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HLA-A, -B, -DRB1 Allele and Haplotype Frequencies and Comparison With Blood Group Antigens in Dialysis Patients in the East Anatolia Region of Turkey

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ABSTRACT

Aim. The first aim of that study was to investigate HLA class I and class II allele and haplotype frequencies in renal dialysis patients who live in East Anatolia in Turkey. Our second aim was to investigate whether there was a relationship between ABO and D blood group antigens and HLA alleles and haplotypes for the study group.

Materials and methods. HLA class I and II polymorphisms in 408 renal dialysis patients were studied using sequence-specific primers (SSP) and sequence-specific oligonucleotides (SSO). Blood group antigens were detected by agglutination methods on microplates.

Results. A total of 16 HLA-A, 34 HLA-B, and 15 HLA-DRB1 alleles were identified. The most frequent HLA-A alleles were *HLA-A*02*, *HLA-A*24*, and *HLA-A*11*. The most frequent HLA-B alleles were *HLA-B*35*, *HLA-B*51*, and *HLA-B*44*. In case of HLA-DRB1; *HLA-DRB1*11*, *HLA-DRB1*04*, and *HLA-DRB1*13* were first 3 alleles with higher frequency, in order. In the combination of those 3 alleles, the most frequent HLA-A-B-DRB1 haplotypes were *HLA-A*02-B*51-DRB1*11*, *HLA-A*11-B*35-DRB1*11*, *A*24-B*35-DRB1*11*. The frequency of ABO, D blood group antigens were observed as 0.168 for A Rh(+), 0.019 for A Rh(−), 0.057 for B Rh(+), 0.013 for B Rh(−), 0.123 for O Rh(+), 0.014 for O Rh(−), 0.018 for AB Rh(+), and 0.001 for AB Rh(−). While A Rh(+) samples with *HLA-A*02* and *HLA-DRB1*11* had the highest frequencies (0.067 and 0.088, respectively), O Rh(+) samples with *HLA-B*51* had the highest frequency (0.06).

Conclusion. According to haplotype frequencies *HLA-A*02-B*51-DRB1*11* is also found at higher frequencies in Bulgarian and Armenian populations. In case of HLA-associated diseases, the east Anatolian population could be susceptible to myastenia gravis, Behçet's disease, and systemic sclerosis due to the high frequencies of *HLA-A*24*, *HLA-B*51*, and *HLA-DRB1*11* respectively. We did not observe a correlation between blood group antigens and HLA alleles or haplotypes in renal dialysis patients.

THE MAJOR HISTOCOMPATIBILITY COMPLEX (MHC), which is also called as the human leukocyte antigen (HLA), is encoded on human chromosome 6 and includes MHC class I, MHC class II, and MHC class III molecules. While MHC class I (A, B, and C)- and class II (DP, DR, DQ)-encoded molecules participate in antigen presentation to T cells, class III molecules consist of some molecules responsible from innate immunity such as complement components and some cytokines tumor necrosis factor-α and -β.[1] MHC class I and class II genes are extremely polymorphic. Each allele at each HLA locus encodes different peptide-binding properties that influence the particular peptides recognized by T cells and thereby regulate the adaptive immune response. Concerning that, one of the most important clinical uses of HLA typing

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involves matching potential organ or tissue donors with recipients who are in need of a transplant. Additionally, determining the MHC class I and II genes is helpful to determine the susceptibility to some organ specific autoimmune diseases.[2,3]

Investigation of HLA matching between donors and recipients forms the basis of solid organ and bone marrow transplantation. A full match of HLA class I and class II not only increases the functional survival of solid organ but also prevents immunologic reactions in recipients such as the graft-versus-host disease in bone marrow transplantation.[4] However, polymorphism on HLA genes makes it difficult to find suitable matching between donors and recipient. That polymorphism is elevated in highly immigrated populations in comparison to the conserved ones. Geographically Anatolia, which covers a major part of Turkey, has had immigration from ancient times till today. In historical order, Hitties, Helens, Romans and Byzatians, and Seljuk Turks were ancient settlers of Anatolia. A thousand years ago, Seljuk Turks immigrated from the far east Asia and then the Ottoman Empire, in which different ethnic populations from East Europe, Africa, Mezopotamia, and Asia lived together on this land. All those distinct ethnic groups formed the present population of Turkish Republic.[5]

Blood groups refer not only to genetically encoded erythrocyte antigens but also the immunologic diversity expressed by other blood constituents, including leukocytes, platelets, and plasma. Most blood group genes are located on the autosomal chromosomes such as ABO locus on chromosome 9 and D antigens locus on chromosome 1 and are inherited according to Mendelian rules of inheritance. The ABO blood group system has the single most important blood group antigens. ABO epitopes are found on many tissues and body fluids, including red blood cells, platelets, and endothelial cells.[6,7]

It has been shown that the frequencies of blood groups A and B differ between populations. More than that, there are examples of protection against several diseases from inheritance of polymorphisms in genes encoding ABH and Lewis antigens.[8] However, there is less knowledge about the correlation between those 2 polymorphic antigens, HLA and blood groups, and their association with renal dialysis patients.

In this study, our main objective was to investigate the frequency of HLA-A, HLA-B, and HLA-DR alleles and haplotypes in patients undergoing renal dialysis in a university hospital, Inonu University Turgut Ozal Medical Center, and dialysis centers in the Eastern Anatolian region in Turkey. Accordingly we compared alelle and haplotype frequencies with the frequencies of blood group antigens (ABO, D) and possible HLA-associated diseases.

MATERIALS AND METHODS

That investigation was approved by Ethic Committee of Malatya Clinical Investigation (Ethic Committee report number 2012/72). Blood samples were collected from 408 patients (208 men and 200 women). Patients with chronic renal disease applied to our center for HLA match analysis either from different dialysis centers in periphery locations at East Anatolia or from the dialysis center of Inonu University Faculty of Medicine Nephrology Unit in Malatya, Turkey, from 2008 to 2012. The exclusion criteria for hemodialysis patients were history of renal transplantation, acute infection, pregnancy, HIV infection, autoimmune diseases such as rheumatoid arthritis, Behcet's disease type I, diabetes, and malignancies. All HLA allele analysis was performed for possible renal transplantation. Forty patients among our study group had renal transplantations at Inonu University Faculty of Medicine in 2010 to 2011.[9] All individuals were of Turkish descent living in 5 different city of East Anatolia, and only scarce information could be obtained from the donors about their ancestors.

Genomic DNA was extracted by EZ-1 isolation kit (QiaGen) from blood samples. Low-resolution polymerase chain reaction-sequence specific primer (PCR-SSP) and polymerase chain reaction-sequence specific oligonucleotide (PCR-SSO) methods was used to determine at the 2-digit-level of HLA-A, -B, and -DRB1 alleles. DNA amplifications were done either by using SSP (Olerup) or SSO (Tepnel Lifecodes) methods. PCR-SSO was performed in Luminex 200 by using a software Luminex 100 Integrated System 2.3. The results were analyzed by using Quicktype for Lifematch 2.6 software. PCR-SSP products were loaded and run in 1.5% agarose gel. Bands were analyzed both under UV light and SCORE software program. ABO and D blood group phenotyping were performed were detected by using the agglutination method.

Statistical Analysis

Allele and haplotype (2, 3, 4) frequencies were estimated by using Arlequin Ver3.1, an integrated software package for population genetics (http://cmpg.unibe.ch7software7arlequin3).[10] Hardy-Weinberg equilibrium (HWE) was tested for each locus separately using the same software by a Markov chain method with exact *P* value estimation. The frequency of blood groups and the relationship between the blood groups and HLA class I and class II alleles was statistically investigated by using Loglinear Analysis in SPSS 10.0.

RESULTS

At the first step of the investigation, we looked into HLA-A, -B, -DR alleles, HLA-AB and HLA-A-B-DR haplotype frequencies of 408 patients under dialysis in at Eastern Turkey. At the second step, we looked into ABO and D blood group antigen frequencies and whether there was a relationship between HLA alleles and blood group antigens in renal dialysis patients.

Allele Frequencies

The frequency distribution at all loci showed that the population sample was in HWE at each locus (Table 1). HLA-A

Table 1. Hardy-Weinberg Equilibrium and Expected Heterozygosity of HLA-A, HLA-B, and HLA-DRB1 Locus

Locus	No. of individuals	Observed heterozygosity	Expected heterozygosity	*P* value
HLA-A	471	0.88323	0.86127	.76445
HLA-B	471	0.87906	0.89897	.68825
HLA-DRB1	471	0.83397	0.85076	.31907

Table 2. HLA-A Allele Frequencies in the Sample Population From East Anatolia Region of Turkey

HLA-A	Allele frequency
*A*01*	0.088
*A*02*	0.175
*A*03*	0.091
*A*11*	0.092
*A*23*	0.018
*A*24*	0.162
*A*25*	0.001
*A*26*	0.042
*A*29*	0.022
*A*30*	0.023
*A*31*	0.012
*A*32*	0.053
*A*33*	0.032
*A*68*	0.037
*A*69*	0.008
*A*74*	0.001

allele frequencies of 408 sample are presented on Table 2. A total of 16 different HLA-A alleles were observed. The 3 most frequent alleles were *HLA-A*02*, *HLA-A*24*, and *HLA-A*11*.

For HLA-B locus, 34 different HLA-B alleles were observed. Among that 34 different alleles, the most prominent frequencies were for *HLA-B*35* and *HLA-B*51*, as shown in Table 3.

In case of HLA-DR, a total of 15 different HLA-DRB1 alleles were observed. The most frequent ones were *HLA-DRB1*11*, *HLA-DRB1*04*, *HLA-DRB1*13*, and *HLA-DRB1*03*, respectively (Table 4).

Haplotype Frequencies

The most frequent 2-locus haplotypes (HLA-A-B) are shown in Table 5. Twenty-one HLA-A-B haplotypes were detected at frequencies higher than 0.01. The most frequent haplotypes were *HLA-A*24-B*51*, *HLA-A*02-B*35*, *HLA-A*24-B*35*, and *HLA-A*11-B*35*, respectively.

In case of 3-locus haplotypes, Table 6 shows HLA-A-B-DR combinations. Among a total of 550 different HLA-A-B-DR combinations, only 4 of them were at frequencies higher than 0.01. The most frequent one was *HLA-A*02-B*51-DRB1*11.*

Frequencies of Blood Group Antigens and Their Relationship With HLA Alleles

The frequencies of ABO blood group antigens were analyzed together with D antigens of patients. We observed that A Rh(+), O Rh(+) were the antigens with frequencies higher than 0.1 (Table 7). Following that, we investigated whether there was a relationship between HLA alleles types and blood group antigens or not. When we analyzed the frequency of HLA-A alleles together with blood group antigens, 87 different combinations were observed. However only 10 of them had a frequency higher than or equal to 0.02. A Rh(+) samples with *HLA-A*02* had the highest frequency (0.067) of overall blood group antigens (Table 8). In case of HLA-B alleles, 142 different combination with blood group antigens were observed. Only 8 of

Table 3. HLA-B Allele Frequencies in the Sample Population From East Anatolia Region of Turkey

HLA-B	Allele frequency
*B*07*	0.037
*B*08*	0.043
*B*13*	0.019
*B*14*	0.011
*B*15*	0.013
*B*18*	0.049
*B*22*	0.001
*B*27*	0.033
*B*35*	0.161
*B*37*	0.016
*B*38*	0.028
*B*39*	0.004
*B*40*	0.011
*B*41*	0.009
*B*42*	0.003
*B*44*	0.058
*B*46*	0.001
*B*48*	0.002
*B*49*	0.034
*B*50*	0.027
*B*51*	0.137
*B*52*	0.043
*B*53*	0.007
*B*55*	0.036
*B*56*	0.002
*B*57*	0.014
*B*58*	0.011
*B*60*	0.009
*B*61*	0.009
*B*62*	0.003
*B*63*	0.013
*B*64*	0.004
*B*65*	0.009
*B*73*	0.001

Table 4. HLA-DR Allele Frequencies in the Sample Population From East Anatolia Region of Turkey

HLA-DRB1	Allele frequency
*DRB1*01*	0.040
*DRB1*03*	0.098
*DRB1*04*	0.106
*DRB1*05*	0.001
*DRB1*07*	0.043
*DRB1*08*	0.015
*DRB1*09*	0.004
*DRB1*10*	0.027
*DRB1*11*	0.218
*DRB1*12*	0.013
*DRB1*13*	0.101
*DRB1*14*	0.056
*DRB1*15*	0.096
*DRB1*16*	0.039
*DRB1*52*	0.001

Table 5. Most Common HLA-A-B Haplotype Frequencies in the Sample Population From East Anatolia Region of Turkey

HLA-A*-B*	Haplotype frequency
*A*01-B*35*	0.026
*A*02-B*07*	0.018
*A*02-B*08*	0.012
*A*02-B*27*	0.012
*A*02-B*35*	0.034
*A*02-B*44*	0.014
*A*02-B*50*	0.014
*A*02-B*51*	0.029
*A*03-B*08*	0.011
*A*03-B*18*	0.013
*A*03-B*35*	0.021
*A*03-B*51*	0.016
*A*11-B*35*	0.033
*A*11-B*51*	0.015
*A*24-B*18*	0.012
*A*24-B*35*	0.033
*A*24-B*51*	0.037
*A*24-B*55*	0.011
*A*26-B*51*	0.012
*A*32-B*51*	0.011
*A*68-B*51*	0.014

them were at 9 frequency higher than or equal to 0.02. O Rh(+) samples with *HLA-B*51* had the highest frequency (0.06; Table 8). HLA-DRB1 and blood group antigens made 82 different combinations and 12 of them had a frequency higher than 0.02. A Rh(+) samples with *HLA-DRB1*11* had the highest frequency (0.088) in that group (Table 8). There were no significant relations between the blood group antigens and HLA-A ($P = .379$), HLA-B ($P = .398$), and HLA-DR ($P = .364$).

DISCUSSION

In our study we investigated the possible HLA alleles, ABO, D blood group antigens, and the relationship between those 2 antigenic structures in 408 dialysis patients in the East Anatolia region of Turkey.

According to the literature and the information at www.alelefrequencies.net website, there are 4 separate investigations about the frequency of HLA alleles and haplotypes in the Turkish population. In one of them, Uyar et al investigated the HLA-A and -B alleles and haplotype frequencies of individuals who lived in İstanbul. They observed *HLA-A*02*, *HLA-A*24*, and *HLA-A*01* and in case of HLA-B, *HLA-B*35*, *HLA-B*51*, and *HLA-B*44* as the most frequent alleles.[11] In another investigation, Saruhan-Direskeneli et al analyzed HLA-DRB1-DQA1 and

Table 6. Most Common HLA-A-B-DRB1 Haplotype Frequencies in the Sample Population From East Anatolia Region of Turkey

HLA-A*-B*-DR*	Haplotype frequency
*A*02-B*51-DRB1*11*	0.014
*A*11-B*35-DRB1*11*	0.012
*A*24-B*35-DRB1*11*	0.011

Table 7. Most Common ABO and D Blood Group Antigen Frequencies in 471 Samples From East Anatolia Region of Turkey

Blood group antigens	Frequency
O Rh(+)	0.123
O Rh(−)	0.014
A Rh(+)	0.168
A Rh(−)	0.019
B Rh(+)	0.057
B Rh(−)	0.013
AB Rh(+)	0.018
AB Rh(−)	0.001

DQB1 polymorphism in Turkish population. They reported that *HLA-DRB1*11:01*, *HLA-DRB1*03:01*, and *HLA-DRB1*07:01* are the most frequent alleles of HLA-DRB1.[12]

However in 2 of them the samples were selected from the individuals that lived in İstanbul, which is one of the most cosmopolitan cities in the world. In the third investigation, Arnaiz-Villena et al investigated HLA alleles and haplotypes in the Turkish population. Accordingly, they observed that *HLA-A*02*, *HLA-B*51*, and *HLA-DRB1*11* are the most frequent HLA alleles in 228 unrelated Turkish individuals, from all over Anatolia including Eastern most parts. In case of extended haplotypes, *HLA-A*24-B*51-DRB1*11* was found to be the most frequent.[13]

Table 8. Most Common HLA Alleles for Each ABO and D Blood Group Antigens

Blood group antigen-HLA	Frequency
O Rh(+)/*HLA-A02*	0.056
O Rh(+)/*HLA-A24*	0.043
O Rh(+)/*HLA-A03*	0.028
O Rh(+)/*HLA-A11*	0.021
A Rh(+)/*HLA-A02*	0.067
A Rh(+)/*HLA-A24*	0.062
A Rh(+)/*HLA-A11*	0.039
A Rh(+)/*HLA-A03*	0.035
A Rh(+)/*HLA-A32*	0.025
A Rh(+)/*HLA-A68*	0.02
O Rh(+)/*HLA-B35*	0.040
O Rh(+)/*HLA-B51*	0.036
O Rh(+)/*HLA-B44*	0.020
A Rh(+)/*HLA-B35*	0.059
O Rh(+)/*HLA-B51*	0.060
O Rh(+)/*HLA-B44*	0.020
O Rh(+)/*HLA-B52*	0.020
B Rh(+)/*HLA-B35*	0.022
O Rh(+)/*HLA-DRB1*11*	0.062
O Rh(+)/*HLA-DRB1*04*	0.035
O Rh(+)/*HLA-DRB1*03*	0.028
O Rh(+)/*HLA-DRB1*15*	0.028
O Rh(+)/*HLA-DRB1*13*	0.027
A Rh(+)/*HLA-DRB1*11*	0.088
A Rh(+)/*HLA-DRB1*04*	0.042
A Rh(+)/*HLA-DRB1*13*	0.041
A Rh(+)/*HLA-DRB1*03*	0.039
A Rh(+)/*HLA-DRB1*15*	0.039
A Rh(+)/*HLA-DRB1*14*	0.020
B Rh(+)/*HLA-DRB1*11*	0.024

We observed similar data with those groups' observation in the case of HLA-A allele. *HLA-A*02*, *HLA-A*24* were as the first 2 alleles with high frequency. In contrast to those 3 investigations, we observed a third and fourth HLA-A allele, *HLA-A*11* and *HLA-A*03*, which are mostly found in Wa population of south-west China *(HLA-A*11:01:01*; 58.4%).[14] Macedonians *(HLA-A*03* 11.9%; *HLA-A*11* 7.6%),[15] and Morrocans *(HLA-A*03*; 10%),[16] and the Greek Cypriot population has *HLA-A*02* (21.4%) and *HLA-A*24* (13.6%) at highest frequencies, which is similar with our study group. In the case of third and fourth HLA-A alleles, *HLA-A*03* 9.1% and *HLA-A*11* 9.7% were observed.[17] Similar to our results, Papassavas et al observed *HLA-A*02* and *HLA-A*24* in highest frequencies, 44.3% and 27.2%, respectively. They also observed *HLA-A*11* and *HLA-A*03* at high frequencies, 16.7% and 11.0%, respectively.[18] In several studies, *HLA-A*02* was observed in other populations geographically near to Turkey, such as Bulgarians (allele frequency-AF- 0.3),[19] Macedonians (25.6%),[15] and Albanians (AF 0.306).[20] *HLA-A*24* allele is also determined at high frequency on Bulgarians (AF 0.118),[19] Albanians (AF 0.159),[20] and Macedonians (16.3%).[15]

In case of HLA-B, we observed *HLA-B*35* and *HLA-B*51* alleles at highest frequency in 35 different HLA-B alleles. In Albanians, *HLA-B*51* (AF 0.172) and *HLA-B*35* (0.141)[20] and in Macedonians *HLA-B*51* (14.8%) and *HLA-B*35* (14.8%)[15] and *HLA-B*51* (AF 0.209)[19] were observed at highest frequencies in Bulgarians. Greek Cypriot population gives *HLA-B*35* as the highest HLA-B allele (25.5%).[17] Accordingly, one of the most interesting comparison was with the Greek population, as *HLA-B*18* and *HLA-B*51* were determined at highest frequencies, 26.8% and 28.51%, respectively. In the Greek population, *HLA-B*35* was the third highest HLA-B allele with 26.4% frequency.[18]

Among HLA-DRB1 alleles, *HLA-DRB1*11*, *HLA-DRB1*13, and *HLA-DRB1*04* had the highest frequencies in our study group. *HLA-DRB1*11* is a major allele for Mediterranean countries and has been shown at high frequencies in Croatians (15.3%),[21] Albanians (AF 0.275),[19] Bulgarians (AF 0.154),[20] and Macedonians (16.6%),[15] also. In the Greek population *HLA-DRB1*11* was determined at the highest frequency *(HLA-DRB1*11:04*, 20.5%).[18] Additionally, *HLA-DRB1*11* was also observed at the highest frequency in North European Russians (14.7%).[22]

In case of A-B haplotype, Arnaiz-Villena et al observed *HLA-A* 24-B*44* and *HLA-A*23-B*49* as the highest-frequency haplotypes and *HLA-A*26-B*38*, and *HLA-A*30-B*13* haplotypes with more than 1 frequency.[13] However, according to our observation, we found completely different haplotypes at highest frequency. *HLA-A*24-B*51*, *HLA-A*11-B*35* and *HLA-A*02-B*51.* Besides that, we did not observe any haplotype *HLA-A*24-B*44*, *HLA-A*23-B*49*, and *HLA-A*26-B*38*. Similar to our data, Uyar et al observed *HLA-A*11-B*35* and *HLA-A*02-B*51* haplotypes in their investigation.[11] In the case of the unrelated Greek populations, *HLA-A*24-B*35*, *HLA-A*02-B*35*, and *HLA-A*02-B*18* were determined as the first 3 haplotypes with higher frequencies, 0.040, 0.028, 0.027, respectively. A02-B51 was determined as the haplotype with the fifth highest frequency (0.020). That also shows us the level of polymorphism of HLA antigens in Anatolian population.

When we investigated 3 haplotypes of the Turkish population, we observed *HLA-A*02-B*51-DRB1*11* (1.4%), *HLA-A*11-B*35-DRB1*11* (1.2%), *HLA-A*24-B*35-DRB1*11* (1.1%) as the first 3 haplotypes in Turkish population. According to the literature, *HLA-A*02-B*51-DRB1*11* found in Armenians and Bulgarians at 2.1% and 2.7%, respectively.[19,23] Arnaiz-Villena et al observed *HLA-A*24-B*51-DRB1*11* (5.3%), *HLA-A*23-B*49-DRB1*11* (2.6%), *HLA-A*02-B*50-DRB1*07* (1.3%), which is different in comparison to our observation.[13] All those distinct data show us the level of polymorphism of HLA antigens in Anatolian population since Anatolia land is on the migration way of distinct conserved populations.

It is known that various autoimmune diseases and also severity of immune response to various pathogens could be associated with specific HLA alleles. Concerning that, *HLA-A*02*, *HLA-A*24*, *HLA-B*51*, and *HLA-DRB1*11* alleles, which are frequently found on our study group, could have a relationship with different autoimmune and infectious diseases. For example, Komlos et al suggested that *HLA-A*02* class I antigens in couples could be related with recurrent spontaneous abortions.[24] In another publication, one Machens et al suggested *HLA-A*24* could be a predictive factor in myasthenia gravis in correlation with thymic pathology.[25] Durrani et al discovered a correlation between *HLA-B*51* frequency and occurence of Adamantiades-Behcet's disease, which is a relapsing systemic vasculitis that may involve the eyes, skin, and almost all other organ systems.[26] In case of HLA class II, Kuwana et al investigated the effect of ethnicity on clinical and serologic expression in patients with systemic sclerosis and anti-DNA topoisomerase I antibody. They have observed that anti-topo-I-positive SSc patients, most of whom had *HLA-DRB1*11* with no difference in clinical expression, in SSc patients with anti-topo I antibody.[27] HLA alleles could affect not only the occurrence but also the severity of specific autoimmune diseases, since those observations were on different ethnic populations with similar HLA allele frequency of our study group, and clinicians must be alert during the examination of patients.

In 1977, Opelz et al showed that male patients with non-O-blood groups who had been given kidney grafts poorly matched for HLA-A and -B loci specificities were at high risk of graft failure. Such a beneficial effect of matching was not found in female patients or male patients with blood group O.[28] An association between ABO blood groups different diseases has also been reported. We investigated a relationship between renal patients undergoing dialysis with their HLA groups and blood group antigens. Accordingly, we observed that A Rh(+) blood group accompanied with *HLA-A*02* and *HLA-DRB1*11* are at highest

frequencies and O Rh(+) blood group accompanied with *HLA-B*51* allele are at highest frequency. In relation with our study, Rios et al investigated the frequencies of ABO blood group in hemodialysis patients in comparison to control healthy individuals. They did not observe a significant difference between hemodialysis patients and healthy individuals in ABO blood groups.[29]

In conclusion, our data confirm and increase the specificity of previous studies investigating the Turkish population. Since the polymorphism on Turkish population is higher than the other populations in the same region, including other populations in Eastern cities especially in South East Anatolia, one should be investigated in detail. Our data are important not only for clinical analysis in transplantation but also in HLA-associated diseases in East Anatolian Turkish population. Since our study group was not specifically divided into groups according to their renal diseases, more specific investigations can be done to analyze the role of blood group antigens and HLA groups on renal dialysis patients.

REFERENCES

1. Margulies DH, Notarajan K, Rossjohn J, et al. Major Histocompatibility complex (MHC) molecules: structure, function, and genetics. In: Paul WE, ed. *Fundamental Immunology*. Philadelphia, PA: Lippincott Williams and Wilkons/Wolters Kluwer Press; 2008: 570–613.
2. Steinmetz M, Inoko H, Kulski JK, et al. An update of the HLA genomic region, locus information and disease associations. *Tissue Antigens*. 2004;64:631–649.
3. Thomson G. HLA disease associations: models for the study of complex human genetic disorders. *Crit Rev Clin Lab Sci*. 1995;32: 183–219.
4. Opelz G, Wujciak T, Dohler B, et al. HLA compatibility and organ transplant survival. Collaborative Transplant Study. *Rev Immunogenet*. 1999;1:334–342.
5. Findley CV, ed. *The Turks in World History*. New York, NY: Oxford University Press; 2005:3–133.
6. Cooling L, Downs T. Immunohematology. In: McPherson RA, Pincus MR, eds. *Henry's Clinical Diagnosis and Management by Laboratory Methods*. Philadelphia, PA: Elsevier Saunders; 2011:674–730.
7. Ravn V, Dabelsteen E. Tissue distribution of histo-blood group antigens. *APMIS*. 2000;108:1–28.
8. Anstee DJ. The relationship between blood groups and disease. *Blood*. 2010;115:4635–4643.
9. Piskin T, Unal B, Koz S, et al. A kidney transplant center's initial experiences in Eastern Turkey. *Transplant Proc*. 2012;44: 1685–1689.
10. Excoffier L, Slatkin M. Maximum likelihood estimation of molecular haplotype frequencies in a diploid population. *Mol Biol Evol*. 1995;12:921–927.
11. Uyar FA, Dorak MT, Saruhan-Direskeneli G. Human leukocyte antigen-A, -B and C alleles and human leukocyte antigen haplotypes in Turkey: relationship to other populations. *Tissue Antigens*. 2004;64:180–187.
12. Saruhan-Direskeneli G, Uyar FA, Bakar Ş, et al. Molecular analysis of HLA-DRB1, -DQA1 and -DQB1 polymorphism in Turkey. *Tissue Antigens*. 2000;55:171–174.
13. Arnaiz-Villena A, Karin M, Bendikuze N, et al. HLA alleles and haplotypes in the Turkish population: relatedness to Kurds, Armenias and other Mediterraneans. *Tissue Antigens*. 2001;57: 308–317.
14. Shi L, Ogata S, Yu JK, et al. Distribution of HLA alleles and haplotypes in Jinuo and Wa populations in Southwest China. *Hum Immunol*. 2008;69:58–65.
15. Arnaiz-Villena A, Dimitroski K, Pacho A, et al. HLA genes in Macedonians and the sub-Sharan origin of the Greeks. *Tissue Antigens*. 2001;57:118–127.
16. Brick C, Bennani N, Atouf O, et al. HLA-A, -B, -DR and -DQ allele and haplotype frequencies in the Moroccan population: a general population study. *Transfus Clin Biol* 2006;13: 346–352.
17. Varnavidou-Nicolaidou A, Karpasitis S, Papleontiou I, Kyriakides GK. HLA-A, -B, -DR Antigens in the Greek Cypriot population. *Transplant Proc*. 1997;29:2920–2921.
18. Papassavas EC, Spyropoulou-Vlachou M, Papassavas AC, Schipper RF, Doxiadis IN, Stavropoulos-Giokas C. MHC class I and class II phenotype, gene and haplotype frequencies in Greeks using molecular typing data. *Hum Immunol*. 2000;61:615–623.
19. Ivanova M, Rozemuller E, Tyufekchiev N, et al. HLA polymorphism in Bulgarians defined by high-resolution typing methods in comparison with other populations. *Tissue Antigens*. 2002;60: 496–504.
20. Sulcebe G, Sanchez-Mazas A, Tiercy JM, et al. HLA allele and haplotype frequencies in the Albanian population and their relationship with the other European populations. *Int J Immunogenet*. 2009;36:337–343.
21. Grubic Z, Zunec R, Cecuk-Jelicic E, et al. Polymorphism of HLA-A, -B, DRB1, -DQA1 and -DQB1 haplotypes in a Croatian population. *Eur J Immunogenet*. 2000;27:47–51.
22. Evseeva I, Spurkland A, Thorsby E, et al. HLA profile of three ethnic groups living in the North-Western region of Russia. *Tissue Antigens*. 2002;59:38–43.
23. Imanishi T, Akaza T, Kimura A, et al. Allele and haplotype frequencies for HLA and complement loci in various ethnic groups. In: Tsuji K, Aizawa M, Sasazuki T, eds. *HLA 1991*. Vol I. Oxford, UK: Oxford University Press; 1992:1065–1220.
24. Komlos L, Klein T, Korostishevsky M. HLA-A2 class I antigens in couples with recurrent spontaneous abortions. *Int J Immunogenet*. 2007;34:241–246.
25. Machens A, Löliger C, Pichlmeier U, et al. Correlation of thymic pathology with HLA in myasthenia gravis. *Clin Immunol*. 1999;91:296–301.
26. Durrani K, Papaliodis GN. The genetics of Adamantiades-Behcet's disease. *Semin Opthalmol*. 2008;23:73–79.
27. Kuwana M, Kaburaki J, Arnett FC, Howard RF, Medsger TA Jr, Wright TM. Influence of ethnic background on clinical and serologic features in patients with systemic sclerosis and anti-DNA topoisomerase I antibody. *Arthritis Rheum*. 1999;42: 465–474.
28. Opelz G, Terasaki PI. Influence of sex on histocompatibility matching in renal transplantation. *Lancet*. 1977;2:419–421.
29. Rios DRA, Fernandes AP, Figueiredo RC, et al. Relationship between ABO blood groups and von Willebrand factor, ADAMTS13 and factor VIII in patients undergoing hemodialysis. *J Thromb Thrombolysis*. 2012;33:416–421.