Frequency of HLA-A and B Antigens in Iraqi Patients with End-Stage Renal Disease Preparing for Transplantation

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ABSTRACT:

BACKGROUND:

The likelihood of developing end-stage renal disease in an individual is determined by interactions between genetic and environmental factors. Human leukocyte antigen is the most polymorphic genetic system in man. Genes of this region influence susceptibility to certain diseases.

OBJECTIVE:

The purpose of the present study is to investigate the association of HLA class I (HLA-A and HLA-B) with the end-stage renal disease in Iraqi patients (Arab and Kurd).

SUBJECTS AND METHODS:

HLA-typing was assessed in 200 patients with end-stage renal disease and 110 healthy controls by microlymphocytotxicity assay.

RESULTS:

A survey of the distribution of HLA-A and HLA-B antigens frequencies yielded a significant variation between patients and healthy control group. Arab patients have significant increase in frequency of HLA-A2 as compared with healthy control (P=0.005). Whereas Kurdish patients revealed significant increase in frequency of HLA-B35 when compared with healthy control (P=0.033).

CONCLUSION:

The current study suggests that high frequency of HLA-A2 in Arab patients and HLA-B35 in Kurdish patients might be associated with susceptibility to risk of end-stage renal disease.

KEY WORDS: end-stage renal disease, HLA.

INTRODUCTION:

End stage renal disease (ESRD) has become a major health problem because it is a devastating medical condition, and the cost of treatment is a huge economic burden [(1)]. The number of patients with ESRD is increasing faster than the number of renal transplantations performed per year worldwide. Renal transplant has become the standard care for the fatal renal diseases. In the world the demand for renal transplant is about 60 patients per million populations. The success of such transplantations correlates with the degree of human leukocyte antigens (HLA) compatibility between recipients and donors [(2)].

Genes of human leukocyte antigens are encoded by major histocompatability complex (MHC) located on short arm of chromosome six. HLA molecule binds and presents peptide to T lymphocytes in cell mediated immune response and plays a key role in shaping the T cell repertoire and is also associated with allograft rejection. HLA antigens are inherited in a co-dominant manner from parents to the offspring [(3)].

The role of the HLA system in the pathophysiology of end-stage renal disease is intriguing, but not completely resolved. Numerous associations and non-associations of HLA antigens with ESRD have been reported in the medical literature. The association between this disease and HLAB-58 was described by Karahan and colleagues in Turkish patients [(4)]. Other study conducted by Crispim *etal*., reported that the antigens positively associated with ESRD were HLA-A78 and HLA-DR11, whereas HLA-B14 antigen was present at a significantly lower in patients and might confer protective role [(5)].

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Moreover, Prasanavar and Shankarkumar were analyzed HLA antigen and haplotype frequencies in 217 renal transplant recipients and live related donors, and they observed that the HLA-A and B antigen frequencies were not significantly different in two groups [6].The purpose of the present study is to investigate the association of HLA class I with the end-stage renal disease in Iraqi patients (Arab and Kurd).

SUBJECTS AND METHODS:

The present study included 200 ESRD patients (110 males and 90 females). Patient's group was divided in to two groups (100 of patients were Arabs, while 100 patients were Kurdish), they were attending to the Al-Karama teaching hospital compared with 110 (60 males and 50 females), [75 were Arab and 35 were Kurdish] healthy age and sex were matched control group.Typing for HLA-A and B antigens was carried out in the HLA-typing laboratory of Al-Karama teaching hospital. Micro-lymphoctotoxicity assay has been applied for HLA-typing (HLA Class I positive and negative control antisera, Biotest, Germany) as described by Terasaki and McClelland [7].Statistical Analysis: Univariate analysis has been applied for the data depending on logistic regression and the results were reported as odds ratio (ORs), which represented the increased or decreased risk for ESRD.

RESULTS:

The frequency of distribution of various HLA-A and HLA-B antigens for two studied groups (patients and healthy groups) were presented in tables (1, 2, 3 and 4). Comparison between ESRD patients and healthy control showed antigens deviations in their frequencies. HLA-A2 antigens was observed with increased frequencies in Arab patients (52.0%) versus (37.3%) in Arab healthy control, with P-values (0.005), table (1). A survey of the distribution of HLA-B frequencies yielded no evident association between HLA-B antigens and Arab patients.Concerning comparison between Kurdish patient and Kurdish healthy control the present results failed to show any significant differences in the frequency of HLA-A antigens between patients and control, table (3),($p>0.05$). In contrast regarding HLA-B locus this study revealed higher frequency of B35 in patients (35.0%) versus healthy control (8.6%), P=0.033, table (4).

Table 1: Antigens frequency of the HLA-A (%, OR, inverse OR, P, EF, PF) of the Arab ESRD patients and the Arab healthy controls.

HLA antigen	Healthy control(N=75)		ESRD cases(N=100)		OR	Inverse OR	P	EF	PF
	N	*%*	*N*	*%*					
HLA-A									
1	17	22.7	20	20.0	0.8	1.2	NS	**	0.050
2	28	37.3	52	52.0	3.6	**	0.005	0.195	**
3	14	18.7	27	27.0	1.6	**	NS	0.068	**
11	9	12.0	10	10.0	0.6	1.6	NS	**	0.048
23	3	4.0	3	3.0	0.7	1.3	NS	**	0.010
24	13	17.3	11	11.0	0.7	1.4	NS	**	0.06
25	1	1.3	1	1.0	0.7	1.3	NS	**	0.010
26	7	9.3	18	18.0	1.8	**	NS	0.039	**
28	9	12.0	13	13.0	1.0	**	NS	**	**
29	3	4.0	6	6.0	1.5	**	NS	0.021	**
30	12	16.0	9	9.0	0.5	1.6	NS	**	0.040
31	2	2.7	1	1.0	1.1	**	NS	0.011	**
32	2	2.7	11	11.0	2.1	**	NS	0.042	**
33	7	9.3	7	7.0	1.0	1.0	NS	**	0.008
34	1	1.3	0	0.0	0.2	4.0	NS	**	**
Blank	22		11						
Total	150		200						

**=Nill

Table 2: Antigens frequency of the HLA-B (%, OR, inverse OR, P, EF, PF) of the Arab ESRD patients and the Arab healthy controls.

HLA antigen	Healthy control (N=75)		ESRD cases (N=100)		OR	Inverse OR	P	EF	PF
	N	*%*	*N*	*%*					
HLA-B									
7	8	10.7	15	15.0	1.5	**	NS	0.021	**
8	8	10.7	13	13.0	1.0	**	NS	**	**
13	5	6.7	8	8.0	0.9	1.1	NS	**	0.036
14	4	5.3	2	2.0	1.0	**	NS	**	**
17	5	6.7	9	9.0	1.4	**	NS	0.025	**
18	3	4	12	12.0	1.9	**	NS	0.057	**
27	3	4.0	7	7.0	2.1	**	NS	0.042	**
35	13	17.3	17	17.0	0.8	1.2	NS	**	0.050
37	3	4.0	1	1.0	0.2	4.1	NS	**	0.030
38	5	6.7	7	7.0	0.9	1.1	NS	**	0.012
39	1	1.3	2	2.0	1.0	**	NS	**	**
40	2	2.7	2	2.0	0.1	6.8	NS	**	**
41	9	12.0	9	9.0	0.6	1.6	NS	**	0.048
44	6	8.0	15	15.0	2.5	**	NS	0.109	**
45	1	1.3	1	1.0	0.7	1.3	NS	**	0.010
47	1	1.3	2	2.0	1.0	**	NS	**	**
49	6	8.0	5	5.0	1.1	**	NS	0.011	**
50	9	12.0	15	15.0	1.3	**	NS	0.034	**
51	14	18.7	17	17.0	1.0	1.0	NS	**	0.008
52	3	4.0	4	4.0	1.0	**	NS	**	**
54	3	4.0	0	0.0	1.0	**	NS	**	**
55	0	0.0	1	1.0	5.4	**	NS		
56	1	1.3	0	0.0	0.2	4.0	NS	**	**
62	1	1.3	1	1.0	0.7	1.3	NS	**	0.010
63	1	1.3	6	6.0	4.7	**	NS	0.047	**
Blank Total	35 150		29 200						

Table 3: Antigens frequency of the HLA-A (%, OR, inverse OR, P, EF, PF) of the Kurdish ESRD patients and the Kurdish healthy controls.

HLA antigen	Healthy control (N=35)		ESRD cases (N=100)		OR	Inverse OR	P	EF	PF
	N	*%*	*N*	*%*					
HLA-A									
1	11	31.4	18	18.0	0.9	1.1	NS	**	0.024
2	20	57.1	43	43.0	1.6	**	NS	0.125	**
3	4	11.4	23	23.0	1.6	**	NS	0.125	**
11	4	11.4	20	20.0	1.7	**	NS	0.074	**
23	2	5.7	3	3.0	0.5	2.0	NS	**	0.028
24	7	20.0	12	12.0	0.5	1.8	NS	**	0.103
25	1	2.9	0	0.0	0.1	8.7	NS	**	**
26	2	5.7	10	10.0	3.4	**	NS	0.063	**
28	3	8.6	11	11.0	1.5	**	NS	0.038	1.5
29	2	5.7	4	4.0	0.5	2.0	NS	**	0.028
30	2	5.7	10	10.0	3.4	**	NS	0.063	**
31	1	2.9	5	5.0	0.7	1.5	NS	**	0.027
32	2	5.7	6	6.0	1.1	**	NS	0.003	**
33	1	2.9	2	2.0	1.1	**	NS	0.001	**
34	0	0.0	0	0.0	0.4	2.8	NS	**	**
Blank	8		33						
Total	70		200						

Table 4: Antigens frequency of the HLA-B (%, OR, inverse OR, P, EF, PF) of the Kurdish ESRD patients and the Kurdish healthy controls.

HLA antigen	Healthy control(N=35)		ESRD cases (N=100)		OR	Inverse OR	P	EF	PF
	N	*%*	*N*	*%*					
HLA-B									
7	0	0.0	7	7.0	4.9	**	NS	0.048	**
8	6	17.1	3	3.0	0.7	1.5	NS	**	0.027
13	0	0.0	2	2.0	0.4	2.8	NS	**	**
14	3	8.6	2	2.0	0.3	3.0	NS	**	0.057
17	1	2.9	6	6.0	2.2	**	NS	0.032	**
18	4	11.4	13	13.0	1.9	**	NS	0.070	**
27	2	5.7	14	14.0	1.1	**	NS	0.010	**
35	3	8.6	35	35.0	3.9	**	0.033	0.202	**
37	2	5.7	0	0.0	0.1	15.0	NS	**	**
38	4	11.4	3	3.0	0.2	4.2	NS	**	0.087
39	1	2.9	2	2.0	1.1	**	NS	0.001	**
40	1	2.9	7	7.0	3.0	**	NS	0.053	**
41	2	5.7	5	5.0	0.7	1.5	NS	**	0.027
44	4	11.4	13	13.0	1.9	**	NS	0.070	**
45	1	2.9	0	0.0	0.1	8.7	NS	**	**
47	1	2.9	0	0.0	0.1	8.7	NS	**	**
49	1	2.9	4	4.0	0.5	2.1	NS	**	**
50	1	2.9	12	12.0	3.4	**	NS	0.063	**
51	5	14.3	22	22.0	1.3	**	NS	0.047	**
52	1	2.9	19	19.0	2.1	**	NS	0.155	**
53	2	5.7	0	0.0	0.1	15.0	NS	**	**
54	1	2.9	0	0.0	0.1	8.7	NS	**	**
55	1	2.9	5	5.0	0.7	1.5	NS	**	0.027
56	1	0.0	1	1.0	0.3	2.9	NS	**	0.019
62	1	2.9	1	1.0	0.3	2.9	NS	**	0.019
63	1	2.9	2	2.0	1.1	**	NS	0.001	**
Blank	20		22						
Total	70		200						

DISCUSSION:

The likelihood of developing ESRD in an individual is determined by interactions between genetic and environmental factors. Familial clustering of nephropathy has repeatedly been observed in all population groups studied and for multiple etiologies of kidney disease. A three- to nine-fold greater risk of ESRD is observed in individuals with a family history of ESRD [8,9]. Moreover it is shown that development of ESRD is associated with different HLA antigens [10]. Several studies indicates epidemiologic differences of ESRD by race but reasons for this are unclear [11].

The present study revealed a significant association of HLA-A2 in Iraqi Arab ESRD patients and HLA-B35 in Iraqi Kurdish ESRD patients (p=0.005; 0.033 respectively), as compared with healthy control. Different results regarding this association was reported, results differ in different population. Similarly to the present results Davood and co-workers noticed that the most frequent detected HLA antigens were A2, A3 and A24 from A loci and B35, B51 and B18 from B loci, and found significant association between susceptibility to ESRD and HLA-A33, A11, B49. So they concluded that polymorphism of HLA class I may influence the susceptibility to ESRD [12]. Furthermore Doxiadis etal., pointed out to the significant increase in frequencies of HLA-B35 and DR5 with high relative risk values in patients [13], meanwhile another report revealed HLA phenotypes which identified as independent risk factors associated with protection against alloantibody sensitization in ESRD such as HLA-DR1, 4, 7, HLA-B12, HLA-A1 and 2, and the only

independent susceptibility atigen was HLA-A36 [14].

In Turkey (2010), Karahan and colleagues reported highly significant frequency of HLA-A3, HLA-A66 and HLA-B18 antigens in patients with ESRD [15], while in other study conducted by Chen demonstrated decrease the frequencies of HLA-B27, B40 and increase frequency of HLA-B35 in patients with ESRD compared with healthy controls [16]. Correspondingly HLA-B27 antigen is most closely linked with renal disease in children in Egypt [17].

CONCLUSION:

The present results denoted the role of HLA-A2 in Arab patients and HLA-B35 in Kurdish patients could be considered as highly significant risk factors for ESRD.

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