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Original Contribution

MAJOR HISTOCOMPATIBILITY CLASS I ANTIGENS AND ALLELE FREQUENCY IN THE AZERI POPULATION

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ABSTRACT
Purpose: The MHC loci display an unprecedented degree of polymorphism that is required to avoid the devastating effects of infectious diseases, which have been the major causes of mortality during mammalian evolution and remain the most serious threat to health in developing countries. We aimed this study to determine of MHC class I antigens and gene frequency in a part of Azerbaijan republic population. Methods: We studied 314 individuals (195 males & 119 females) referred to Iran Red Crescent Society clinic in Baku and HLA typing was performed using serologic method. Results: The most frequent HLA antigens were found to be HLA-A2 (36.9%), HLA-B35 (36.6%) and HLA-CW4 (31.8%). Conclusions: We concluded that Azeri population may be susceptible to diabetic retinopathy, posttransplantation diabetes mellitus, autoimmune adrenal deficiency, renal failure, Behcet disease and HIV infection. Our findings support the idea that Azeri population may be resistant to melanoma, pre-eclampcia and multiple sclerosis.

Key words: MHC; Class I; Azerbaijan

INTRODUCTION

The major histocompatibility complex (MHC) is a large group of genetic loci on the short arm of chromosome 6 that were originally discovered through research on models of transplant compatibility. A number of these loci encode the human leukocyte antigens HLA class I and HLA class II, which we now know to be key molecules in the antigen presentation system at the core of adaptive immunity (1). The classical MHC spans ~4 Mb and comprises over 160 protein-coding genes. Compared with other similar-sized sections of the human genome, the MHC holds the most, and some of the longest recognized associations with disease (2). The MHC loci display an unprecedented degree of polymorphism compared to other regions of the human genome. It has been argued that this degree of polymorphism within a population is required to avoid the devastating effects of infectious diseases, which have been the major causes of mortality during mammalian evolution and remain the most serious threat to health in developing countries (1). The MHC influences numerous chronic inflammatory and autoimmune conditions, including type I diabetes, multiple sclerosis and Crohn's disease. MHC variants also confer susceptibility to many infectious diseases, such as malaria and HIV (2). Therefore, insight of HLA polymorphism distribution is important in detecting of genetic risk of many diseases. Thus, we designed this study to determine of MHC class I antigens and gene frequency in a part of Azerbaijan republic population.

MATERIALS AND METHODS

Subjects of this study were the individuals from different parts of Republic of Azerbaijan referred to Iran Red Crescent Society clinic in Baku. Using sequential sampling method, 314 individuals (195 males & 119 females) were selected. Blood samples were collected into tubes containing 10 000 IU of preservative-free heparin and, within 15 minutes, isolation of the

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lymphocytes was started using Ficoll-Hypaque density gradient method.

HLA typing was performed using serologic method, based on manufacture's instruction (Euro clone, Italy) immediately using commercially available trays with mono- and polyclonal antisera purchased from BAG Health Care GmbH (Amtsgerichtsstrabe1-5 35423 lich/Germany). The usual grading scale of 1 to 5 was used, in which 5 represented the positive control with nearly total cell kill and 1 was the negative control with the lowest number of dead cells (normally not more than 1%-2%). For the C locus, the antibodies included on the trays were restricted to the seven antisera.

Phenotype frequencies were calculated by direct count and Gene frequencies using the following formula:

$$GF=1-\sqrt{(1-AF)}$$

where G_f is the gene frequency and A_f is the antigen frequency, based on the assumption of Hardy-Weinberg equilibrium as described by Motta et al. (3).

Collected data were analyzed by SPSS software.

RESULTS

Ages of subjects were ranged from 18 to 54 years. The most frequent HLA-A antigens were found to be A2 (36.9%), A24 (28.0%), A3 (24.8%), A1 (18.7%) and A30 (16.2%) respectively **(Table 1)**. These results about HLA-B were B35 (36.6%), B51 (30.2%), B13 (10.2%), B18 and B44 (9.8%) respectively **(Table 2)**. Furthermore results showed CW4 (31.8%) as the most frequent HLA-C antigens **(Table 3)**. The least frequent HLA-A antigens were found to be A36 and A80 (0%), A35 and A74 (0.3%) **(Table 1)**. These results about HLA-B were B48, B54, B59, B61, B63-B7, B75, B76 and B82 (0%) **(Table 2)**. Furthermore results showed CW5 (7.9%) as the least frequent HLA-C antigens **(Table 3)**.

DISCUSSION

There are several prominent disease associations with class I HLA alleles (4).HLA molecules play a key role in the selection and establishment of the antigen-specific T cell repertoire (5).

In this analytical descriptive study, HLA class I distribution was assessed in a part of Azerbaijan republic. In our study we found the most frequent HLA-A as A2, A24, A3, A1 and A30 respectively. Several studies have shown the influence of the complex Human Leukocyte Antigen (HLA) A2 and others genes in the clinical status, risk and therapeutic response of some psychiatric disorders (6). Findings of some studies strongly suggest an association between HLA-A2 and vitiligo (7). Results have been showed HLA-A24 is not a protective factor for proliferative diabetic retinopathy, but is a risk factor of its development. Other researchers suggest an association between HLA-A3, A1 and melanoma (8, 9). It is reported HLA-A30 to be predisposing genes for Posttransplantation diabetes mellitus (10).

Table 1. *HLA-A antigens distribution and gene frequencies of Azeri subjects*

HLA-A Antigen	Number	Frequency	Gene frequency
A1	59	0.187	0.099
A2	116	0.369	0.206
A3	78	0.248	0.133
A9	2	0.006	0.003
A10	3	0.009	0.0045
A11	49	0.156	0.082
A19	2	0.006	0.003
A23	19	0.060	0.030
A24	88	0.280	0.152
A25	2	0.006	0.003
A26	34	0.108	0.056
A28	4	0.012	0.006
A29	16	0.050	0.026
A30	51	0.162	0.085
A31	13	0.041	0.021
A32	18	0.057	0.029
A33	14	0.044	0.022
A34	9	0.028	0.014
A35	1	0.003	0.0015
A36	-	0	0
A66	4	0.012	0.006
A68	20	0.063	0.033
A69	2	0.006	0.003
A74	1	0.003	0.0015
A80	-	0	0

Table 2. *HLA-B antigens distribution and gene frequencies of Azeri subjects*

HLA-B Antigen	Number	Frequency	Gene frequency
B7	26	0.083	0.042
B8	24	0.077	0.039
B13	32	0.102	0.052
B14	18	0.057	0.029
B15	9	0.029	0.015
B16	4	0.013	0.0065
B17	3	0.009	0.0045
B18	31	0.098	0.050
B21	5	0.015	0.0075
B27	18	0.057	0.029
B35	115	0.366	0.203
B37	15	0.047	0.023
B38	25	0.079	0.040
B39	4	0.013	0.0065
B40	2	0.006	0.003
B41	17	0.054	0.027
B42	2	0.006	0.003
B44	31	0.098	0.050
B45	4	0.012	0.006
B46	1	0.003	0.0015
B47	3	0.009	0.0045
B48	-	0	0
B49	22	0.070	0.035
B50	8	0.025	0.0125
B51	95	0.302	0.164
B52	18	0.057	0.028
B53	3	0.009	0.0045
B54	-	0	0
B55	11	0.035	0.017
B56	8	0.025	0.0125
B57	18	0.057	0.028
B58	2	0.006	0.003
B59	-	0	0
B60	8	0.025	0.0125
B61	-	0	0
B62	7	0.022	0.011
B63	-	0	0
B64	-	0	0
B65	-	0	0
B67	-	0	0
B73	2	0.006	0.003
B75	-	0	0
B76	-	0	0
B78	3	0.009	0.0045
B82	-	0	0

Table 3. *HLA-C antigens distribution and gene frequencies of Azeri subjects*

HLA-C Antigen	Number	Frequency	Gene frequency
CW1	44	0.140	0.072
CW2	39	0.124	0.064
CW3	30	0.095	0.048
CW4	100	0.318	0.174
CW5	25	0.079	0.040
CW6	82	0.261	0.140
CW7	98	0.312	0.170

Our study also showed most frequent HLA-B as B35, B51, B13, B18 and B44. Some results has been showed associations between HLA B35 and genetic renal and autoimmune adrenal disorders (11, 12). HLA B51 have been associated with Behcet disease (13). Other results suggest positive association between HLA B13 and celiac disease and pre-eclampcia (14, 15). It is shown correlation between HLA B18 and renal failure (16). HLA B*44 appears to influence disease course, preserving brain volume and reducing the burden of T2 hyperintense lesions in subjects with Multiple sclerosis (17).

Our results about HLA-C showed most frequent genotypes as CW4. Role of HLA CW4 in chronic HIV has been showed (18).

We concluded that Azeri population may be susceptible to diabetic retinopathy, posttransplantation diabetes mellitus, autoimmune adrenal deficiency, renal failure, Behcet disease and HIV infection. Our findings support the idea that Azeri population may be resistant to melanoma, pre-eclampcia and multiple sclerosis.

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