27Cw2. The present HLA data reveal that the populations in geographic regions of Turkey are homogenous. [Turk J Med Res 1993; 11(1): 32-36]*

Key Words: HLA antigens, Linkage disequilibrium

The HLA region has been shown to be the most polymorphic genetics system thus far known in man (7). It is known that the linkage-disequlibrium between these HLA alleles is remarkably different in each population of the world (4,3). Thus each population tends to have different HLA gene frequencies and set of characteristic haplotypes.

Turkey, lying between 36-42° E and 26-45° N is a country situated in west of Asia and southeast of Europe. It has a population of nearly fifty-five million. The population of Turkish consists of 99.2% Muslims and 0.8% Christians. Turkey has seven geographical regions.

HLA antigen distribution in several ethnic groups of the world has been reported (2,3). Although, few reports are also available on Turkish population, this study is the largest (6).

In this study, we have characterised distribution of HLA antigens and compared it with European Caucasoid populations and other populations.

## MATERIALS AND METHODS

A total of 2180 individuals, mainly healthy parents of potential kidney recipients, living in the different geographical regions (Blacksea, Mediterranean, Egean, Middle Anatolia, East Anatolia, Marmara, Southeast Anatolia regions) were included in the study.

HLA-typing: All 2180 Turkish donors were tested for class I antigens by the two-stage microlymphocytotoxicity assays (11).

Following HLA antigens were appointed:

A-locus: 1,2,3,9,10,11,28.

B-locus: 5,7,8,12,13,14,15,18,27,35,40,w4,w6, w22, w51, w55.

C-locus: w2, w4.

Statistical analysis: Gen frequencies were calculated by the formula (10):

gf: I-Zilrf"

gf: gene frequency

af: frequency of the antigen

Haplotype frequencies were estimated from the phenotypes of random individuals, according to the equation of Ceppellini et al (5).

xij: PiPj+A

xij: The haplotype frequency corresponding to the i specificity at one locus and the j spesicificity at another locus.

Pi and Pj: The gene frequencies of the antigens forming the haplotype.

Delta (A): The linkage disequilibrium parameters for these antigens. The delta values were calculated from 2x2 tables according to the equation of Mattiuz et al (8), where

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$$\Delta: \frac{d}{n} - \frac{(b+d)\,(c+d)}{n}$$

The frequencies of the phenotypes ++, +-, -+ and — are represented by a,b,c and d respectively and n: a+b+c+d. Tests of significant linkage disequilibrium were made using a chi-square test. All significance levels are two-sided and are not corrected for multiple comparisons.

## RESULTS

*Antigen frequencies (AF) and gene frequencies (GF):* The HLA-A antigen and gene frequencies observed among 2180 Turkish are summarized in Table 1. The most common A-locus antigens in all geographic regions were A2 (38.2%, for total population), A9 (29.18%) and A1 (20.88%). The HLA-A11 antigen was found higher in Southeast Anatolia and Marmara regions (respectively, 21.56% and 22.3).

The HLA-B and C antigens and genes frequencies are summarized in Table 2. The most common B locus antigens for 2180 donors were B5 (30%). B55 (24.7%) and B12 (12. %). The HLA-B13 frequency was relatively lower in Marmara region (1.31%) than other regions. The HLA-B7 antigen was relatively found higher in Mediterranean region (23.6%). The antigens Bw51 (1.05%), B15 (1.14%), Bw55 (1.37%), B14 (3.21%) and B18 (3.55%) were found infrequently.

The HLA-C antigen and gene frequencies are summarized in Table 2. Cw2 and Cw4 antigen frequencies were found 6.42% and 31.15%, respectively.

*Haplotype frequencies (HF) and linkage disequilibrium:* Significant two-locus haplotype associations and delta values for HLA class I alleles in geographic regions are summarized in Table 3. Statistically significant positive linkage disequilibrium ($p<0.05$) was found for 9 different haplotypes in total population, although, in each geographic regions there were some differences. The most frequently observed class I two-locus haplotypes were B35Cw4 (hf:854), A2B5 (hf:525), B27Cw2 (hf:321) and A1B8 (hf:300). The strongest linkage disequilibrium between class I alleles was found for B35Cw4 (delta:650), A1B8 (delta:340) and B27Cw2 (delta:310).

## DISCUSSION

In this study, we have determined the antigen and gene frequencies for HI_A-A,B and C in population living in the different geographic regions of Turkey. HLA-A.B and C phenotype frequencies of Turkish, European Caucasoids, Japanese Orientals, Negroes, Greeks and Tunisian papulations are shown in Table 4 (2,1,9).

When Turkish population are compared to European Caucasoids, few differences in antigen frequencies can be seen. In Turkish, the frequencies of A2, A9 and A1 are higher. The frequencies of HLA-A are

Table 1. AF* and GF* of HLA-A antigens in Turkish population from 7 different geographic regions

| HLA-A ant. | 1 n:102 | 2 n:130 | 3 n:694 | 4 n:784 | 5 n:300 | 6 n:76 | 7 n:94 | TURKEY n:2180 |
|---|---|---|---|---|---|---|---|---|
| A1 | 18.60* | 26.90 | 19.16 | 23.97 | 15.00 | 18.42 | 22.50 | 20.88 |
| | 9.70** | 14.50 | 8.30 | 13.00 | 7.80 | 9.60 | 11.90 | 11.00 |
| A2 | 36.27 | 43.84 | 42.36 | 35.96 | 33.00 | 38.15 | 38.70 | 38.20 |
| | 20.00 | 25.00 | 24.00 | 20.00 | 18.00 | 21.00 | 21.70 | 21.00 |
| A3 | 19.60 | 10.00 | 18.01 | 12.50 | 19.00 | 15.78 | 10.75 | 15.40 |
| | 10.00 | 5.00 | 9.00 | 5.90 | 10.00 | 8.20 | 5.50 | 8.00 |
| A9 | 29.41 | 26.90 | 26.94 | 30.22 | 32.66 | 22.30 | 34.40 | 29.18 |
| | 16.00 | 14.00 | 13.90 | 17.00 | 18.00 | 11.80 | 19.00 | 15.80 |
| A10 | 2.94 | 11.53 | 8.64 | 7.65 | 5.00 | 5.26 | 6.45 | 7.50 |
| | 1.40 | 5.00 | 4.40 | 3.00 | 2.90 | 2.60 | 3.20 | 3.80 |
| A11 | 21.56 | 13.00 | 8.35 | 11.22 | 11.00 | 22.30 | 7.52 | 11.10 |
| | 11.40 | 6.00 | 4.20 | 5.70 | 5.60 | 11.80 | 3.80 | 5.60 |
| A28 | 3.92 | 7.69 | 11.67 | 10.20 | 9.33 | 13.15 | 12.90 | 10.32 |
| | 2.00 | 4.00 | 6.00 | 5.00 | 4.70 | 6.80 | 6.60 | 5.30 |
| A32 | 5.88 | 0.00 | 0.86 | 1.90 | 1.66 | 1.31 | 0.00 | 1.14 |
| | 3.00 | 0.00 | 0.40 | 0.80 | 0.83 | 0.60 | 0.00 | 0.53 |

* Antigen frequency %

** Gene frequency %,

1. Southeast Anatolia
2 Egean
3 Blacksea
4 Middle Anatolia
5 East Anatolia
6 Marmara
7 Mediterranean

Table 2. AF and GF of HLA-E and C antigens in Turkish population from 7 different geographic regions

| HLA-A ant. | 1 n:102 | 2 n:130 | 3 n:694 | 4 n:784 | 5 n:300 | 6 n:76 | 7 n:94 | TURKEY n:2180 |
|---|---|---|---|---|---|---|---|---|
| B5 | 20.50 | 21.50 | 26.90 | 35.00 | 33.66 | 26.30 | 23.60 | 30.00 |
| | 10.80 | 11.30 | 14.50 | 19.00 | 18.50 | 14.15 | 12.50 | 16.30 |
| B7 | 7.84 | 6.15 | 9.50 | 10.33 | 12.30 | 9.20 | 23.60 | 10.41 |
| | 4.00 | 3.00 | 4.80 | 5.00 | 6.30 | 4.70 | 12.50 | 5.00 |
| B8 | 6.86 | 8.46 | 8.35 | 6.63 | 8.00 | 13.15 | 9.67 | 7.85 |
| | 3.40 | 4.30 | 4.20 | 3.00 | 4.00 | 6.80 | 5.00 | 4.00 |
| B12 | 19.60 | 7.69 | 13.80 | 11.86 | 11.60 | 9.20 | 10.75 | 12.40 |
| | 10.00 | 4.00 | 7.10 | 5.60 | 6.00 | 4.70 | 5.50 | 6.40 |
| B13 | 5.88 | 11.53 | 6.30 | 10.20 | 7.60 | 1.31 | 13.90 | 8.35 |
| | 3.00 | 6.00 | 3.20 | 5.10 | 3.80 | 0.60 | 7.20 | 4.20 |
| B14 | 0.98 | 0.76 | 3.00 | 3.82 | 5.33 | 0.00 | 1.07 | 3.21 |
| | 0.30 | 0.40 | 1.50 | 1.78 | 2.70 | 0.00 | 0.50 | 1.60 |
| B15 | 0.98 | 0.76 | 1.58 | 0.89 | 0.66 | 1.31 | 2.15 | 1.14 |
| | 0.40 | 0.40 | 0.70 | 0.40 | 0.33 | 0.60 | 1.00 | 0.60 |
| B18 | 3.92 | 6.15 | 3.00 | 3.18 | 2.60 | 5.26 | 3.22 | 3.35 |
| | 0.15 | 3.10 | 1.50 | 1.60 | 1.30 | 2.60 | 1.60 | 1.60 |
| B27 | 4.90 | 6.92 | 7.78 | 6.88 | 5.00 | 5.26 | 9.60 | 6.88 |
| | 2.50 | 3.50 | 3.90 | 3.50 | 2.90 | 2.60 | 5.00 | 3.50 |
| B35 | 27.38 | 34.70 | 25.92 | 24.36 | 21.66 | 23.67 | 20.40 | 24.70 |
| | 14.10 | 18.00 | 12.30 | 11.50 | 11.20 | 12.20 | 10.60 | 12.60 |
| B40 | 10.78 | 9.23 | 11.81 | 6.50 | 7.30 | 21.00 | 6.45 | 9.17 |
| | 5.50 | 4.70 | 6.00 | 3.00 | 3.70 | 11.10 | 3.20 | 4.70 |
| Bw4 | 63.70 | 63.84 | 61.95 | 61.47 | 61.30 | 64.47 | 63.40 | 62.00 |
| | 40.00 | 39.80 | 38.31 | 37.50 | 37.70 | 40.00 | 39.50 | 38.00 |
| Bw6 | 60.78 | 44.60 | 43.22 | 42.47 | 48.00 | 39.47 | 44.00 | 44.40 |
| | 37.00 | 25.00 | 24.64 | 23.80 | 27.80 | 22.00 | 25.10 | 25.00 |
| Bw22 | 9.80 | 3.85 | 5.30 | 2.55 | 3.30 | 0.00 | 1.07 | 3.76 |
| | 5.00 | 1.90 | 2.60 | 1.00 | 1.50 | 0.00 | 0.50 | 1.80 |
| Bw51 | 0.00 | 0.76 | 0.86 | 1.65 | 1.00 | 0.00 | 1.07 | 1.05 |
| | 0.00 | 0.40 | 0.43 | 0.80 | 0.50 | 0.00 | 0.50 | 0.50 |
| Bw55 | 6.86 | 0.76 | 2.16 | 0.50 | 1.00 | 0.00 | 0.00 | 1.37 |
| | 3.40 | 0.40 | 1.00 | 0.20 | 0.50 | 0.00 | 0.00 | 0.68 |
| Cw2 | 2.94 | 10.76 | 7.34 | 5.99 | 4.33 | 9.20 | 5.37 | 6.42 |
| | 1.40 | 5.50 | 3.70 | 3.00 | 2.10 | 4.70 | 2.70 | 3.20 |
| Cw4 | 32.35 | 25.38 | 27.95 | 33.80 | 35.30 | 26.30 | 29.00 | 31.15 |
| | 17.70 | 13.60 | 15.00 | 18.00 | 19.50 | 14.15 | 15.70 | 17.00 |

1 Southeast Anatolia
2 Egean
3 Blacksea
4 Middle Anatolia
5 East Anatolia
6 Marmara
7 Mediterranean

similar of Turkish in European Caucasoid and Greek population. In Japanese Orientales, HLA-A1 is lower from other populations.

Although few differences in antigen frequencies among geographic regions can be seen, A2, A9 and A1 are the most common A-locus antigens. The most common B locus antigens for Turkish are B5, B35 and B12, respectively. Ersoy revealed that the frequency of A2 and A9 are higher in Turkish population, too (6). There are also same frequency in Caucasion European population. In Japanese population, B5, B40 and B15 are the most common B locus antigens. In negroes, B12, B5 and B7 are higher B locus antigens.

The lower B locus antigen is B15 for Turkish, but it is B14 for Caucasion European population, B13 for Greeks and Negroes and B18 for Japanese population.

The most common HLA alleles in linkage disequilibrium in Turkish population are B35Cw4, A1B8 and B27Cw2. In Caucasions and Greeks, the higher delta value is observed for A1B8 haplotype (2). A1B17 haplotype is the most common HLA alleles in Tunisian.

There are some differences for HLA haplotype among geographic regions of Turkey (Table 3). But B35Cw4 is the most common HLA allele in all regions.

Table 3. Significant two-locus haplotype associations and delta values for HLA class 1 alleles

| Region | Haplotype | Haplotype frequency x 10 | value x10 | P |
|---|---|---|---|---|
| Southeast Anatolia | A1B40 | 343 | 290 | <0.05 |
| | A1Bw22 | 358 | 310 | <0.05 |
| | A2B13 | 340 | 280 | <0.05 |
| | A9B18 | 224 | 220 | <0.01 |
| | A28B8 | 176 | 170 | <0.05 |
| | B27Cw2 | 303 | 300 | <0.001 |
| | B35CW4 | 990 | 840 | <0.001 |
| Egean | A9B12 | 350 | 300 | <0.05 |
| | B27Cw2 | 400 | 390 | <0.001 |
| | Bw6Cw2 | 490 | 360 | <0.05 |
| | B35Cw4 | 740 | 620 | <0.001 |
| Blacksea | A1B8 | 164 | 130 | <0.01 |
| | A1B35 | 220 | 160 | <0.01 |
| | A2B27 | 190 | 100 | <0.05 |
| | A2Bw4 | 390 | 300 | <0.05 |
| | A2Cw2 | 280 | 200 | <0.001 |
| | A10B35 | 180 | 150 | <0.001 |
| | B27Cw2 | 330 | 320 | <0.001 |
| | B35Cw4 | 560 | 460 | <0.001 |
| Middle Anatolia | A1B8 | 239 | 200 | <0.01 |
| | A1B35 | 189 | 180 | <0.01 |
| | A2B5 | 650 | 270 | <0.01 |
| | B27Cw2 | 391 | 390... | <0.001 |
| | B35Cw4 | 572 | 560 | <0.001 |
| | Bw4Cw4 | 590 | 170.. | <0.05 |
| East Anatolia | B27Cw2 | 198 | 140.. | <0.01 |
| | B35Cw4 | 980 | 800 | <0.001 |
| | B40Cw4 | 210 | 140 | <0.05 |
| Marmara | A1B8 | 480 | 420 | <0.05 |
| | A28B8 | 490 | 450 | <0.05 |
| | B27Cw2 | 220 | aiO | <0.05 |
| | B35Cw4 | 486 | 370 | <0.001 |
| Mediterranean | A1B8 | 470 | 420 | <0.01 |
| | A9B7 | 621 | 450 * | <0.05 |
| | A9B35 | 650 | 480 | <0.05 |
| | B35Cw4 | 930 | 790 | <0.0001 |
| TURKEY (Total) | A1B8 | 300 | | <0.001 |
| | A2B5 | 525 | 183 | <0.001 |
| | A2B27 | 183 | 110 | <0.01 |
| | A2Cw2 | 147 | so n * | <0.01 |
| | A10B35 | 130 | 100 | <0.001 |
| | A11Cw4 | 200 | 110 | <0.05 |
| | B27Cw2 | 321 | 310 | <0.001 |
| | B35Cw4 | 854 | 650 | <0.001 |
| | Bw6Cw4 | 172 | 200 | <0.001 |

**Table** 4. G F of HLA-A.B and C antigens of different population

| HLA antigens | ,TURKEY | GREEKS | TUNISIAN | CAUCASION EUROPEAN | JAPANESE ORIENTALIS | NEGROES |
|---|---|---|---|---|---|---|
| A1 | 11.00 | 13.00 | 13.30 | 14.90 | 0.50 | 3.30 |
| A2 | 21.00 | 28.80 | 19.80 | 26.00 | 24.60 | 14.70 |
| A3 | 8.00 | 6.30 | 10.00 | 11.60 | 0.50 | 7.40 |
| A9 | 15.80 | 20.70 | 20.40 | 11.90 | 36.10 | 13.70 |
| A10 | 3.80 | 5.70 | 3.80 | 5.60 | 9.90 | 4.20 |
| A11 | 5.60 | 6.20 | 4.60 | 5.90 | 9.00 | 0.60 |
| A28 | 5.30 | 3.20 | 46.50 | 4.00 | 0.50 | 8.70 |
| A32 | 0.53 | | 5.13 | 4.50 | 0.10 | 1.50 |
| BS | 16.30 | 14.00 | 7.10 | 9.60 | 19.30 | 8.90 |
| B7 | 5.00 | 5.70 | 7.60 | 8.80 | 5.90 | 8.90 |
| B8 | 4.00 | 5.10 | 9.50 | 8.20 | 0.10 | 2.90 |
| B12 | 6.40 | 9.40 | 11.60 | 12.10 | 6.70 | 11.00 |
| B13 | 4.20 | 1.80 | 1.30 | 2.80 | 2.00 | 0.70 |
| B14 | 1.60 | 2.60 | 41.00 | 3.00 | 0.10 | 4.10 |
| B15 | 0.60 | 3.60 | 1.30 | 5.80 | 9.00 | 1.30 |
| B18 | 1.60 | 10.20 | 4.10 | 5.80 | 0.00 | 3.90 |
| B27 | 3.50 | 3.30 | 4.10 | 3.90 | 0.40 | 1.50 |
| B35 | 12.60 | 18.50 | 7.60 | 9.50 | 7.30 | 6.20 |
| B40 | 4.70 | 3.70 | 6.00 | 5.10 | 15.40 | 1.80 |
| Bw4 | 38.00 | — | — | — | — | — |
| Bw6 | 25.00 | — | — | — | — | — |
| Bw22 | 1.80. | | | 2.80 | 11.30 | 0.80 |
| Bw51 | 0.50 | — | — | — | | — |
| Bw55 | 0.68 | — | — | | — | — |
| Cw2 | 3.20 | — | — | 9.70 | 9.70 | 22.50 |
| Cw4 | 17.00 | — | — | 22.10 | 22.10 | 29.30 |

In conclusion, the present HLA data reveal that, except for minor differences, the populations in geographic regions of Turkey are homogenous.

## Türk toplumunda HLA-A, B ve C antijenlerinin dağılımı

*Türkiyenin farklı coğrafi bölgelerinde yaşayan 2180 kişinin HLA-A, BveC antijenleri tayin edildi ve HLA-A, B ve C antijen frekansları literatürle karşılaştırıldı. Tüm coğrafi bölgelerde en sık izlenen A ve B lokus antijenleri A1, A2, A9, B5, B35 ve B12 idi. HLA lokusları allelleri arasındaki bağlantı dengesizliği incelendi. Türk toplumundan bağlantı dengesizliğinde en sık izlenen HLA allelleri B35Cw4, A1B8 ve B27Cw2 idi. Bu çalışmadan elde edilen HLA verileri Türkiyenin farklı coğrafi bölgelerinde yaşayan toplulukların homojen olduğunu göstermektedir.*
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