HLA prevalence in Iraqi patients with ischemic heart disease

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Summary:

Background: The etiology of ischemic heart disease (IHD) is believed to have an immunological component. Association with human leukocyte antigens (HLAs) has been previously reported, particularly with DR6.

Patients and methods: 75 cardiac patients were admitted to the coronary care unit, Baghdad Teaching Hospital over the period October 2008-May 2009 with the clinical diagnosis of acute coronary syndrome and STEMI myocardial infarction their ages range was (25-82) years the number of male was (55) (73.3%) and female was (20) (26.7%). All cases have routine ECG, cardiac marker's measurements, routine haematological, Biochemical test and 2mls of blood reserved for HLA study.

Results: It was found that HLA-DR1 (8%) (P 0.001) has significant risk factor in the development of ischemic heart disease while HLA B (62%) (P 0.0009) has a protection factor in ischemic heart disease.

Conclusions: Our result suggests that strong relation between the incidence of acute ischemic episode (acute coronary syndrome and STEMS myocardial infarction and HLA-DR1) which mean that there may be predisposing genetic factor for the development ischemic heart disease.

Key words: Ischemic Heart Disease, Human Leukocyte Antigens.

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Introduction:

Ischemic heart disease is a complex of clinical symptoms of various pathogenesis caused by insufficient oxygen and nutritional compounds supply in relation to the actual requirement of the myocardium. However the most important factors for increased incidence of ischemic heart disease is the presence of predisposing factors like age, sex, atherogenic diet smoking, lack of physical activity, obesity, excessive consumption of Alcohol, abnormal lipid profile, high Blood pressure, Hyperglycemia, elevated concentration of homocysteine and fibrinogen. Another important role in the development of ischemic heart disease is the genetic factor.(1,2) Since they affect the development ischemic heart disease via the process of polymorphism in which there will be genetically transmitted mutation of DNA. Another aspect of association of ischemic heart disease is HLA system. The major histocompatibility complex (MHC) is a complex locus, composed of a large cluster of genes located on the short arm of chromosome 6 (3). MHC products are expressed on surface of a variety of cell in human, these are known as HLA-Ags (3, 4). The human MHC, comprises three major classes (I, II, III) of genes involved in the immunr response.

Class I: molecules are a glycoprotein's and dividend two families, HLA Ib encoded by genes at the A, B and C loci in the HLA on chromosome 6(5, 6, 7, 8). C locum in immunologically important.

Class II: molecules are the MHC class II genes encode a glycoprotein.

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These molecules are consist of two non covalently linked polypeptide chains, α chain and β chain encoded by DR-DQ and DP regions (6, 9) (DP immunologically most important).

The MHC region between class I and class II is called class III region contain several different genes coding for complements C2, C4, BF, two cytokines (TNF α and β), two HSP (hsp 70-1& 70-2) "one of family produced by cells in response to heart and injuries" and 21 hydroxylase "an enzyme important in steroid metabolism"(10, 11).

Patients and Methods:

75 cardiac patients with history of acute coronary syndrome and acute myocardial infarction (STEMS) admitted to the coronary care unit, Baghdad teaching hospital over the period October 2008-May 2009. Their age range was age 55±30 (25-82) the Number of male were 55 and female were 20 and (value) and the male to female into was 2.7:1. 50 healthy central (age, sex, matched) were enrolled in this study. Both patients and control went thought the same uniform questionnaire, which includes (clinical history, clinical examenation, routine blood test, cardiac markers, electrocardiography, and echocardiography). These patients did not have any other chronic disorders like malignancy, reneal falure, thyroid disorder, diabetes mellitus, and connective tissue disease.

Both groups were typed for HLA-class I (A&B) and class II (DR-DQ) antigens. The basic material for typing with Histo-type DNA-ssp sequence specific primers kit is purified kit. The test procedure was done by using the sequence specific primers (ssp). This method is based in the fact that primer extension and hence successful polymerase chain

reaction (PCR) relies on the exact match at the 3-end of both primers

Results:

The frequency of distribution of various class I HLA-Ags for both patients & control groups were show in tables (1and 2). The HLA-A locus, comparison between IHD patients and healthy control groups showed no significant association between several antigens regarding their frequencies distribution. Studying HLA-B locus, it has been found the B7 was showing increased frequencies in healthy control group in compassion to patients (15.0% Vs 5.0%) then patients and therefore this may represent a protective factor against the disease with p value 0.009. Studying the DR- allels, It has been found that DR-1showing high frequency in patients group in comparison to control group (p value <0.001) an shown in table 3.

Table-1: Antigens frequency of the HLA-A (%, P) of the IHD patients and healthy control.

HLA antigen	Healthy control		Ischemic heart cases		P
Total	No=50		No=75		
HLA-A	N	%	N	%	
1	15	30.0	25	25.0	NS
2	33	58.0	35	52.0	NS
3	6	12.0	11	11.0	NS
9	3	6.0	5	5.0	NS
10	1	2.0	3	3.0	NS
11	5	10.0	7	7.0	NS
23	2	4.0	5	5.0	NS
24	10	20.0	18	180	NS
25	1	2.0	3	3.0	NS
26	3	6.0	4	4.0	NS
28	4	8.0	2	2.0	NS
29	3	6.0	2	2.0	NS
30	3	6	4	4.0	NS
31	2	4.0	4	4.0	NS
32	2	4.0	2	2.0	NS
33	2	4.0	3	3.0	NS
34	1	2.0	2	2.0	NS
36	1	2.0	4	4.0	NS

Table-3 below revealed the importance of DR-alleles through their frequencies in IHD patients in comparison with healthy controls. As shown, DR1 found in high frequencies in patients compared to healthy control groups with (P value <0.0001).

A survey of the distribution of HLA-DQ frequency yielded no evident association between DQ Ag and IHD patients, (table-4).

So from all what had been mentioned previously it appeared that DR-1 formed a big significant difference between patients and the normal persons since it's P value was <0.0001, while the strongest protective antigen was HLA-B7 with P value (0.009).

Table-2: Antigens frequency of the HLA-B (%, P) of the IHD patients and healthy control.

HLA antigen	Health control		IHD cases		P
Total	No=50		No=75		
HLA-B	N	%	N	%	
5	3	6.0	4	4.0	NS
7	35	62.0%	3	3.0	0.009
8	7	14.0	9	9.0	NS
12	0	0.0	3	3.0	NS
13	0	0	0	0.0	NS
14	4	8.0	9	9.0	NS
15	1	2.0	3	3.0	NS
17	2	4	1	1.0	NS
18	5	10.0	5	5.0	NS
21	1	2.0	8	8.0	NS
22	0	0	0	0.0	NS
27	3	6.0	6	6.0	NS
35	4	8.0	2	2.0	NS
37	3	6	3	3.0	NS
38	5	10.0	7	7.0	NS
39	12	22.0	18	18.0	NS
40	2	4.0	1	1.0	NS
41	3	6	3	3.0	NS
44	6	12.0	4	4.0	NS
45	1	2.0	0	0.0	NS
47	1	2.0	1	1.0	NS
49	1	2	0	0.0	NS
50	1	2	1	1.0	NS
51	7	14.0	8	8.0	NS
52	1	2	0	0.0	NS
53	3	6.0	2	2.0	NS
54	0	0.0	1	1.0	NS
55	1	2.0	6	6.0	NS
56	1	2.0	2	2.0	NS
57	1	2.0	1	1.0	NS
60	0	0.0	1	1.0	NS
62	1	2.0	3	3.0	NS
63	1	2.0	2	2.0	NS
70	1	2.0	1	1.0	NS
73	0	0.0	2	2.0	NS

Table-3: Antigens frequency of the HLA-DR (%, P) of the IHD patients and healthy control.

HLA antigen	Healthy control		IHD cases		P
	N0=50		No=75		
HLA-DR	N	%	N	%	
1	4	8.0	62		0.001
2	6	12	11	11.0	NS
3	10	20	12	18.0	NS
4	20	32.0	24	24.0	NS
5	2	4.0	4	4.0	NS
6	1	2	0	0.0	NS
7	32	52.0	44	48.0	NS
8	3	6.0	2	2.0	NS
9	1	2.0	0	0.0	NS
10	5	10.0	8	8.0	NS
11	3	3.0	6	6.0	NS
13	1	2.0	1	1.0	NS
14	2	4.0	4	4.0	NS
15	3	6	4.0	0.7	NS
52	5	10.0	6	6.0	NS
53	3	6.0	4	4.0	NS

Table-4: Antigens frequency of the HLA-DQ (%, P) of the IHD patients and healthy control.

HLA antigen	Healthy control		IHD cases		P
Total	No=50		No=75		
HLA-DQ	N	%	N	%	
1	13	26	26	26.0	NS
2	13	26.0	26	26.0	NS
3	10	20.0	18	18.0	NS
4	8	16.0	13	13.0	NS

Discussion:

The role of genetic factors in the etiology of different types of heart diseases was documented many decades ago. As a result, the investigative efforts were focused on the genetic markers of susceptibility to this disease. Moreover, the high familial incidence of heart diseases suggests the possibility of a linkage or an association of disease with MHC (8, 12), however, this study is the first report on the association of HLA class I and II with IHD in Iraqi patients.

In the present work, there was a significant association of HLA-DR1 with IHD patients (p= 0.001). This result is in agreement with what reported by some researchers regarding significant statistical association of IHD with DR locus in comparison with healthy control group (6, 13).

Different results regarding this association was reported, results differ in different population. For instance Limas reported the association of HLA-Ag with IHD and observed an increase frequency of HLA-DR6 in Americans patients (7), other study reported by Palikhe and collegues revealed an increased frequency of HLA-A2 in Finland patients (13, 14). Howover, other scientist failed to confirm such association (15, 16).There is no clear reason why some studies should be different from those already published, other than possible differenc,(17, 18, 19) arising from geographically and ethnically different populations.

So generally an immunological basis for IHD remains likely, but this disease is probably a heterogeneous condition and it may be that a strong immunological component is not a feature of all groups (20).

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