Research Article

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HLA class I and II alleles may influence susceptibility to adult dermatomyositis in a Mexican mestizo population

Objective: To investigate the possible association between HLA and Dermatomyositis (DM) in the Mexican mestizo population.

Methods: HLA class I (A and B) and class II (DRB1* and DQB1*) were determined in 36 Mexican mestizo patients with DM and 72 healthy controls.

Results: A positive association was identified among alleles HLA A*01:01 (OR 3.5 (1.30-9.54), p<0.012), A* 03:01 (OR 5 (2.11-11.81), p<0.0002), B* 07:02 (OR 3.9 (1.63 - 9.50), p<0.0002), DRB1* 09:01 (OR 5 (2.11-11.81), p<0.032) and DRB1*01:02 (OR 33.04 (1.86-588.09), p<0.017), and the presence of DM. Protective alleles were identified for the development of disease to DRB1* 16:01 (OR 0.12 (0.015-0.093), p<0.043) and DQB1* 03:02 (OR 0.10 (0.02-0.46), p<0.002).

Conclusions: In this study, identification of alleles related to DM in a Mexican mestizo-population showed the participation of HLA in its development, as reported in other-populations.

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Introduction

Dermatomyositis (DM) is a form of idiopathic inflammatory myopathy (IIM) which, together with polymyositis (PM) and inclusion body myositis, is part of a heterogeneous group of musculoskeletal diseases [1]. Frequency of DM as an independent entity from other inflammatory myopathies is unknown, but DM is the most common. The condition affects more women than men, including children and adults. DM occurs with varying degrees of predominantly distal muscle weakness without affecting facial muscles. Usually it develops slowly over weeks or months [2]. This condition is characterized by skin lesions which, in most cases, precede muscle weakness. These include heliotrope rash on the upper eyelids; erythematous rash on the face, neck and anterior chest or back and shoulders, knees, elbows or malleolus; Gottron's papules, raised purple rash or bumps on the knuckles, predominantly in metacarpophalangeal and interphalangeal joints; and dilated capillary loops in the nail bed with thickened and distorted cuticles. The lateral and palmar fingers may become rough and cracked with dark horizontal lines [2,3]. There may be manifestations in other organs and systems such as joint contractures; oropharyngeal dysphagia with involvement of striated muscle and upper esophagus; atrioventricular conduction disturbances, tachyarrhythmia, myocarditis; pulmonary manifestations involved with thoracic muscle involvement or interstitial lung disease; subcutaneous calcifications and general symptoms such as fever, malaise, weight loss and arthralgia [2]. DM can be associated with other connective tissue diseases and an increase in the frequency of cancer, especially ovarian, gastrointestinal tract, lung, breast and non-Hodgkin lymphoma [2,3].

Criteria proposed by Bohan and Peter allow establishing the clinical diagnosis of DM [4,5] according to dermatological findings [6]. For characterization and classification of DM, myopathological patterns can also be used. Although this condition may manifest itself as clinically homogeneous, there are at least two distinct clinic pathological types: vascular pathology of muscle fiber atrophy and mitochondrial changes seen predominantly in

children. Interstitial lung disease is rare. The second pattern shows prominent connective tissue pathology with necrosis and regeneration of the muscle fiber. This pattern occurs mainly in adults and is associated with interstitial lung disease [7]. IIM can also be divided into multiple serogroups according to the presence of myositis-specific autoantibodies or to myositis-associated antibodies, which are associated with various epidemiological, clinical, prognostic and immunogenetic patterns [8,9].

In regard to the etiology of IIM, environmental factors have been proposed that trigger the phenomenon of autoimmunity in a genetically predisposed host [10,11]. This concept is supported by reports of family groups with IIM and according to those who develop the disease after exposure to environmental agents in certain geographical areas and during certain times of the year [12].

The principal genetic risk factor for IIM is related to chromosomal region 6p21.3 that regulates HLA [13,14].

Some studies have described alleles of the ancestral HLA haplotype (HLA-A1~B8~DRB1*03:01 ~DQA*05:01) as risk factors for multiple autoimmune diseases, conferring very high possibilities of autoimmunity without being associated with specific diseases [12].

On the other hand, the ancestral European haplotype HLA- In the North American Caucasian population, allele HLA-A*68 are a significant risk factor for DM and are also associated with the binding of alleles DQA1*03:01 and DQA1*05:01 [15,16].

The African-American population with DM shares the DRB1*03:01 allele as a risk factor with the European-American population [17]. In the Caucasian population of the UK, an association of DQB1*02 with DM and PM and DRB1*07 and DQA1*02 with DM has been found [18] and in the Chinese population of DRB1*07 and DQA1*01:04 with DM [19]. DRB1*03:01, DQA1*03:01 and DQA1*05:01 are considered to be the principal risk factors for the juvenile form of DM in the Caucasian population [15-20]. In the present study we investigate the association of HLA with Mexican mestizo patients with DM.

Methods

We carried out a case-control study (1:2) in the Hospital Juárez de México (HJM). Thirty six patients from the Rheumatology Service were included. Patients were diagnosed with DM according to the criteria of Bohan and Peter [4,5]. There were 72 healthy subjects included from the database of the live kidney donor program. The population belongs to Mexican mestizo ethnicity, according to the trihibrid model (admixture of Amerindian, European and African populations) [21]. The subjects were born in Mexico and have a family history of Mexican ascendance in at last three generations. The research protocol was approved by Ethics in Investigation Committee with a registration number 1758/09.09.08. All the participants signed an informed consent that includes the management of genetic material.

HLA typing

Study subjects were genotyped for HLA class I (A and B) and class II (DRB1 and DQB1) using PCR-SSP technique (Invitrogen ABDRDQ SSP UniTray®, Life Technologies Corporation, Brown Deer, WI, USA). Alleles obtained were valid in the IMGT/HLA database that allows retrieving the information about one particular allele as mentioned in WHO's Committee of Nomenclature [22-26].

Statistical analysis

HLA allele and haplotype frequencies were obtained by gene counting. Hardy–Weinberg (HW) equilibrium and LD were calculated with Arlequin ver. 3.1 and the strength of association was given as odds ratio (OR) with a 95% confidence interval (CI); p values ≤0.05 were considered significant with MedCalc Software

Table 1. Demographic characteristics of dermatomyositis group and controls

Variable	Dermatomyositis	Controls	p
Size	n=36	n=72	
Age - Years			
Median	40.5	37	>0.05
Interquartile range	33.5-47	32-43	
Number - Sex (%)			
Female	27 (75)	41 (56.9)	<0.05
Male	9 (25)	31 (43.1)	

Table 2. HLA A frequencies in dermatomyositis groups and controls

HLA A*allele	PATIENTS n = 36	CONTROLS n=72	OR (CI) °	p °°
0.042361	0.1527	0.0486	4.08 (1.42-11.72)	0.0089
0.046528	0	0.0277	0.2 (.011- 4.05)	0.305
0.050694	0	0.0069	0.6 (0.026-16.39)	0.799
0.1375	0.0277	0	10.2 (0.48-216.33)	0.134
0.084028	0.1944	0.2152	0.08 (0.43-1.78)	0.722
0.085417	0.0138	0	6 (0.24-150.71)	0.271
0.090972	0.0138	0	6 (0.24-150.71)	0.271
0.106944	0	0.0069	0.6 (0.026-16.39)	0.799
0.118056	0	0.0069	0.6 (0.026-16.39)	0.799
0.125694	0.25	0.0625	5 (2.11-11.81)	0.0002
0.13125	0	0.0069	0.6 (0.026-16.39)	0.799
0.1375	0	0.0069	0.6 (0.026-16.39)	0.799
0.459028	0.0138	0.0486	0.5 (0.113-2.763)	0.475
0.461111	0	0.0208	0.27 (0.01-5.47)	0.4
0.470833	0	0.0069	0.6 (0.026-16.39)	0.799
0.475694	0.0138	0	6 (0.24 -150.71)	0.271
0.959028	0.0277	0.0277	1 (0.17-5.592)	1
0.968056	0	0.0069	0.6 (.026 - 16.39)	0.799
1.001389	0.0277	0.0972	0.26 (0.05-1.200)	0.085
1.042361	0	0.0277	0.2 (.011- 4.05)	0.305
1.084028	0.0138	0.0069	2 (0.12-32.67)	0.622
1.085417	0	0.0208	0.27 (0.01-5.47)	0.4
1.209028	0.0277	0.0347	0.8 (1.50-4.19)	0.786
1.250694	0	0.0347	0.17 (0.009-3.20)	0.24
1.292361	0.0138	0.0833	0.3 (0.06-1.44)	0.136
1.29375	0.0138	0.0069	2 (0.12-32.67)	0.622
1.334028	0.0416	0.0069	6.2 (0.63-60.86)	0.116
1.375694	0	0.0208	0.27 (0.01-5.47)	0.4
1.380556	0	0.0069	0.6 (.026-16.39)	0.799
1.500694	0	0.0069	0.6 (.026-16.39)	0.799
1.792361	0	0.0069	0.6 (.026-16.39)	0.799
2.834028	0	0.0416	2 (0.64-6.73)	0.216
2.836806	0	0.0277	0.21(0.011-4.05)	0.305
2.853472	0	0.0069	0.6 (0.026-16.39)	0.799
3.084028	0.0138	0.0416	0.3 (0.036-2.595)	0.278
3.085417	0	0.0069	0.6 (0.026-16.39)	0.799
3.0875	0.0138	0.0138	0.9 (0.084-10.61)	0.964
3.334028	0.0138	0	6 (0.24-150.71)	0.271

°Odds Ratio (OR), 95% Confidence Interval (CI), °° p< 0.05

Table 3. HLA B frequencies in dermatomyositis groups and controls

HLA B* allele	PATIENTS n = 36	CONTROLS n = 72	OR (CI) °	p °°
0.293056	0.2083	0.0625	5 (1.90-13.09)	0.001
0.296528	0	0.0069	0.65 (0.026-16.39)	0.799
0.395139	0.0138	0	6 (0.24-150.71)	0.271
0.433333	0.0138	0	6 (0.24-150.71)	0.271
0.316667	0.0277	0.0069	4 (0.36-45.83)	0.253
0.334028	0.013	0.013	0.9 (0.08-10.61)	0.964
0.334722	0.013	0	6 (0.24-150.71)	0.271
0.336111	0	0.0069	0.65 (0.026-16.39)	0.799
0.359028	0.0138	0	6 (0.24-150.71)	0.271
0.542361	0.0138	0.0138	0.9 (0.08-10.61)	0.964
0.584028	0.0277	0.0208	1.3 (0.219-8.22)	0.749
0.584722	0.0138	0.0416	0.3 (0.038-2.743)	0.301
0.625694	0.0277	0.0208	1.3 (0.21-8.22)	0.749
0.626389	0.0277	0.0208	1.3 (0.21-8.22)	0.749
0.63125	0	0.0069	0.65 (0.026-16.39)	0.799
0.631944	0.0138	0.0277	0.5 (0.054-4.49)	0.53
0.632639	0	0.0069	0.65 (0.026-16.39)	0.799
0.634028	0	0.0069	0.65 (0.026-16.39)	0.799
0.636111	0.0277	0.0069	4 (0.36-45.83)	0.253
0.636806	0.0277	0	10.2 (0.48-216.33)	0.134
0.638194	0	0.0069	0.65 (0.026-16.39)	0.799
0.645139	0	0.0069	0.65 (0.026-16.39)	0.799
0.658333	0.0138	0	6 (0.24-150.71)	0.271
0.695139	0.0138	0	6 (0.24-150.71)	0.271
0.750694	0.0416	0.0138	3 (0.49-18.36)	0.234
0.759722	0	0.0069	0.65(0.026-16.39)	0.799
1.125694	0.0138	0	6 (0.24-150.71)	0.271
1.127778	0.0138	0	6 (0.24-150.71)	0.271
1.130556	0	0.0069	0.65 (0.026-16.39)	0.799
1.459028	0.138	0.118	1 (0.52-2.78)	0.662
1.460417	0.0138	0.0138	0.9 (0.08-10.61)	0.964
1.461806	0.0416	0.0625	0.5 (0.17-2.48)	0.652
1.471528	0	0.0069	0.65 (0.026-16.39)	0.799
1.472222	0	0.0138	0.37 (0.01-7.85)	0.525
1.475694	0	0.0069	0.65 (0.026-16.39)	0.799
1.476389	0	0.0069	0.65 (0.026-16.39)	0.799
1.477778	0	0.0138	0.4 (0.018-8.296)	0.548
1.483333	0	0.0069	0.65 (0.026-16.39)	0.799
35:60	0	0.0069	0.65 (0.026-16.39)	0.799
35:63	0	0.0069	0.65 (0.026-16.39)	0.799

°Odds Ratio (OR), 95% Confidence Interval (CI) , °° p< 0.05

Table 3a. HLA B frequencies in dermatomyositis groups and controls

HLA B* allele	PATIENTS n = 36	CONTROLS n = 72	OR (CI) °	p °°
1.584028	0	0.0138	0.37 (0.017-7.85)	0.525
1.625694	0.0138	0.0347	0.39 (0.04-3.41)	0.396
1.626389	0	0.0069	0.65 (0.026-16.39)	0.799
1.629167	0	0.0069	0.65 (0.026-16.39)	0.799
1.63125	0.0277	0	10 (0.48-216.33)	0.134
1.638194	0	0.0138	0.37 (0.017-7.85)	0.525
1.667361	0	0.0277	0.21 (0.011-4.05)	0.305
1.668056	0.0416	0.0625	0.65 (0.17-2.48)	0.531
1.68125	0.0138	0	6 (0.24-150.71)	0.271
1.709028	0	0.0069	0.65 (0.026-16.39)	0.799
1.713889	0	0.0069	0.65 (0.026-16.39)	0.799
1.750694	0	0.0069	0.65 (0.026-16.39)	0.799
1.834722	0.0277	0.0069	4 (0.36- 45.83)	0.253
1.844444	0	0.0069	0.65 (0.026-16.39)	0.799
44:166	0.0138	0	6 (0.24-150.71)	0.271
1.875694	0.0138	0.0138	0.9 (0.0845-10.61)	0.964
2.001389	0	0.0069	0.65 (0.026-16.39)	0.799
2.042361	0	0.0138	0.37 (0.017-7.85)	0.525
2.043056	0	0.0069	0.65 (0.026-16.39)	0.799
2.084028	0.055	0.0277	2 (0.499-8.48)	0.317
2.125694	0	0.0277	0.21 (0.011--4.054)	0.305
2.135417	0	0.0069	0.65 (0.026-16.39)	0.799
2.167361	0	0.0208	0.27 (0.01-5.47)	0.4
2.172222	0	0.0069	0.65 (0.026-16.39)	0.799
2.209028	0.0138	0.0138	0.9 (0.08-10.61)	0.964
2.254167	0	0.0069	0.65 (0.026-16.39)	0.799
2.292361	0	0.0277	0.2 (0.011-4.05)	0.305
2.334028	0	0.0138	0.37 (0.017-7.85)	0.525
2.335417	0	0.0069	0.65 (.026-6.39)	0.799
2.339583	0	0.0138	0.37 (.017-7.859)	0.525
3.250694	0	0.0069	0.65 (0.026 - 16.39)	0.799

°Odds Ratio (OR), 95% Confidence Interval (CI) , °° p< 0.05

Version 16.4.3 -Last modified: April 26, 2016, © 1993-2016 [27,28].

Results

Demographic characteristics are described in Table 1. Median age of diagnosis of patients with DM was 37 years (interquartile range, IQR, 31-43 years) Table 1.

A total of 195 genotype alleles were obtained: HLA class I: 40 A and 71 B. In HLA class II there were 58 DRB1 and 26 DQB1. and were identified to be associated with the presence of alleles A*01:01 [OR 4.08 (1.42-11.72), p 0.0089], A*03:01 [OR 5 (2.11-11.81) p=0.0002], B*07:02 [OR 5 (1.90-13.09), p= 0.001], DRB1*01:02 [OR 33.09 (1.86-588.09) p=0.017] and DRB1*09:01 [OR 10.6 (1.22-93.14), p=0.032], were identified to be associated with the presence of DM and DRB1*16:01 [OR 0.082 (0.018-0.36), p= 0.011], DQB1* 03:02 [OR 0.10 (0.02-0.46), p=0.002] as protective of disease (Tables 2-5).

Haplotypes frequencies in dermatomyositis

Table 4. HLA DQB1 frequencies in dermatomyositis groups and controls

HLA DQB1 allele	PATIENTS n = 36	CONTROLS n=72	OR (CI) °	p °°
0.084028	0.0972	0.1111	0.8 (0.33-2.19)	0.755
0.085417	0.0138	0	6 (0.24-150.71)	0.271
0.086806	0.0138	0	6 (0.24-150.71)	0.271
0.09375	0.0138	0	6 (0.24-150.71)	0.271
0.094444	0.0138	0	6 (0.24-150.71)	0.271
0.104861	0.0277	0	10.24 (0.48-216.33)	0.134
0.125694	0.1388	0.215	0.58 (0.27-1.27)	0.18
0.126389	0.0277	0.208	0.10 (0.02-0.46)	0.002
0.127083	0.0138	0.0138	1 (0.08-11.21)	1
0.129861	0.0277	0	10.24 (0.48-216.33)	0.134
0.131944	0.0138	0	6 (0.24-150.71)	0.271
0.132639	0.0138	0	6 (0.24-150.71)	0.271
0.134722	0.0138	0	6 (0.24-150.71)	0.271
0.145833	0.0138	0	6 (0.24-150.71)	0.271
0.167361	0.1944	0.2152	0.87 (0.43 -1.78)	0.722
0.168056	0.0138	0	6 (0.24-150.71)	0.271
0.170139	0.0138	0	6 (0.24-150.71)	0.271
0.176389	0.0138	0	6 (0.24-150.71)	0.271
0.209028	0.1111	0.0625	1.87 (0.69-5.08)	0.216
0.228472	0.0138	0	6 (0.24-150.71)	0.271
0.238194	0.0138	0	6 (0.24-150.71)	0.271
0.24375	0.0138	0	6 (0.24-150.71)	0.271
0.250694	0.0833	0.1388	0.56 (0.21-1.47)	0.241
0.251389	0.0277	0.0347	0.79 (0.15- 4.19)	0.786
0.288889	0.0138	0	6 (0.24-150.71)	0.271
0.297917	0.0138	0	6 (0.24-150.71)	0.271
0.336111	0.0138	0	6 (0.24-150.71)	0.271

°Odds Ratio (OR), 95% Confidence Interval (CI) , °° p< 0.05

groups present the highest prevalence not only shows that the haplotype A*02:01~B*35:01~DRB1*08:01~DQB1*04:01 that occurs with high frequency in the mestizo population Table 6.

Discussion

There is a growing body of evidence to suggest that differences in the impact of HLA class II alleles on the susceptibility to DM and PM may exist among different ethnic groups and geographic locations. In addition to the above information, it was demonstrated that the group of IIM is not genetically identical as reported in Caucasian population studies. Therefore, the study of DM independently in Mexican mestizos was of interest [18]. In the Mexican mestizo population, this is the first report that established the possible HLA associations with DM.

In our study, HLA-A*01:01, HLA-A*03:01, HLA-B*07:02, HLA-DRB1*01:02 and HLA-DRB1*09:01 were significantly associated with the presence of DM. Strength of association of each of the alleles can change in accordance with its presence in the healthy population. Unlike our results, for the genotypes published by Williams and Gorodezky in a healthy Mexican mestizo open population [29-31]. Alleles HLA-A*01:01 and HLA-B*07:02 are reported as part of the polymorphism of some groups of healthy Mexican mestizos with a frequency of 9-14%. In the case of HLA-A*03:01, it was documented with a frequency lower than the previous (0.024%) [32,33].

In Caucasian and Asian ethnicities, HLA-A*01:01 and HLA-B*07:02 were reported with the highest frequency [24]. In the case of

Table 5. HLA DRB1 frequencies in dermatomyositis groups and controls

HLA DRB1* allele	PATIENTS n = 36	CONTROLS n=72	OR (CI) °	p °°
0.042361	0.0833	0.055	1.5 (0.51-4.36)	0.437
0.043056	0.0972	0	33.09 (1.86-588.09)	0.017
0.04375	0	0.0069	0.65 (0.026 - 16.39)	0.799
0.047222	0.0138	0	6 (0.24-150.71)	0.271
0.049306	0.0277	0	10.2 (0.48-216.33)	0.134
0.052083	0	0.0069	0.6 (.026-16.39)	0.799
0.05625	0.0138	0	6 (0.24-150.71)	0.271
0.125694	0.0555	0.0208	2.7 (0.60-12.70)	0.191
0.169444	0.0138	0	6 (0.24-150.71)	0.271
0.167361	0.0152	0.173	0.85 (0.39-1.86)	0.698
0.170139	0.0138	0	6 (0.24-150.71)	0.271
0.175	0	0.0069	0.65 (0.026-16.39)	0.799
0.177083	0	0.0069	0.65 (0.026-16.39)	0.799
0.181944	0	0.0069	0.65 (0.026-16.39)	0.799
0.234722	0.0277	0	10.2 (0.48-216.33)	0.134
0.209722	0.0138	0	6 (0.24-150.71)	0.271
0.292361	0.0694	0.0277	2.6 (0.67-10.04)	0.162
0.299306	0.0138	0	6 (0.24-150.71)	0.271
0.302778	0.0138	0	6 (0.24-150.71)	0.271
0.334028	0.0415	0.0625	1.53 (0.40-5.84)	0.531
0.336111	0	0.0069	0.6 (0.026-16.39)	0.799
0.339583	0.0138	0	6 (0.24-150.71)	0.271
0.354861	0	0.0138	0.37 (0.01-7.85)	0.525
0.375694	0.0416	0.0069	10.6 (1.22- 93.14)	0.032
0.378472	0.0138	0	6 (0.24-150.71)	0.271
0.417361	0	0.0069	0.65 (.026-16.39)	0.799
0.459028	0.0277	0.0555	0.48 (0.10- 2.34)	0.369
0.459722	0.0138	0.0208	0.66 (0.067-6.47)	0.723
0.461806	0	0.0069	0.65 (0.026-16.39)	0.799
0.463194	0	0.0069	0.37 (0.01-7.85)	0.525
0.469444	0	0.0138	0.37 (0.01-7.85)	0.525
0.473611	0.0138	0	6 (0.24-150.71)	0.271
0.475694	0	0.0069	0.65 (0.026-16.39)	0.799
0.542361	0.0277	0.0208	1.34 (0.21- 8.22)	0.749
0.54375	0.0138	0	6 (0.24-150.71)	0.271
0.545139	0	0.0625	0.09 (0.005-1.71)	0.111
0.546528	0.0138	0	6 (0.24-150.71)	0.271
0.549306	0.0138	0	6 (0.24-150.71)	0.271
0.550694	0.0138	0	6 (0.24-150.71)	0.271
0.551389	0.0138	0	6 (0.24-150.71)	0.271
0.590278	0.0138	0	6 (0.24-150.71)	0.271

°Odds Ratio (OR), 95% Confidence Interval (CI) , °° p< 0.05

Table 5a. HLA DRB1 frequencies in dermatomyositis groups and controls				
HLA DRB1* allele	**PATIENTS n = 36**	**CONTROLS n=72**	**OR (CI) °**	**p °°**
0.584028	0.0277	0	10.24 (0.48-216.33)	0.134
0.584722	0.0138	0.0486	0.27 (0.033 -2.28)	0.232
0.586111	0	0.0277	0.21 (0.011-4.05)	0.305
0.590278	0	0.0277	0.21 (0.011-4.05)	0.305
0.59375	0.0138	0	6 (0.24-150.71)	0.271
0.599306	0.0138	0	6 (0.24-150.71)	0.271
0.602083	0	0.0069	0.65 (0.026-16.39)	0.799
0.615278	0	0.0069	0.65 (0.026-16.39)	0.799
0.625694	0.0277	0.0208	1.34 (0.21-8.22)	0.749
0.667361	0.0138	0.104	0.082 (0.018-0.36)	0.011
0.668056	0	0.0069	0.65 (0.026-16.39)	0.799
°Odds Ratio (OR), 95% Confidence Interval (CI) , °° p< 0.05				

HLA-A*03:01, this was described in populations from five continents [34].

HLA-DRB1*01:02 allele was not reported in the healthy Mexican mestizo population [28].

According to our results, these alleles were identified as probable genetic risk factors for the occurrence of DM in conjunction with HLA-A*03:01. In the control group, HLA-DQB1*03:02 and HLA-DRB1*16:01 were identified as protective alleles for developing DM. HLA-DQB*1 03:02 was reported in the Mexican mestizo population with a frequency of 0.485, whereas HLA-DRB1*16:01 was not identified [19].

Previous studies in the Mexican mestizo population did not find HLA alleles as a risk factor for IIM, but only identified the presence of anti-Mi-2 antibodies associated with HLA-DRB1*04 and HLA DQA1*03 [35] Alleles found in this study associated with the presence of DM were different from those reported in Caucasian, Chinese and Afro-American populations [15-17,19].

Results of this study indicate that haplotype A*02:01~B*35:01~DRB1*08:01~DQB1*04:01 in dermatomyositis groups present the highest prevalence not only shows that the haplotype that occurs with high frequency in the mestizo population Table 6. This is not included in the haplotypes reported by Williams and Gorodezky in an open Mexican mestizo population [29,31].

We consider that this study of DM, independent of other types of IIM, contributes to determining the genotypes associated with this disease. This is the first report of a genetic association with DM in a Mexican mestizo population with a limited number of patients. These data will be valid in future studies to determine if DM is genetically different from other IIM, as reported in other populations [17-19].

Conclusion

In our study, HLA-A*01:01, HLA-A*03:01, HLA-B*07:02, HLA-DRB1*01:02 and HLA-DRB1*09:01 were significantly associated with the presence of DM, DRB1*16:01 and DQB1* 03:02 as alleles protective of disease in Mexican mestizo population and to have greater validity the results obtained necessary to expand the sample number of cases–controls.

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Conflict of Interest

NA, not conflict of interest

Ethical Approval

The research protocol was approved by Ethics committee in research of the Hospital Juárez de México with a registration number 1758/09.09.08.

Clinical trial registration

All the participants signed an informed consent that includes the management of genetic material.

Table 6. Haplotypes frequencies in dermatomyositis groups

NO.	HAPLO TIPO HLA CLASE I Y II	HF° n = 36
1	A*01:01~ B*07:02 ~DRB1*04:01~ DQB1*03:01	0.013889
2	A*02:11~ B*39:09~ DRB1*14:23~DQB1*02:15	0.013889
3	A*01:01~ B*40:21~ DRB1*04:01~ DQB1*04:14	0.013889
4	A*02:01~ B*15:16~ DRB1*08:09~ DQB1*03:01	0.013889
5	A*03:01 ~B*15:101~ DRB1*01:01~ DQB1*03:01	0.013889
6	A*26:01 ~B*07:02~ DRB1*14:01~ DQB1*04:01	0.013889
7	A*23:01~ B*35:01 ~DRB1*04:01~ DQB1*03:07	0.013889
8	A*24:02 ~B*15: ~02 DRB1*09:01~ DQB1*03:07	0.013889
9	A*03:01~ B*18:01~ DRB1*04:05~ DQB1*05:01	0.013889
10	A*29:01~ B*27:04 ~DRB1*14:15 ~DQB1*02:01	0.013889
11	A*02:01 ~B*35:01~ DRB1*08:01 ~DQB1*04:01	0.013889
12	A*02:03 ~B*15:02 ~DRB1*04:01~ DQB1*04:01	0.013889
13	A*01:01 ~B*08:02~ DRB1*01:01~ DQB1*05:43	0.013889
14	A*68:01 ~B*44:166~ DRB1*13:01~ DQB1*06:01	0.013889
15	A*01:01 ~B*39:09 ~DRB1*01:11 ~DQB1*03:01	0.013889
16	A*32:01~ B*15:16~ DRB1*13:104~ DQB1*04:01	0.013889
17	A*03:01~ B*15:01 ~DRB1*03:01~ DQB1*02:01	0.013889
18	A*74:06~ B*07:02~ DRB1*13:07~ DQB1*03:01	0.013889
19	A*03:01~ B*50:01~ DRB1*04:0~1 DQB1*03:01	0.013889
20	A*68:01~ B*35:03~ DRB1*14:01 ~DQB1*03:01	0.013889
21	A*32:01~ B*44:02 ~DRB1*11:01 ~DQB1*06:01	0.013889
22	A*68:01~ B*07:02~ DRB1*07:01~ DQB1*05:01	0.013889
23	A*02:01~ B*18:01~ DRB1*01:01 ~DQB1*02:16	0.013889
24	A*03:01~ B*08:01~ DRB1*16:01~ DQB1*04:02	0.013889
25	A*68:01~ B*14:02~ DRB1*01:11~ DQB1*03:01	0.013889
26	A*03:01~ B*35:05~ DRB1*13:14~ DQB1*04:01	0.013889
27	A*02:01~ B*15:01~ DRB1*11:22~ DQB1*02:01	0.013889
28	A*68:01~ B*40:02~DRB1*01:08~ DQB1*02:01	0.013889
29	A*03:01~ B*35:01~ DRB1*13:13~ DQB1*05:51	0.013889
30	A*11:01 ~B*15:17~ DRB1*13:70~ DQB1*03:11	0.013889
31	A*31:01 ~B*07:02 ~DRB1*01:21~ DQB1*05:29	0.013889
32	A*32:01~ B*50:01 ~DRB1*09:05 ~DQB1*06:56	0.013889
33	A*02:01 ~B*40:02 ~DRB1*04:01~ DQB1*03:14	0.013889
34	A*31:03~ B*15:17~ DRB1*14:02~ DQB1*03:02	0.013889
35	A*74:01~ B*35:05~ DRB1*11:02~ DQB1*05:01	0.013889
36	A*80:01~ B*35:05~ DRB1*13:03~ DQB1*06:01	0.013889
37	A*03:01~ B*08:01~ DRB1*13:01~ DQB1*02:01	0.013889
38	A*31:01~ B*15:48 ~DRB1*03:01 ~DQB1*06:01	0.013889
39	A*01:07 ~B*18:01~ DRB1*13:11 ~DQB1*03:01	0.013889
40	A*02:01 ~B*53:01~ DRB1*08:01~ DQB1*04:01	0.013889

HF°= Haplotypes frequencies

Table 6a. Haplotypes frequencies in dermatomyositis groups		
NO.	**HAPLO TIPO HLA CLASE I Y II**	**HF° n = 36**
41	A*01:01~ B*15:10~ DRB1*07:16~ DQB1*02:01	0.013889
42	A*03:01~ B*45:0~1 DRB1*03:01~ DQB1*06:01	0.013889
43	A*03:01~ B*07:02~ DRB1*04:01 ~DQB1*02:05	0.013889
44	A*01:01 ~B*14:01~ DRB1*15:01~ DQB1*06:124	0.013889
45	A*02:01~ B*35:01~ DRB1*04:28 ~DQB1*02:01	0.013889
46	A*01:01~ B*07:02 ~DRB1*01:02~ DQB1*05:01	0.013889
47	A*26:03~ B*07:02 ~DRB1*01:02~ DQB1*05:01	0.013889
48	A*01:07 ~B*35:01~ DRB1*01:02~ DQB1*02:31	0.013889
49	A*03:02 ~B*27:01~ DRB1*07:0~1 DQB1*03:03	0.013889
50	A*01:01~ B*07:19 ~DRB1*01:01~ DQB1*04:05	0.013889
51	A*02:01 ~B*35:01~ DRB1*07:01~ DQB1*04:01	0.013889
52	A*03:01 ~B*07:02~ DRB1*15:01~ DQB1*06:69	0.013889
53	A*02:01~ B*44:166~ DRB1*04:01 ~DQB1*04:01	0.013889
54	A*11:01~ B*07:02~ DRB1*01:01 ~DQB1*05:01	0.013889
55	A*29:01 ~B*07:02 ~DRB1*11:01 ~DQB1*02:03	0.013889
56	A*11:01~ B*44:02 DRB1*04:01 DQB1*03:02	0.013889
57	A*03:02 ~B*44:16~ DRB1*01:01~ DQB1*04:01	0.013889
58	A*02:01~ B*07:02~ DRB1*07:01~ DQB1*03:03	0.013889
59	A*03:02 ~B*07:02 ~DRB1*04:01~ DQB1*04:01	0.013889
60	A*01:07~ B*35:01~ DRB1*03:0~1 DQB1*03:01	0.013889
61	A*03:01~ B*35:01~ DRB1*04:01 ~DQB1*04:01	0.013889
62	A*03:01~ B*07:02 ~DRB1*07:11~ DQB1*03:10	0.013889
63	A*02:01~ B*07:36 ~DRB1*01:02~ DQB1*04:01	0.013889
64	A*03:02~ B*50:01~ DRB1*01:02~ DQB1*05:01	0.013889
65	A*01:01~ B*13:01~ DRB1*01:01~ DQB1*05:01	0.013889
66	A*23:01 ~B*39:01~ DRB1*04:28~ DRB1*09:01	0.013889
67	A*02:01~ B*35:01~ DRB1*07:01 ~DQB1*02:31	0.013889
68	A*01:01~ B*07:02~ DRB1*03:01 ~DQB1*06:01	0.013889
69	A*02:01~ B*07:02 ~DRB1*01:01~ DQB1*04:01	0.013889
70	A*24:02~ B*35:01 ~DRB1*09:01~ DQB1*06:02	0.013889
71	A*03:01~ B*07:02~ DRB1*08:01~ DQB1*04:01	0.013889
72	A*26:03 ~B*14:02 ~DRB1*15:01 ~DQB1*06:02	0.013889
HF°= Haplotypes frequencies		

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