

FEATURES OF THE DISTRIBUTION OF HLA- ANTIGENS AMONG PEOPLE OF THE UZBEK NATIONALITY IN THE SAMARKAND REGION

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Abstract: *The study of the HLA genetic profile of the population was carried out using the most complete set of modern HLA typing reagents. For the first time, the study of the HLA phenotype was carried out for a wide range of alleles of the A, B and DR loci, separately among the residents of the city and the village inhabiting the Samarkand region.*

Keywords: *immunogenetic, HLA, pathogenesis, antigens, genes and haplotypes*

ОСОБЕННОСТИ РАСПРЕДЕЛЕНИЯ HLA-АНТИГЕНОВ СРЕДИ ЛИЦ УЗБЕКСКОЙ НАЦИОНАЛЬНОСТИ В САМАРКАНДСКОЙ ОБЛАСТИ

Аннотация: *Изучение генетического профиля HLA населения проведено с использованием наиболее полного набора реагентов HLA-типирования. Впервые проведено изучение фенотипа HLA по широкому спектру аллелей локусов A, B и DR, отдельно среди жителей города и села Самаркандской области.*

Ключевые слова: *иммуногенетика, HLA, патогенез, антигены, гены и гаплотипы.*

INTRODUCTION

At present, the study of the characteristics of the immunogenetic profile of various ethnic groups, determined by race, historical conditions of development, and the relationship of populations, is of particular relevance. Knowledge of the “normal” distribution of HLA antigens characteristic of individual populations is important both for identifying HLA associations and diseases characteristic of certain regions and for understanding the genetic basis of their pathogenesis. On the other hand, it is of interest to use HLA data - the phenotype of a population along with historical, linguistic and other studies in order to establish the origin of various ethnic groups [1, 2, 4, 10,12].

To date, among studies on the distribution of HLA genes in the Uzbek population, their predominant number has been carried out in the regions of the Tashkent region and the Ferghana Valley [3, 5, 6, 7, 11].

For other regions, clear and reliable data is not enough. Obviously, such studies will deepen the modern characterization of the HLA-genetic profile of the Uzbek population [8, 9].

To achieve the set goals and objectives, we examined 86 practically healthy, unrelated residents of the city of Samarkand and the Samarkand region, Uzbek nationality, aged 17 to 52 years. Immunological, immunogenetic and biochemical methods of research were carried out in 86 persons, in the city center of clinical immunology and AIDS, together with the staff of the Institute of Immunology of the Academy of Sciences of the Republic of Uzbekistan. Typing of HLA class II antigens (DR) was carried out in 82 examined individuals.

When studying the surveyed population, we took into account regional differences in residence (urban, rural), gender and age characteristics. A total of 61 women and 25 men were examined, of which 50 lived in rural areas and 36 in the city of Samarkand.

When examining rural residents, a comparative assessment of the immune status was carried out depending on the working conditions (cotton growers and factory workers).

In the examination of patients, an important place belonged to the study of the anamnesis of diseases, family anamnesis with the compilation of a family pedigree. The survey included persons without clinical signs of the following diseases: chronic tonsillitis, hepatitis, diabetes mellitus, hypertension, atherosclerosis, etc.

Methods

Immunogenetic research methods

Immunogenetic research methods were carried out on the basis of methodological recommendations set out in the guidelines of Yu. M. Zaretskaya (1983) and V. I. Konenkov (1999).

In the 1960s, a method for serological typing of HLA antigens was developed, using the principle of a microlymphocytotoxic test, which consists in the selective interaction of HLA molecules on the surface membrane of the lymphocytes of the examined patient with specific HLA antibodies and complement, leading to cell death, which is determined in a light microscope .

Therefore, in our work, the HLA phenotype was established in a standard microlymphocytotoxic test (Terasaki P. I., 1964) using a panel of HLA antiserum of the St. Petersburg Research Institute of Hematology and Blood Transfusion. When conducting the microlymphocytotoxic test, the recommendations of the NIH (National Institute of Health, USA) were taken into account, according to which, when digging lymphocytes into the wells of the Terasaki plate, the “shooting” technique was used, which largely ensured the purity of the “readable” wells.

This method is based on the combination of the corresponding antibodies with the lymphocyte antigens of the subject in the presence of a rabbit complement, which is a mixture of serum of 10-14 non-immunized rabbits. If there are corresponding HLA antigens on the surface of lymphocytes, then a lymphocytotoxic reaction occurs, as a result of which the permeability of the membrane of mononuclear cells is disturbed, and they are intensely stained with a dye, while living cells remain unstained.

Results

The distribution of HLA antigens, genes and haplotypes in a healthy Uzbek population of the Samarkand region was investigated using the most complete set of typing reagents.

The results of studies of the frequencies of HLA antigens and genes in the examined population of 86 practically healthy individuals are presented in (Table 1)

As the analysis showed, in locus A, the antigens A2 (31.4%), A9 (32.4%), A19 (38.4%) are found with the highest frequency. The HLA-A10 antigens were detected in the phenotype in 25.6% and A28 in 19.8% of the examined individuals. HLA antigens, A1 (15.1%), A3, A24 (17.4%), A11, A26 (12.8%), A30 (11.6%), were often found. The low frequency of occurrence in the phenotype of the examined individuals is typical for HLA antigens - A23, A29, A31, A33 (2.3%), A36 (1.2%).

Of the split antigens, the A24 antigen occurs most frequently (17.4%), making the main contribution to the frequency of the A9 antigen. Another subtype of specificity A9-antigen A23 can be attributed to less common antigens (2.3%) of the A locus.

Among the locus antigens in the population, the most common were HLA antigens B13 (26.7%), B5 (20.9%), HLA antigens B7 (17.4%), B35 (11.6%), B27 (10.5%), less common (from 6 to 12%) antigens B8, B12, B17, B22, B27, B35, B40. The lowest frequency in the population is characteristic of HLA antigens B16, B39, B53, B56, B75.

A rather high frequency of the blank in locus B (0.1624%) indicates the presence of unidentified antigens in these loci, which are rare antigens specific to Mongoloids.

In the DR locus, the most common antigen was HLA-DR7 (37.8%), DR1(28.19%), DR 2 (22.0%), DR9 (23.2%), DR15 (20.7%), DR8 and DR12 antigens were detected with the lowest frequency in the DR locus (2.4%).

The data presented in Table 4 on the distribution of HLA antigens in the Uzbek population indicate the presence of both similarities and distinctive features in comparison with the distribution of HLA antigens inherent in the world populations of Caucasoids and Mongoloids.

Thus, in the surveyed population, a number of antigens occur with frequencies similar to the average frequencies in Caucasoid HLA populations - A9, A11, A19, A23, A24, A28, A33, B7, B22, B50, B53, B55, DR1, DR3. DR13.

However, HLA antigens are more common than in Caucasoids: A10, A30, B42 and less common A1, A2, B8, B15, B39, B40, which is more typical for Mongoloids.

An intermediate position between the average frequencies in Mongoloids and Caucasians is occupied by the frequencies of HLA antigens: A3, A19, A24, A30, A36, B41, B42, B52, B55, B60, DR8.

Thus, according to the nature of the distribution of HLA antigens, the Uzbek population has common features with both Caucasoids and Mongoloids, and also has peculiar features of the distribution of HLA antigens. The most characteristic differences, both from the populations of Caucasoids and Mongoloids, are the reduced frequencies of occurrence of HLA antigens B12, DR6 and, on the contrary, the increased frequencies of B13, DR9 antigens. Table 2 presents the results of calculating the frequencies of HLA haplotypes and the values of linkage disequilibrium (D) for the alleles that make up the haplotype. Among Uzbeks, the following haplotypes are found with the highest frequency: A2-B13, A30-B13, A30-B14, A9-B35, A32-B44, A32-B46, A19-DR4, A24-DR6, A26-DR8, A24-DR13, B22- DR2, B14-DR4, B27-DR8.

The highest values of non-equilibrium linkage (gametic association) are determined for HLA haplotypes A2-B13, A19-DR4, A30-B13, A9-B35. Haplotypes characterized by significant positive linkage disequilibrium are of the greatest importance for the analysis of the genetic structure, being a more individual characteristic of the HLA genetic profile of the population than the frequencies of HLA antigens. These indicators well reflect the HLA-genetic features of the Uzbek population.

The results of the studies carried out are consistent with anthropological and ethnogenetic information about the origin of the Uzbeks, indicating a mixture of different ethnic groups belonging to the Mongoloids and Caucasoids during the formation of the population. The peculiarities of the HLA genetic profile of the Uzbek population, which are clearly manifested in the analysis of the frequencies of HLA antigens, haplotypes, and the values of linkage disequilibrium, allow us to expect the peculiarity of associations of HLA antigens with diseases, characteristic of this ethnic group, the possibility of identifying HLA markers of diseases that are different from other populations, and as well as the originality of associations of HLA antigens with the parameters of the immune status of healthy individuals.

It was of interest to conduct a comparative analysis of the features of the HLA-genetic profile among urban and rural residents of the surveyed population. Table 3 shows the results of the distribution of the frequency of occurrence of HLA antigens in the urban population.

According to the results of the study, it can be seen that in locus A (Table 3), the most common antigen was A9 (33.3%), A10 (36.1%), A19 (44.4%). HLA antigen A2, A28 was found in 22.2% of the examined persons. Less common were A1, A3 (16.7%), A11, A30 (13.5%), A24, A26 (11.1%) and few (less than 3%) HLA antigens A33, A36, A68.

In locus B, HLA antigens B13 (25.0%) were found with the highest frequency, HLA antigens B5, B7, B8, B22 were also often detected (11.1%). Antigens (from 6 to 9%) B12, B14, B41, 42, B49, B51, B60 (5.6%), B17, B27, B35, B44, B46 (8.3%) were encountered with moderate frequency. Less common (less than 3%) B18, B39, B48, B50, B55 (2.8%)

At the DR locus, the antigens DR7 (38.9%) and DR9 (30.6%) were found with the highest frequency. DR4 antigens were detected in 25.0%, DR1 and DR2 in 22.0% of the examined population. Antigens DR3, DR5 (19.4%), DR11 (13.9%), DR13 (11.1%) were encountered with moderate frequency. Less common (from 3 to 6%) antigens DR12, DR10, DR 8.

From Table 4 shows that among the rural population with the highest frequency at the A locus, HLA antigens A2 (38.0%), A19 (34.0%) were found. A9 (26.0%), A24 (22.0%) were common, and antigens A3, A10 (18.0%), A1, A26 (14.0%), A11, A69 (12.0%) were detected with moderate frequency. A32 was detected in 6% and antigens A23, A29, A69 in 4% of the examined persons.

By locus B, B5, B13 (28.0%) were the most common. The B7 antigen was frequently encountered (22.0%). HLA antigens B35 (14.0%), B27 (12.0%) and B17 (10%) were encountered with moderate frequency in the examined individuals. HLA antigen B8 was detected in 8% and antigens B15, B18, B22, B60 in 6% of the rural population. HLA antigens B12, B14, B41, B50, B51, B55 turned out to be less common (from 2 to 4%).

At the DR locus, HLA antigens DR7 (37.0%) and DR1 (32.6%) were found with the highest frequency. Antigens DR2 (21.7%), DR3, DR5, DR9, DR11, DR13, DR15 (17.4%) were often detected. Antigens (from 4 to 9%) DR4, DR8, DR6, DR10, DR14 turned out to be less common.

Thus, the study of the HLA phenotype of the examined individuals revealed some features of the HLA genetic profile of the urban and rural population. Table 5 illustrates the results of statistically significant differences in the ratios of the frequencies of occurrence of HLA antigens in urban and rural residents. According to the data obtained, it can be seen that the HLA phenotype of people of Uzbek nationality among the urban population is characterized by an increased detection of HLA antigens A9 ($P<0.05$), A19 ($P<0.05$) and DR4 ($P<0.005$).

We also evaluated the distribution of HLA antigens depending on the sex of the examined individuals. With the general similarity of the HLA-immunogenetic profile in the compared groups, a slightly reduced frequency of occurrence of HLA antigens A32, B14, B49, DR4 among females attracted attention. These data are shown in Table 6.

Taking into account the data obtained on the peculiarity of the HLA genetic profile of rural and urban residents, as well as some features of the distribution of HLA antigens in connection with the sex of the examined individuals, we considered it appropriate to establish the frequencies of HLA antigens for specific population groups that can be used as characteristic for them. Further, data reflecting the specifics of the distribution of HLA antigens in the examined groups.

As can be seen, A9 locus (40.00%) was found with a high frequency among the residents of the city at the A locus. HLA antigens A10, A24 were detected in 25%, A1 in 20.8% of the examined persons of this group. A30 belonged to 15% and A2, A3, A26, A32 - 10% of the examined individuals of this group.

At locus B, antigen B13 (25.0%) was detected more in relation to other antigens of this locus, B17, B35 were detected in 15.0% and B60 in 12.5% of the examined individuals of this group. Of all the examined antigens, only 10.0% of individuals belonged to HLA antigens B5, B7, B12, B22, B40, B44. Less common HLA antigens were B8, B14, B15, B16, B18, B27, B39, B41, B48, B51, B55, B75 (5.0-6.25%).

At the DR locus, the DR9 antigen (40.0%) turned out to be the most detectable. HLA antigens DR7 (35.0%), examined individuals of this group. The frequency of occurrence of the HLA antigen DR11 was 25.0% and DR1 20.0%. HLA antigens DR3, DR4 were detected in 15.0% and DR2 and DR15 in 10.0% of the examined individuals of this group. Less than a percentage of the frequency of occurrence belonged to HLA antigens DR6, DR12, DR13 (5.0%).

Analysis of the distribution of HLA antigens by locus A in the group of males living in the urban region showed that antigens A19 (50.0%), A2, A10 (37.5%) prevailed in this locus. Also, HLA antigens A9, A3 were detected with a high frequency (25.0%). Antigens A1, A28 were detected in 18.75%, A11, A26, A30 in 14.1%. HLA antigens A24, A33 were detected less (6.3%).

At locus B, antigens B5 (31.3%) and B13 (25.0%) were encountered with high frequency. The percentage of occurrence of HLA antigens B8, B12, B466 is 18.8%. The lowest frequencies of antigens were typical for HLA antigens B14, B15, B41, B44, B50, B51, B55 (6.3%).

According to the DR locus, it can be said that highly detectable antigens were characteristic of the HLA antigen DR7 (43.8%), DR4 (37.5%), DR15 (31.3%). The frequency of occurrence of antigens DR1, DR2, DR3 was equal to 25.0%. DR6, DR9, DR13 were found in 18.8% of the examined persons and DR 8, DR10, DR12 in 6.3% of the examined persons.

An analysis of the distribution of HLA antigens in the group of women from the village showed that for locus A, the highest percentage of the frequency of occurrence falls on antigens A2, A19 (34.1%). Also, HLA antigens A9 (26.82%), A10 (24.4%) were detected with a high frequency. HLA antigens met with frequency A1, A3 (14.6%), A24 (13.3%), and A11, A69 (12.2%). Less common were A30 antigens (9.7%), A23, A29, A68, A32, A33, A36 antigens (from 2.5 to 4.9%).

At the B locus, HLA antigens B13 (26.8%), B5 (24.4%), B7 (22.0%) were common. B35 was found in 14.6% of the examined individuals of this group. The percentage of occurrence of HLA antigens B8, B17, B22, B27, B40 was 9.8%. Also antigens B18, B42 met 7.3%. From 2.5-5%, antigens B12, B15, B21, B41, B50, B51, B52, B56, B60 were encountered.

At the DR locus, DR1 was characteristic, which was found in 36.84% of the examined individuals of this group. HLA-DR7 was also found in 34.2% of individuals. The frequency of occurrence of antigens DR2, DR15 was 21.1%, antigens DR3, DR5, DR9, DR11 were 15.8%. HLA antigens DR6, DR13 (10.5%), DR10 (7.9%) were encountered with moderate frequency and much less often HLA - antigens DR4, DR8 (2.5-3.5%)

An analysis of studies in a group of males living in a rural region showed that in locus A, A2 (55.5%) was the highest frequency HLA antigen. HLA antigen A3, A19, A32 (33.3%), A9, A28 (22.2%) met with the highest frequency. Antigens A10, A24, A30, A69 met with a frequency of 11.1%.

By locus, B13 (33.3%) turned out to be highly detectable antigens. B22, B27 (22.2%). In 11.1% of cases, HLA antigens B5, B14, B15, B17, B35, B40, B42, B55, B60 were found

At the DR locus, the most frequently detected antigens were HLA DR2 and DR7 (50.0%). DR9, DR11, DR15 were detected in 25.0% of cases, the frequency of occurrence of antigens DR1, DR3, DR4, DR5, DR9 was 12.5%

It can be seen that the most significant differences compared to the general population are among urban residents in the frequency of occurrence of antigens A11, A24, DR9, DR11, among rural women in HLA DR1. Among males in the group of urban dwellers, HLA phenotypes A10, A19, B12, DR4, DR15 prevailed, men living in the countryside - A2, A3, A32, DR2 and DR7, among the latter, HLA-DRI phenotypes were less common.

Thus, the studies of the distribution of HLA antigens among people of Uzbek nationality living in the Samarkand region made it possible to obtain characteristics of the HLA genetic profile of this population for class A, B and DR antigens and to determine some of its features in connection with gender and region of residence.

Discussion

It should be noted that the relevance of the study of human immunodeficiencies in recent years is largely determined by the progress in deciphering their genetic code. At the same time, research to study and establish the relationship between individual HLA specificities and immune status are one of the important areas of modern immunology. The development of this problem is associated, first of all, with the progress in the development of the serotyping methodology, which requires significant efforts to create typing panels from many hundreds and thousands of human sera to ensure the detection of individual HLA specificities.

In our study, systems A, B, DR manufactured by the St. Petersburg Institute of Hematology and Blood Transfusion of the Ministry of Health of the Russian Federation were used.

It should be noted that intensive studies on the characterization of the HLA - genetic profile of various ethnic groups began in the 80-90s of the last century. Population studies of people of Uzbek nationality living in the Tashkent, Fergana, Samarkand regions of Uzbekistan were also carried out.

Conducted at different times, these studies covered a limited number of tested HLA antigens, mainly class I, from today's standpoint. Less studied HLA is a class II polymorphism. In addition, as already mentioned, studies were carried out in different regions of Uzbekistan and revealed differences in the frequencies of HLA alleles, probably characteristic of the population of a particular region. Therefore, we considered it appropriate to study the distribution of HLA - antigens, genes and haplotypes in a healthy Uzbek population of the Samarkand region using the most complete set of typing reagents.

A more detailed study of the antigens of the HLA system showed that this population has peculiar features of the distribution of HLA antigens of class I and II of the histocompatibility system. Previous studies [7,8] at the end of the last century on the study of antigens in healthy individuals of Uzbek nationality living in the Samarkand region showed that in the surveyed population the most common antigens were A2, A3 and A9, which is an approximate proof in our work. Among the antigens of the locus in the most widespread, according to the data of the mentioned authors, was the HLA - B5 antigen, the HLA - B13, B35 antigens were also often found, and among the antigens of the DR class, HLA - DR4, DR5 were most often detected. It should be noted that in these studies, a total of 8 antigens were identified at the A locus (A1, A2, A3, A9, A10, A11, Aw19, A28), and 15 antigens at the B locus (B5, B7, B8, B12, B13, B14, B15, B16,

B17, B18, B21, Bw22, B27, B35, B40) and at the DR-6 locus of histocompatibility antigens (DR1, DR2, DR3, DR4, DR5, DR7).

To date, the study of antigens in the surveyed population has already revealed 62 antigens, of which 18 antigens were detected at the A locus, 14 antigens at the B-30 locus and 14 antigens at the DR locus. The highest percentage of unidentified alleles was at the B locus, which may be a subject for further study. The data obtained in this study show that in the Uzbek population of the Samarkand region, all the studied HLA antigens are found with different frequencies. Typical HLA antigens for the examined population were A2, A9, A10 and A19, B5, B7, B13, DR1, DR2, DR7, DR9 and DR15. The most complete range of possible diversity of alleles is presented in the A and DR loci, judging by the low frequency of the blank allele in these loci (0.0930 and 0.0419, respectively). This value is somewhat higher in the B locus (0.1624).

A feature of the examined population is an increased frequency of HLA-antigen B13 (26.74%).

Thus, according to the nature of the distribution of HLA antigens, the examined population has common features with both Caucasoids and Mongoloids, and also has individual features. The results of the study can serve as a basis for studying the association of HLA antigens with diseases in this population.

As it is known, HLA haplotypes are more individual characteristic of the HLA genetic profile of a population than the frequency of HLA antigens. For the surveyed population, characteristic haplotypes were A2-B13, A19-DR4, A9-B35, A30-B13. In the same haplotypes, the highest values of nonequilibrium linkage of alleles are noted.

In recent years, it has become known that the polymorphism of the HLA system, in addition to the established interracial and interethnic differences, also has intraethnic differences. Thus, it is clear that the polymorphism of the HLA system, characteristic of each particular population group, has a significant impact on the biological stability of this group.

The study of the difference in HLA antigens between the urban and rural population showed that the urban region was characterized by an increase in the distribution of HLA antigens: A9, A19 and DR4.

Comparative characteristics of gender differences showed that the frequency of HLA - antigens A32, B14, B49 and DR4 was somewhat higher in the male groups of the surveyed population.

Conclusion

The HLA-genetic profile of the Uzbek population of the Samarkand region was established for a wide range of alleles of the A, B and DR loci. An increased frequency of occurrence of HLA haplotypes A2-B13, A9-B35, A19-DR4 and A30-B13 in the examined population was revealed. In the same haplotypes, the highest values of nonequilibrium linkage of alleles are noted.

Table 1

Distribution of HLA antigens in the examined population
(n=86, DR, n=82)

HLA-antigene	A%	G	HLA-antigene	A%	G	HLA-antigene	A%	G
A1	15,2	0,0787	B15	4,7	0,0235	DR1	28,1	0,1518
A2	31,4	0,1717	B16	1,2	0,0058	DR2	22,0	0,1165

A3	17,4	0,0914	B17	9,3	0,0476	DR3	18,3	0,0961
A9	32,4	0,1660	B18	4,7	0,0235	DR4	13,4	0,0695
A10	25,6	0,1373	B21	4,7	0,0235	DR5	18,3	0,0961
A11	12,8	0,0661	B22	9,3	0,0416	DR6	9,8	0,0500
A19	38,4	0,1224	B27	10,5	0,0538	DR7	37,8	0,2114
A23	2,3	0,117	B35	11,6	0,0599	DR8	3,7	0,0185
A24	17,4	0,0914	B39	1,2	0,0058	DR9	23,2	0,1235
A26	12,8	0,0661	B40	8,2	0,0416	DR10	4,9	0,0247
A28	19,8	0,1043	B41	3,5	0,0176	DR11	15,9	0,0827
A29	2,3	0,0117	B42	4,7	0,0235	DR12	2,4	0,0123
A30	11,6	0,0599	B44	3,5	0,0176	DR13	9,8	0,0500
A31	2,3	0,0117	B46	3,5	0,0176	DR15	20,7	0,1097
A32	9,3	0,0476	B48	1,2	0,0058	DRbl		0,0420
A33	2,3	0,0117	B49	2,3	0,0117			
A68	4,7	0,0235	B50	2,3	0,0117			
A69	7,00	0,0355	B51	3,5	0,0176			
Abl	-	0,0560	B52	2,3	0,0117			
			B53	1,2	0,0058			
B5	20,93	0,1108	B55	2,3	0,0117			
B7	17,44	0,0914	B56	1,2	0,0058			
B8	9,30	0,0476	B60	5,8	0,030			
B12	6,98	0,0355	B75	1,2	0,0058			
B13	26,74	0,1441	Blb		0,203			
B14	3,49	0,0176						

Note: Abl - A-blank - the frequency of an unidentified, empty allele; A is the frequency of occurrence of the antigen, %; G is the frequency of occurrence of the gene.

Table 2

Frequencies of HLA haplotypes with statistically significant and positive D values in the general population

HLA- haplotype	D	H
A2-B13	3304*	5509
A9-B35	2304*	3209
A19-DR4	3008*	4382
A24-DR6	1733*	2168
A26-DR13	1733*	2168
A26-DR8	1019*	1135

A30-B13	2368*	3332
A30-B14	1034*	1139
A32-B17	1435*	1662
A32-B44	1063*	1147
A32-B46	1063*	1147
B5-DR10	1436*	1697
B14-DR4	1039*	1135
B22-DR2	1712*	2173
B27-DR8	1049*	1143

*Note: D-value of haplotype linkage disequilibrium (X 100000); H – haplotype frequency (X 100000); *-P<0.05*

Table 3

The frequency of occurrence of HLA antigens in the urban population of Uzbek nationality (n=36)

AG	n	AG%	G%	AG	N	AG%	G%	AG	n	AG %	G%
A1	6	16,7	0,0874	B21	-	-	-	DR1 1	5	13,9	0,072 0
A2	8	22,2	0,1179	B22	4	11,1	0,0570	DR1 2	2	5,6	0,028 4
A3	6	16,7	0,0874	B27	3	8,3	0,0424	DR1 3	4	11,1	0,057 0
A9	1 2	33,3	0,1833	B35	3	8,3	0,0424	DR1 4	-	-	-
A10	1 3	36,1	0,2006	B39	1	2,8	0,0141	DR1 5	9	25,0	0,134 0
A11	5	13,5	0,0700	B40	-	-	-				
A19	1 6	44,4	0,2500	B41	2	5,6	0,0284				
A23	-	-	-	B42	2	5,6	0,0284				
A24	4	11,1	0,0570	B44	3	8,3	0,0424				
A25	-	-	-	B46	3	8,3	0,0424				
A26	4	11,1	0,057	B48	1	2,8	0,0141				
A28	8	22,2	0,1179	B49	2	5,6	0,0284				
A29	-	-	-	B50	1	2,8	0,0141				
A30	5	13,5	0,0700	B51	1	2,8	0,141				
A31	-	-	-	B55	1	2,8	0,0141				
A32	5	13,5	0,0700	B56	-	-	-				

A33	1	2,8	0,0112	B60	2	5,6	0,0284				
A36	1	2,8	0,0112	B75	-	-	-				
A68	2	4,0	0,0203	B60	2	5,6	0,0284				
A69	-	-	-	B75	-	-	-				
Abl											
B5	4	11,1	0,0570	DR1	8	22,2	0,1180				
B7	4	11,1	0,0570	DR2	8	22,2	0,1180				
B8	4	11,1	0,0570	DR3	7	19,4	0,1022				
B12	2	5,6	0,0284	DR4	9	25,0	0,1340				
B13	9	25,0	0,1340	DR5	7	19,4	0,1022				
B14	2	5,6	0,0284	DR6	4	11,1	0,0570				
B15	1	2,8	0,0141	DR7	14	38,9	0,2183				
B16	-	-	-	DR8	1	2,8	0,0141				
B17	3	8,3	0,0424	DR9	11	30,6	0,1670				
B18	1	2,8	0,0141	DR10	1	2,8	0,0141				

Note: AG - antigen, AG% - frequency of occurrence of antigen, n - number of examined persons

Table 4

The frequency of occurrence of HLA antigens among people of Uzbek nationality living in the rural population (n=50, DR, n=46)

AG	n	AG%	G%	AG	N	AG%	G%	AG	n	AG %	G%
A1	7	14,0	0,0727	B18	3	6,0	0,0305	DR9	8	17,4	0,0912
A2	19	38,0	0,2126	B21	-	-	-	DR10	3	6,5	0,0331
A3	9	18,0	0,0945	B22	3	6,0	0,0305	DR11	8	17,4	0,0912
A9	13	26,0	0,1398	B27	6	12,0	0,0619	DR12	-	-	-
A10	9	18,0	0,0945	B35	7	14,0	0,0730	DR13	4	8,7	0,0445
A11	6	12,0	0,0620	B39	-	-	-	DR14	4	8,7	0,0445
A19	17	34,0	0,1876	B40	-	-	-	DR15	8	17,4	0,0912
A23	2	4,0	0,0203	B41	1	2,0	0,0101				
A24	11	22,0	0,117	B42	2	4,0	0,0203				
A25	-	-	-	B44	-	-	-				

A26	7	14,0	0,0727	B46	-	-	-				
A28	9	18,0	0,0945	B48	-	-	-				
A29	2	4,0	0,0203	B49	-	-	-				
A30	5	10,0	0,0514	B50	1	2,0	0,0101				
A31	2	4,0	0,0203	B51	1	2,0	0,0101				
A32	3	6,0	0,0305	B52	-	-	-				
A33	1	2,0	0,0101	B53	-	-	-				
A36	-	-	-	B55	1	2,0	0,0101				
A68	2	4,0	0,0203	B56	-	-	-				
A69	6	12,0	0,0620	B60	3	6,0	0,0305				
				B75	1	2,0	0,0101				
B5	14	28,0	0,1520								
B7	11	22,0	0,1170	DR1	15	32,6	0,1791				
B8	4	8,0	0,0408	DR2	10	21,7	0,1152				
B12	2	4,0	0,0203	DR3	8	17,4	0,0912				
B13	14	28,0	0,1515	DR4	2	4,3	0,0218				
B14	1	2,0	0,0101	DR5	8	17,4	0,0912				
B15	3	6,0	0,0305	DR6	4	8,7	0,0445				
B16	-	-	-	DR7	17	37,0	0,2063				
B17	5	10,0	0,0514	DR8	2	4,3	0,0218				

Note: AG - antigen, AG% - frequency of occurrence of antigen, n - number of examined persons

Table 5

Differences in the distribution of HLA antigens between the urban and rural population of the surveyed population

HLA antigen	General population n=86		Urban population n=36		Rural population n=50	
	A%	G%	A%	G%	A%	G%
A9	32,4	0,1660	33,3	0,1833	26,0*	0,1398
A19	32,6	0,1661	44,4	0,2500	34,0*	0,1876
DR4	13,41	0,0695	25,0	0,1340	4,0***	0,0510

*Note: * - significant compared with the data of the urban region group (* - $P < 0.05$; ** - $P < 0.01$); A% - frequency of antigen occurrence; G% frequency of occurrence of a gene*

Table 6

Differences in the distribution of HLA antigens between females and males of the surveyed population

HLA antigen	General population (n=86)		women n=61 (DR, n=57)		Men n=25 (DR, n=25)	
	A%	G%	A%	G%	A%	G%
A32	9,30	0,0476	5,0*	0,0254	19,2	0,1012
B14	3,49	0,0176	1,6**	0,0081	7,6	0,0388
B49	2,33	0,0117	0**	0	7,6	0,0388
DR4	13,41	0,0695	7,7**	0,0393	28,0	0,1515

*Note: * significant in comparison with the data of the group of males (* - $P < 0.05$; ** - $P < 0.01$); A% is the frequency of antigen occurrence; G% frequency of occurrence of a gene*

REFERENCES

1. Abdukarimovna D. G. et al. ANALYSIS OF THE RELATIONSHIP OF THE HLA-PHENOTYPE WITH THE LEVEL OF IMMUNOREACTIVITY OF THE ORGANISM //Web of Scientist: International Scientific Research Journal. – 2022. – T. 3. – №. 9. – С. 429-438.
2. Alekseev L.P., Khaitov R.M. 1996. Molecular genetics of the HLA system //Int .J. Immunorehab., No. 26., P 59-65.
3. Alekseev L. P., Khaitov R. M., Sechkin A. V. 2001. HLA and medicine // Modern. prob. allergol. immunol. and immunopharmacology". Abs. report 4 congresses of RAAKI. - Moscow, P. 240-260.
4. Iskhakov A. T., Rakhimova D. A. 1993. Biological organization of the HLA system // Med. magazine Uzbekistan. - - No. 3., P. 67-70.
5. Khaitov R. M., Alekseev L. P. 2002. Genomics of the major histocompatibility complex: clinical aspects // Sat. modern samples allergol., immunology and immunopharmacology. V Congress of RAACA. -M., P. 9-28.
6. Khaitov R. M., Alekseev L. P., Yazdovsky V. V. 1991. HLA-associated genetic control of some indicators of immunoreactivity in normal and pathological conditions // Methodological aspects of modern immunology. -N., P. 117-129
7. Khaitova N. M. Alekseev L. P. Yazlovsky V. V., Polunin V. V. 1988. HLA and some indicators of immunoreactivity in healthy lindens of the Uzbek nationality // Immunology, No. 2., P. 63-66
8. Chereshev V. A., Kevorkov N. V., Bakhmetiev B. A., Shirshv S. V., Osipenko A. V., Raev M. B. Shirsheva I. V. 2001. Physiology of the immune system and ecology / / Immunology., No. 3., P. 12-18.
9. Chereshev V. A., Yushkov B. G., Klimin V. G., Lebedev E. V. 2002 Immunophysiology. - Yekaterinburg: UrORAN. 258 p.
10. Душанова Г. А. и др. Современное состояние проблемы массовых иммунологических обследований //Образование и наука в России и за рубежом. – 2020. – №. 12. – С. 62-74.

11. Н.Р. Аралов, С.Х. Зиядуллаев, Г.А. Душанова [Hla-ХОБЛ и маркеры бронхиальной астмы: общность и различия](#) // Международный журнал фармацевтических исследований 12 (1), 1233-1237.
12. Зиядуллаев С., Душанова Г., Ахмедова Г. [LBPS 02-51 роль системных металлопротеиназ и их ингибиторов при сердечной недостаточности](#). - Гипертония, 2016.