Human Leukocyte Antigens and Susceptibility to Atopic Dermatitis
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Abstract:

Background: Atopic dermatitis (AD) is a chronic inflammatory skin disease belongs to atopic allergic diseases resulting from the interaction between environmental and genetic factors. Many HLA alleles are involved in the etiopathology of atopic dermatitis.

Objective: the association between HLA-A, and B genes and the atopic dermatitis.

Patients and methods: HLA A and B genotyping were practiced for 40 atopic dermatitis patients and 80 healthy controls using the microlymphocytotoxicity complement dependent technique.

Results: A total of 40 patients with atopic dermatitis were studied. Patients' age ranged from 2 to 48 years with a mean of 19.33± 11.29. The other control group, their ages ranged from 15 to 50 years with a mean of 20.45 ± 12.03. Females were more than males. HLA typing of atopic dermatitis patients showed A9 (14,31.82, 0.17), B6(16, 36.36, 0.20) and B35 (8, 18.18, 0.10) were the highest absolute numbers, phenotype frequencies and genotype frequencies respectively while the control group demonstrated A1(24, 30, 0.16), A2( 28, 35, 0.19), B6(33, 41.25,0.23), B35(21, 26.25, 0.14) were the dominant ones. There was a significant difference in HLA typing between atopic dermatitis patients and control group in the following alleles (A1, A36, B41, B42, B53 had an association with atopic dermatitis Iraqi Arab Muslims patients. Alleles of HLA- A36, B41, B42, B53 had an association with atopic dermatitis. Alleles of HLA- A1 and B14 appear to be protective against atopic dermatitis.

Conclusions: Genetic factors have a role in the development and expression of atopic dermatitis. Alleles of HLA- A36, B41, B42, B53 had an association with atopic dermatitis. Alleles of HLA- A1 and B14 appear to be protective against atopic dermatitis.

Key words: Atopic, Human Leukocyte Antigens and microlymphocytotoxicity.

Introduction:

The atopic diseases include atopic dermatitis, asthma and hay fever, are among the most common chronic diseases. They are major causes of illness and disability and represent an important public health issue. Atopic dermatitis (AD) is a chronic inflammatory skin disease with onset typically in early childhood

It is an important manifestation of atopy that is characterized by the formation of IgE to environmental allergens. In developed countries, the prevalence of atopic dermatitis is approximately 15%, with a steady increase over the past decades. Atopic dermatitis is a chronic relapsing inflammatory skin disorder associated with interactions between environmental and genetic factors. Among environmental factors is food allergy is found in 35 to 45% of children with moderate to severe AD. Among various food allergens, hen's egg, particularly egg white, is one of the most common causes of food allergy and is correlated with AD severity. Current breakthroughs in genetic methodology have greatly increased our understanding of the contribution of genetics to susceptibility to AD.

One candidate gene that may be involved is human leukocyte antigen (HLA), because it plays a major role in immune response regulation and is associated with predisposition to a large number of immunologically mediated diseases. The HLA, the major histocompatibility complex (MHC) in humans has been known to reside on chromosome 6 and encodes cell-surface antigen-presenting proteins and many other proteins related to immune system function. HLA class I molecules are an important regulatory function in inflammatory responses. HLA class II molecules have extensive molecular polymorphisms, confined to the peptide-binding groove and presented antigen to T cells via T cell receptors. It had been found that HLA-DRB1 polymorphism is associated with AD particularly HLA-DRB1*11:01 was significantly increased in Korean children with AD compared with controls.

Thus the aim of this study is to determine the frequency of HLA alleles in Iraqi patients affected by AD.

Patients and Methods:

Patients group consisted of 40 Iraqi Arab Muslims patients with atopic dermatitis who were diagnosed by their consultant in dermatology, presented to Baghdad Medical City –Department of Dermatology from Baghdad Province. The inclusion criteria were only patients diagnosed as atopic dermatitis and treated with atopic dermatitis medications and came to follow –up. The exclusion criteria were all other atopic diseases.

The second control group consisted from 80 Iraqi Arab Muslims volunteers from hospital employees and their relatives.

The permission of medical ethics committee was obtained from Al-Kindy Medical College. The Ethical Committee of the Al-Kindi College of Medicine, Baghdad University and Baghdad Medical City Teaching Hospital approved the study, and all samples were obtained with informed consent in accordance with the Al-Kindi Teaching Hospital Declaration.

HLA typing was done for them using serological method by microlymphocytotoxicity test, which was developed by Terasaki and McClelland (1964). This test is a complement dependent reaction, in which antibodies recognize antigens on the surface of lymphocytes and form antigen-antibody complexes. The formed antigen-antibody complexes thus are able to activate the added rabbit complement which results in death of reacted cells. Then by a dye exclusion technique, it is possible to score the reaction and to determine the HLA-phenotype. Statistical analysis was done using...
Results:
A total of 40 patients with AD were studied. Patients' age ranged from 2 - 48 years with a mean of 19.33 ± 11.29 years. Twenty-four of them were female and the rest were males. The age and sex distribution of patients are described in Table-1. The other control group, their ages ranged from 15 - 50 years with a mean of 20.45 ± 12.03 years. Fifty of them were female and the rest were males.

<table>
<thead>
<tr>
<th>Sex</th>
<th>AD patients</th>
<th>No.</th>
<th>%</th>
<th>Healthy control</th>
<th>No.</th>
<th>%</th>
<th>*P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>24</td>
<td>60</td>
<td></td>
<td>50</td>
<td>62.5</td>
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<td>0.134</td>
</tr>
<tr>
<td>Male</td>
<td>16</td>
<td>40</td>
<td></td>
<td>30</td>
<td>37.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Age at sampling Mean ± SD: 19.33 ± 11.29 for AD patients and 20.45 ± 12.03 for control group, respectively. There was a significant difference in HLA typing between AD patients and control group in the following alleles (A1, A36, B14, B41, B42, and B53) as revealed in Table-2. Odd ratio was highest in A9 and B41 as shown in table -1.

HLA typing of AD patients showed A9 (14, 31.82, 0.17), B6 (16, 36.36, 0.20) and B35 (8, 18.18, 0.10) were the highest absolute numbers, phenotype frequencies and genotype frequencies respectively (Table-2) while the control group demonstrated A1(24, 30, 0.16), A2(28, 35, 0.19), B6(33, 41.25, 0.23), B35(21, 26.25, 0.14) were the dominant ones (Figure -1-2).

Table-1: Age and sex distribution of AD patients and control group.

Table-2: HLA typing of AD patients and control group.
Discussion:
Atopic dermatitis is a chronic inflammatory skin disorder belongs to the group of allergic disorders (1). A multifactorial cause for AD has been suggested, like genetic as well as environmental factors influencing disease development (5).

HLA system plays an important role in disease development. In our study, we found that alleles of HLA typing in Iraqi Arab Muslims affected by AD were more frequent in A9=31.82, B6= 36.36 and B35=18.18 (Table-2) while the control group demonstrated A1= 30, A2= 35, B6= 41.25, B35= 26.25 were the dominant ones (Figure -1-2 A and B).

There was a significant difference in HLA typing between AD patients and control group in the following alleles (A1, A36, B14, B41, B42, and B53) as revealed in table-2-. Other study in Tunis showed that HLA-A32 could be a protective marker against atopic dermatitis for Tunisian patients, in contrast to HLA-B, DR and DQ alleles that seemed to have no importance in AD pathogenesis (9).

Others demonstrated the frequencies of HLA phenotypes A1, B8 and A3, B7 in the patients group and control did not differ significantly and the frequency of HLA-DR7 was strikingly low (10) while in our study we found a significant difference in HLA-A1.

HLA typing differs according to ethnic background of studying group. In Koreans, a study showed the frequency of HLA-A24 was significantly increased in patients with atopic dermatitis compared to controls (11).

The exact mechanism underlying the effect of HLA genes on AD development is due to HLA class II alleles play key roles in antigen presentation to
CD4+ T lymphocytes via T cell receptors and thus influence specific IgE response to several allergens (12).

Saeki et al (13) reported that the frequency of HLA-DRB1*13:02 was increased in patients with severe AD and high serum IgE compared with controls. There is a possible association between peculiar HLA antigens and atopic dermatitis (14). Thus, genetic and genomic analysis of complex diseases will play an important role in identification of new molecular targets for intervention with pharmaceutical and biological drugs (15).

The difference in HLA association with AD in our study and other studies in different countries may be due to race, ethnicity, religion and family study that differ from one country to other. Moreover, ethnicity found to have a significant role in both disease susceptibility and disease expression (16). In summary, our studies emphasize previous studies indicating that genetic factors do have a role in the development and expression of AD in association with environmental factors like food allergy. Environmental factors may possibly trigger the disease in genetically susceptible subjects

Conclusions:
Genetic factors have a role in the development and expression of AD. Alleles of HLA-A36, B41, B42, and B53 had an association with AD Iraqi Arab Muslims patients. Alleles of HLA-A1 and B14 appears to be protective against AD

References

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