

HLA Diversity in Iraqi Population: Molecular Typing

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Abstract:

Background: Human leukocyte antigen (HLA) is the most polymorphic system in human. The distribution of HLA- alleles varies in different populations.

Objective: This study was conducted to highlight on alleles frequency of HLA in Iraqi population by using molecular technique.

Patients and methods: Two hundred individuals were genotyped for HLA class I and II alleles by polymerase chain reaction sequence-specific oligonucleotides (PCR-SSO).

Results: The present study observed that the alleles with highest frequency for HLA-A,B,C,DR and DQ region were: [A*02(27.75%), A*01(10.75%), B*51(17.75%), B*35(9%), C*04(26.75%), C*07(20.25%), DRB1*02(17.5%), DRB1*07(17%), DQB1*01(25.5%) and DQB1*03(21.75%)].

Conclusion: The frequency of HLA alleles in Iraqi Arabs partly different when compared with some populations around the world, however; this data is useful in field of response to vaccines and therapy, anthropology and could be provide standard control for future Iraqi studies about the HLA association with different diseases.

Key words: HLA; Iraq; PCR.

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Introduction:

Human leukocyte antigen (HLA) is the most polymorphic system in human. The primary function of HLA is the regulation of the immune system by present processed peptide to T-cell, it is associate with certain diseases with unknown specific mechanisms (1, 2). The HLA system is consisted of three regions, the class I region contains the classical HLA-A, B, and-C genes, and the class II region contains the classical HLA-DR, -DP and-DQ genes. While the class III region include genes for complement components (C2, C4, factor B), 21-hydroxylase, tumor necrosis factors (TNFs), and others (3, 4). Alleles of HLA are inherited as an HLA haplotype in a Mendelian law from each parent. Certain HLA haplotypes are present more frequently in some populations than other, for example, HLA-A1, B8, DR17 is the most presence HLA haplotype in Caucasians (2).

Certain HLA-alleles are common while other alleles vary in frequency among various ethnic groups. For example, HLA-A1 antigen occurs in 15 % of Caucasians, 3.3 % of African Black, and 0.5 % of Japanese (5), while in Iraqi people occurs in 22.92 % (6). Differences in the frequency of HLA alleles may participate in geographic variation of the susceptibility to different diseases, such as infectious, metabolic and autoimmune diseases (7). This study was conducted to highlight on frequency of HLA alleles in Iraqi Arab population by using molecular technique.

Patients and methods:

Two hundred unrelated Iraqi Arab subjects (105 males and 95

females) were included in this study from 2012 till 2015.

Two ml of blood sample was collected from each individual kept in EDTA tube for DNA extraction. The HLA genotyping done by PCR-SSO method according to the manufacturer's instructions in the HLA-typing laboratory of Al-Karama teaching hospital, Baghdad (PCR-SSO kit: Innogenetics-Line Probe Assay, INNO—LiPA; Belgium).

Statistical analysis: The results were presented in terms of percentage frequencies and gene frequency. The gene frequency was calculated as following (8):

$$S=1-\sqrt{1-AG}$$

S=gene frequency

AG=frequency of certain allele

Results:

The frequency of class I and class II HLA-alleles for unrelated Iraqi Arab individuals are presented in tables (1,2,3,4,5). This study showed that the HLA-class-I alleles with highest frequencies were A*02 (27.75 %), A*01(10.75%), B*51(17.75%), B*35(9%), C*04(26.75%) and C*07(20.25%), while for class II alleles were: DRB1*02(17.5%), DRB1*07(17%), DQB1*01(25.5%) and DQB1*03(21.75%).

On the other hand the alleles with minimal frequencies for HLA-class-I were: A*36(0.25%), A*69(0.25%), B*81(0.25%), B*82(0.25%), C*17(1.25%), C*18(1.25%), while for class II were: DRB1*17(0.50%), DQB1*8(0.50%) and DQB1*9(0.50%).

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Table-1: Distribution of HLA-A alleles in Iraqi Arab population.

HLA-A alleles	No. of Positive cases	%	Gene frequency	HLA-A alleles	No. of Positive cases	%	Gene frequency
A*01	43	10.75	0.05	A*31(19)	18	4.5	0.023
A*02	111	27.75	0.149	A*32(19)	9	2.25	0.012
A*03	32	8	0.04	A*33(19)	13	3.25	0.017
A*9	2	0.50	0.003	A*34(10)	4	1	0.006
A*11	23	5.75	0.029	A*36	1	0.25	0.002
A*23(9)	13	3.25	0.017	A*66(10)	11	2.75	0.014
A*24(9)	31	7.75	0.04	A*68(28)	12	3	0.016
A*25(10)	3	0.75	0.004	A*69(28)	1	0.25	0.002
A*26(10)	19	4.75	0.024	A*74(19)	13	3.25	0.017
A*29(19)	9	2.25	0.012	A*80	2	0.50	0.003
A*30(19)	30	7.50	0.039				
TOTAL					400		

Table-2: Distribution of HLA-B alleles in Iraqi Arab population.

HLA-B alleles	No. of Positive cases	%	Gene frequency	HLA-B alleles	No. of Positive cases	%	Gene frequency
B*07	24	6	0.031	B*48	2	0.50	0.003
B*08	29	7.25	0.073	B*49(21)	16	4	0.021
B*13	15	3.75	0.019	B*50(21)	22	5.5	0.028
B*14	4	1	0.006	B*51(5)	71	17.75	0.089
B*15	24	6	0.031	B*52(5)	13	3.25	0.017
B*17	2	0.50	0.003	B*53	4	1	0.006
B*18	16	4	0.021	B*54(22)	3	0.75	0.004
B*27	12	3	0.016	B*55(22)	8	2	0.011
B*35	36	9	0.047	B*56(22)	4	1	0.006
B*37	10	2.5	0.013	B*57(17)	3	0.75	0.004
B*38(16)	11	2.75	0.014	B*58(17)	9	2.25	0.012
B*39(16)	9	2.25	0.012	B*59	2	0.50	0.003
B*40	16	4	0.021	B*60(40)	2	0.50	0.003
B*41	10	2.5	0.013	B*78	3	0.75	0.004
B*44(12)	14	3.50	0.018	B*81	1	0.25	0.002
B*45(12)	2	0.50	0.003	B*82	1	0.25	0.002
B*46	2	0.50	0.003				
TOTAL					400		

Table-3: Distribution of HLA-C alleles in Iraqi Arab population.

HLA-C alleles	No. of Positive cases	%	Gene frequency
C*01	12	3	0.016
C*02	25	6.25	0.032
C*03	21	5.25	0.027
C*04	107	26.75	0.145
C*05	25	6.25	0.032
C*06	39	9.75	0.05
C*07	81	20.25	0.107
C*08	18	4.50	0.023
C*12	38	9.50	0.049
C*14	8	2	0.011
C*15	8	2	0.011
C*16	8	2	0.011
C*17	5	1.25	0.007
C*18	5	1.25	0.007
TOTAL	400 (NO. of individuals=200)		

Table-5: Distribution of HLA-DQ alleles in Iraqi Arab population.

HLA-DQ -B1 alleles	No. of Positive cases	%	Gene frequency
DQ*01	102	25.5	0.134
DQ*02	76	19	0.10
DQ*03	87	21.75	0.11
DQ*04	35	8.75	0.045
DQ*05(1)	18	4.50	0.023
DQ*06(1)	69	17.25	0.089
DQ*07(3)	9	2.25	0.012
DQ*08(3)	2	0.50	0.003
DQ*9(3)	2	0.50	0.003
TOTAL	400 (NO. of individuals=200)		

Discussion

It is well known that there are many studies regarding the HLA association with different diseases in Iraq, but few studies are available about the distribution of HLA- alleles in Iraqi population. To our knowledge, present study is the first in Iraq about the HLA distribution in Iraqi Arab population by using molecular technique (PCR-SSO). Current findings showed high frequencies of some HLA alleles among Iraqi Arabs which includes: A*02, A*01, B*51, B*35, C*04, C*07, DRB1*02, DRB1*07, DQB1*01 and DQB1*03.

Table-4: Distribution of HLA-DR alleles in Iraqi Arab population.

HLA-DR-B1 alleles	No. of Positive cases	%	Gene frequency
DR*01	40	10	0.052
DR*02	70	17.5	0.089
DR*03	45	11.25	0.057
DR*04	59	14.75	0.073
DR*07	68	17	0.089
DR*08	13	3.25	0.017
DR*9	3	0.75	0.004
DR*10	7	1.75	0.009
DR*11 (5)	15	3.75	0.019
DR*12 (5)	6	1.50	0.008
DR*13(6)	15	3.75	0.019
DR*14(6)	18	4.50	0.023
DR*15(2)	21	5.25	0.027
DR*16(2)	18	4.50	0.023
DR*17 (3)	2	0.50	0.003
TOTAL	400 (NO. of individuals=200)		

Interestingly, present results confirm the outcome of previous Iraqi study done by serotyping method (Microlymphocytotoxicity assay) which found that the highest frequencies of HLA-A alleles were: HLA-A2 (38.48%) and A1 (22.92%), while the highest frequencies for HLA-B, HLA-C HLA-DR and HLA-DQ alleles were: B51(20%), B35 (19.8%), CW4(23.4%),CW7(19.28%), DR2 (27.75%), DR3 (27.25%), DQ1(23.25%) and DQ3 (23.25%) (6). Moreover, other Iraqi study conducted by Ad'hiyah in 2009 was investigate the HLA- A, B, DR and DQ antigens by serotyping method in 145 non related Iraqi individuals revealed that the antigens with highest frequencies were: A19,A2, B5 and B35 regarding the HLA-class I antigens while for HLA class II antigens were DR2, DR1, DQ2 and DQ3 (9), however, these results in comparison with the current study showed some variation, for example the most frequent alleles in Iraqi population were A2 and DQ1 regarding the HLA-A and DQ antigens in present study while in study done by Ad'hiyah were A19 and DQ2. The difference in picture of HLA distribution of both studies may be due to the disadvantages of serotyping method of HLA-typing especially with low size of samples (in HLA-serotyping method, some alleles were blank with no results). On the other hand the HLA-B and HLA-DR-alleles of both studies showed approximated results regarding the first allele with highest frequency.

Other local study conducted by Lafta, in 1999 (the HLA typing done for only HLA-A and -B antigens with serotyping method) revealed that the A2 and B 51 antigen were with highest frequency: (38.7 %), (20.5%) respectively (10). The

present study showed some variation when compared with other communities like Saudis (11), Turkish (12) Indian (13) and others. The antigen with highest frequency for HLA-A-locus was A2 (43 %, 33% and 56%) for Saudis, Iranian and Turkish respectively, while for HLA-B locus were B50 (37%), B5 (42%) and B5 (33%) in Saudis, Iranian and Turkish respectively, however; for HLA-C locus was Cw4 (48 % and 15%) in Saudis and Iranian respectively. In addition the antigen with highest frequency for HLA-DR locus were DR7 (35%), DR11 (29%) and DR4 (34%) in Saudi, Tunisian and Indian respectively and for HLA-DQ locus were DQ1 (51%) in both Saudis and Tunisian. The reason for this variation may be in partial due to gene drift (association between some genes by chance) or gene flow (admixture among different populations (14), sample size and method used in HLA typing. Current work confirmed the concept of race variation, which showed that the some alleles occur at higher or lower frequency in Iraqis as compared with other population. Define which HLA alleles are existent in the population give knowledge about the origin of this population and the genetic susceptibility to various diseases. Different HLA genotypes have been associated with susceptibility to different diseases such as viral infections (15).

Conclusion:

The frequency of HLA alleles in Iraqi Arabs partly different when compared with some populations around the world, however; this data is useful in field of response to vaccines and therapy, anthropology and could be provide standard control for future Iraqi studies about the HLA association with different diseases.

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