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Association of HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302 and DQB1*0303 Alleles with population Uygur patients of vitiligo

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Abstract

Vitiligo is associated with different human leukocyte antigens (HLAs), but the relationship of HLAs and Uygur population people is unknown. The study aimed to investigate whether there is an association between HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, and DQB1*0303 and the incidence of vitiligo in a Chinese Uygur population and further evaluate their effect on the clinical features of vitiligo. A total of 308 Chinese Uygur patients with vitiligo and 310 healthy controls were included in the study. HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302 and DQB1*0303 allele distribution was investigated by polymerase chain reaction (PCR), the sequence-specific primer method. Family history, clinical types, phase, etc. were evaluated. The data were analyzed by the chi-square test. A significant difference was found in the distribution of HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, and DQB1*0303 between the vitiligo patients and healthy subjects in the studied population. A comparison of the clinical features of DRB1*1201/02 (+) and DRB1*1201/02 (-) patients revealed a significant difference between localized and generalized vitiligo patients, (OR: 0.55, 95% CI: 0.31–0.99, P = 0.044). The progressive phase of vitiligo was more common for DRB1*1201-positive patients than for HLA-DRB1*1201/02-negative patients (OR: 3.18, 95% CI: 1.48–6.82, P = 0.002). The other clinical features were similar in both groups. In conclusion, our findings suggest that HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, and DQB1*0303 are associated with vitiligo susceptibility, and DRB1*1202/02-positive patients have some obvious clinical differences from DRB1*1202/02-negative patients in the Chinese Uygur population.

Keywords: Chinese Uygur population; HLA-DQA1*0302; HLA-DQB1*0303; HLA-DRB1*0701/02; HLA-DRB1*1201/02; Vitiligo

Introduction

Vitiligo, which is one of the most common pigmentation disorders, is a multifactorial, depigmenting disorder of the skin characterized by a loss of functional melanocytes, resulting in the appearance of milky-white patches on the skin [1]. Multiple HLA-II alleles have been found to be associated with vitiligo in different populations [2-6]. The previous findings highlight both the similarity and differences of vitiligo major histocompatibility complex (MHC) genetic associations in different races and nationalities[7]. According to the study of Shen et al.[8], HLA alleles and haplotypes are different in the Chinese Uygur and Han ethnic group. HLA-DQA1*0302, DQB1*0303, DRB1*1201/02, and DRB1*0701/02 allele distribution is shown to be associated with the pathogenesis of vitiligo in other population. Nevertheless, there are neither further detailed clinical data nor genetic mutation information concerning the ethnic Uygur vitiligo patients. Whether there is a relation between vitiligo and HLA-DQA1*0302, DQB1*0303, DRB1*1201/02, and DRB1*0701/02 is unknown. Therefore, it's essential to investigate the association between HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, DQB1*0303 and vitiligo of Uygur population. This study aimed to investigate whether there is an association between HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, DQB1*0303 and vitiligo incidence in a Chinese Uygur population, and to explore the role of HLA alleles in clinical character of vitiligo.

Materials and methods

Study population

We performed HLA alleles analysis in 308 Uygur patients with vitiligo compared with 310 healthy controls. In the cases, males / females was 148/160, and the age range was 0–68, with an average age of 24.42 ± 14.09. In the controls, the males/females ratio was 134/176, the age ranged from 4 to 78, and the average age was 33.35 ± 15.74 (Table 2). All the patients were recruited consecutively from May 2007 to Dec 2008 from the outpatient and inpatient clinics at the Department of Dermatology, People's Hospital of Xin Jiang Uygur Autonomous Region, Urumqi, China. The diagnosis of vitiligo was made by two independent dermatologists according to the method Alain Taieb and Mauro Picardo Stand (2010). Patients with a suspected presence of other possible causes of hypopigmentation, for example, that resulting from diseases, such as tinea versicolor, anemia nevus, mottled disease, albinism, pityriasis alba, senile white spots, etc., were not included in the study. Patient information was collected through face-to-face interviews conducted by dermatologists using standard instruments. Clinically, the cases were classified as stable or progressive disease. We defined *stable vitiligo* as the condition that has not progressed for at least three months. *Progressive disease* was defined as development of new lesions or extension of old lesions within three months before examination [9]. The information contained also patient demographics, age of onset, current age, and gender. Family histories were also collected. Clinical subtypes of vitiligo in this study were subclassified as vitiligo, including vitiligo vulgaris (scattered macules), acrofacial vitiligo (distal parts of the extremities and face), and vitiligo universalis (complete or nearly complete depigmentation over the body). Localized vitiligo included

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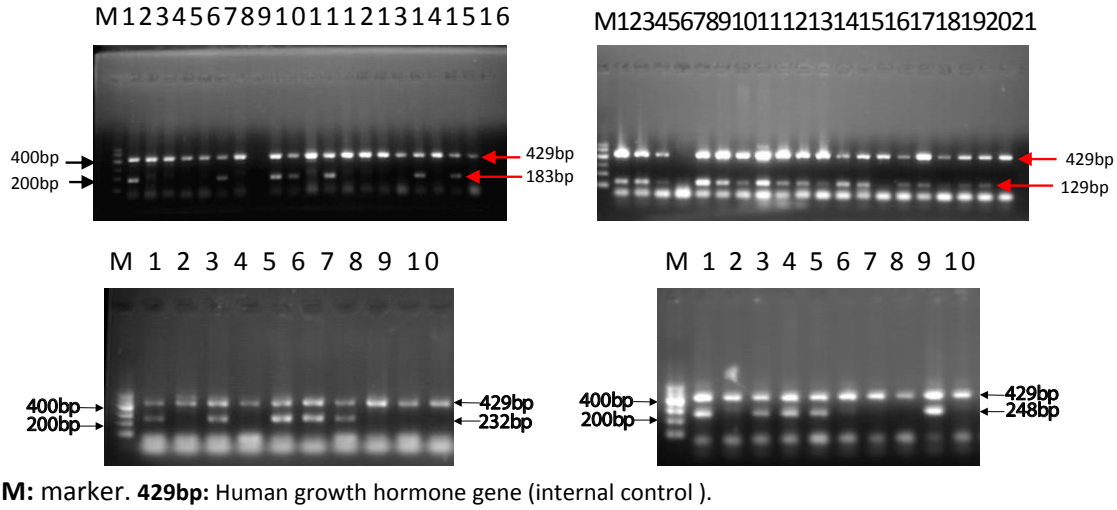
Allele	Forward Primer	Reverse Primer
HLA-DQAI*0302	5'-TTCACTCGTCAGCTGACCAC-3	5'-CAAATTGCGGGTCAAATCTTCT-3' (183bp)
HLA-DQBI*0303	5'-GACGGAGCGCGTGCGTCT-3'	5 '- CTGTTCCAGTACTCGGCGT -3 ' (129 bp)
HLA-DRB1*0701/02	5'-CCTGTGGCAGGGTAAGTATA-3'	5'-CCCGTAGTTGTGTCTGCACAC-3' (232bp)
HLA-DRB1*1201/02	5'-AGTACTCTACGGGTGAGTGTT-3'	5'-CTCTGTGAAGCTCTCCACAG-3' (248bp)
Human growth hormone gene (internal control)	5'-GCCTTCCCAACCATTCCCTTA-3	5'-TCACGGATTTCTGTTGTGTTTC-3' (429 bp)
The amplifying primers of HLA—DQAI*0302, DQBI*0303, DRB1*0701/02 and DRB1*1201/02 were described by Olerup et al.		

Table 1: Amplifying primers sequences [1].

Variables	Cases (n = 308)	Controls (n = 310)
Males/females	148/160	134/176
Mean age(range)	24.42 ± 14.09 (0–68)	33.35 ± 15.74 (4–78)
Family history	--	--
With family history	39 (12.66%)	0
Without family history	269 (87.34%)	310
Clinical types	--	--
Localized vitiligo	100 (32.47%)	--
Generalized vitiligo	208 (67.5%)	--
Segmental vitiligo	33 (10.71%)	--
Focal vitiligo	33 (10.71%)	--
Vitiligo vulgaris	51 (16.56%)	--
Universal vitiligo	10 (3.25%)	--
Acrofacial vitiligo	16 (19.75%)	--
Stable phase	123 (39.93%)	--
Progressive phase	185 (60.07%)	--

Table 2: Proband characteristics.



M: marker. **429bp:** Human growth hormone gene (internal control).

Figure 1: The electrophoresis results of HLA-DQA1*0302, DQB1*0303, DRB1*0701/02 and DRB1*1201/02. (A) 183bp:HLA-DQA1*0302 (positive: 1,6,8,10,11; negative: 2-5,7,9,12-15). The sixteenth channel represent blank control. (B): 129bp: HLA-DQB1*0303 (positive: 1-3,5-13,15-19; negative: 14,20). The twenty-first channel represents blank control. The fourth channel represents amplification failure. (C): 232bp: HLA-DRB1*0701/02 (positive: 1, 3, 5, 6,7; negative: 2,4,8-10). (D): 248bp: HLA-DRB1*1201/02 (positive: 1,3-5,9; negative: 2,6-8,10).

segmental (limited depigmentation spreading within the segment over a period of 6–24 months and then stopping) and focal types (one or more macules in one area). The age of onset less than 20 years or younger were categorized as having early-onset vitiligo, whereas those whose onset started when they were older than 20 were classified as having late-onset vitiligo [10]. A total of 310 controls were clinically assessed to be without vitiligo, other autoimmune disorders, systemic disorders or family history of vitiligo (including first-, second-, and third-degree relatives), and from local unrelated subjects presenting for health examination. All the participants provided written informed consent. This study was approved by the Medical Ethics Committee of the People's Hospital of Xin Jiang Uygur Autonomous Region, Urumqi, China.

Genotyping

HLA alleles detection were peformed by polymerase chain reaction, sequence-specific primer method (PCR-SSP)[11]. The amplifying-primer sequences of HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, DQB1*0303, and human growth hormone gene (internal control) are shown in Table 1. Control primers were included in all

Variables	Positive (%)	Negative (%)	*P*-value	OR (95% CI)
HLA-DRB1*1201/02 genotyping				
Case	81 (26.30%)	227 (73.70%)	<0.001	2.56 (1.67–3.90)
Control	38 (12.26%)	272 (87.74%)		
HLA-DRB1*0701/02				
Case	139 (45.13%)	169 (54.87%)	<0.001	2.21 (1.58–3.10)
Control	84 (27.10%)	226 (72.90%)		
HLA-DQA1*0302				
Case	119 (38.64%)	189 (61.36%)	0.002	1.72 (1.23–2.42)
Control	83 (26.77%)	227 (73.23%)		
HLA-DQB1*0303				
Case	181(58.77%)	127(41.23%)	<0.001	4.10 (2.91–5.76)
Control	80 (25.81%)	230 (74.19%)		

Chi-squared test for categorical variables.

HLA: Human Leucocyte Antigen; OR: Odds Ratio; CI: Confidence Interval

Table 3: Distribution of HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, and DQB1*0303.

Clinical characteristics	HLA-DRB1*1201/02genotyping		P-value	OR(95% CI)
	Positive (n = 81)	Negative (n = 227)		
Onset				
Median age of onset (±Q)	19.75 (±12.60)	21.41 (±13.77)	0.528	1.18 (0.70-1.99)
Early-onset	50 (61.73%)	131 (57.71%)		
Late-onset	31 (38.27%)	96 (42.29%)		
Family history				
With family history	8 (9.88%)	31 (13.66%)	0.707	0.88 (0.43-1.76)
Without family history	73 (90.12%)	19 6 (86.34%)		
Clinical types				
Localizised vitiligo	19 (23.46%)	81 (35.68%)	--	--
Generalizised vitiligo	62 (76.54%)	146 (64.32%)	--	--
Segmental vitiligo	7 (8.64%)	26 (11.45%)	0.044	0.55(0.31-0.99)
Focal vitiligo	12 (14.82%)	55 (24.23%)	--	--
Vitiligo vulgaris	44 (54.32%)	96 (42.29%)	--	--
Universal vitiligo	2 (2.47%)	8 (3.52%)	--	--
Acrofacial vitiligo	16 (19.75%)	42 (18.50%)	0.284	--
Stable phase	20 (24.69%)	124 (54.63%)	--	--
Progressive phase	103 (75.31%)	61 (45.37%)	0.002	3.18 (1.48-6.82)

Chi-squared test for categorical variables; Q means interquartile range;
HLA: Human Leucocyte Antigen; OR: Odds Ratio; CI: Confidence Interval

Table 4: Clinical comparison of clinical features of HLA-DRB1*1201/02-positive and -negative patients.

PCR reactions as a positive control for PCR amplification. Primers were synthesized by Shanghai Sheng Gong Biological Engineering Technology Service Co, Ltd. (Shanghai, China).

HLA-DRB1*1201/02, DRB1*0701/02: The final volume of all PCR reactions was 25 μL. PCR reaction mixtures consisted of 13.1 μL ddH_2O, 2.5 μL 10×PCR buffer, 2.5 μL 2 mmol/L of each dNTP, 1.5 μL 25 mmol/L of $MgCl_2$, 1 μL (20 μmol/L) of each allele-specific primer, 0.5 μL of control primer pairs, 2 μL of template DNA, and 0.4 U of Taq polymerase (5 U/μL). HLA-DQAl*0302: 35 cycles of the reaction were conducted, more specifically: initial denaturation at 94 °C for 5 min; 45 s of denaturation at 94 °C, 45 s of primer annealing at 57.5 °C, and 30 s of primer extension at 72 °C in each cycle, followed by a single round of elongation at 72 °C for 10 min. HLA-DQBl*0303: 35 cycles of the reaction were conducted, more specifically: initial denaturation at 94 °C for 5 min; 45 s of denaturation at 94 °C, 45 s of primer annealing at 59 °C, and 30 s of primer extension at 72 °C in each cycle, followed by a single round of elongation at 72 °C for 10 min. Six microliters of the PCR products were used for electrophoresis with 1.5 percent agarose gel containing 2 μL of 0.5 μg/mL ethidium bromide. The gels were run for 30 min at 150 mV. UV transmission gel imaging was used to scan and analyze the graphs after electrophoresis.

Statistical Analysis

All data analysis was performed using a statistical package (version 15.0, SPSS Inc., Chicago, IL, USA). Continuous data, such as age, are described using means ± standard deviations or median (range) for normally distributed data. We compared categorical data and proportions by the chi-squared test. All statistical analyses were two-sided, and significance was assigned at $P < 0.05$. Odds ratios (ORs) and 95% confidence intervals (95% CI) were also assessed.

Results

Electrophoresis

The electrophoresis results were presented in Figures 1 and 2.

Proband distribution of alleles

As shown in Table 3, the frequency of HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, and DQB1*0303 alleles in vitiligo patients was significantly higher than that in the healthy controls (HLA-DRB1*1201/02: OR = 2.56, 95% CI: 1.67–3.90, $P < 0.001$; HLA-DQB1*0707/02: OR = 2.21, 95% CI: 1.58–3.10, $P < 0.001$;

HLA-DQA1*0302: OR = 1.72, 95% CI: 1.23–2.42, P = 0.002; HLA-DQB1*0303: OR = 4.10, 95% CI: 2.91–5.76, P < 0.001).

The phase of the disease

The progressive phase of vitiligo was more common in DRB1*1201–positive patients than in HLA-DRB1*1201/02-negative patients. As shown in Table 4, 75.31% of the patients in the HLA- DRB1*1201/02-positive group were in the progressive phase, compared with 45.37% of patients in the HLA- DRB1*1201/02 –negative group (P = 0.002, OR =3.18, 95% CI: 1.48-–6.82). The frequency of vitiligo in the progressive phase was also higher in the DQB1*0303-positive patients than in negative patients (62.98% vs. 44.09%, P = 0.212, OR = 0.75, 95% CI: 0.47–1.18); however, the difference did not reach a significant level (Table 5).

Clinical types

Age of the patients at the onset of vitiligo

As presented in (Tables 4,7) HLA-DRB1*1201/02, DQA1*0302-positive patients manifested an earlier disease onset than did the negative patients, with a median age of onset of 19.75 ± 12.60 years vs. 21.41 ± 13.77 years for HLA-DRB1*1201/02-positive and -negative patients, and 21.06 ± 13.00 years vs. 21.54 ± 13.77 years for DQA1*0302, respectively. However, there was no significant genotypic difference in HLA-DRB1*1201/02 or DQA1*0302 between early-onset and late-onset patients.

The family history

The HLA-DRB1*1201, DQA1*0302, DQB1*0303-positive groups showed decreasing frequency of family history compared to the

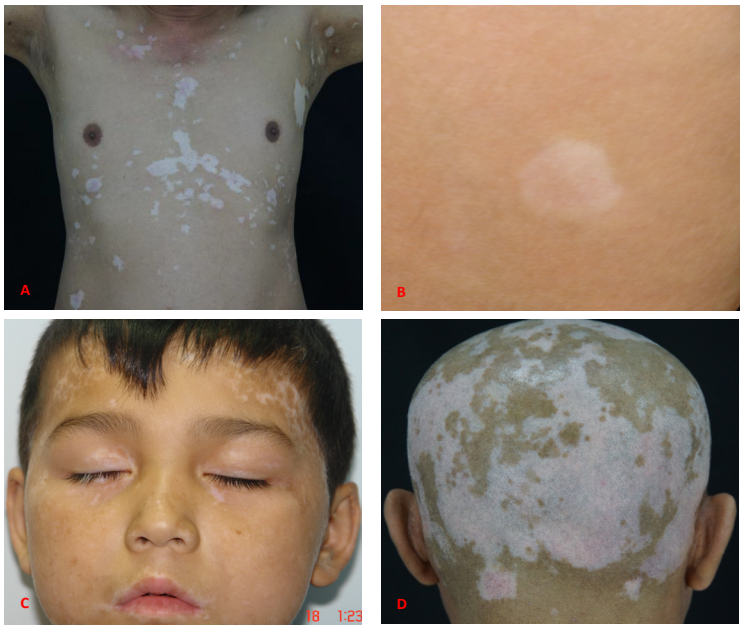


Figure 2: Different phases or types of vitiligo. A: Progressive phase, generalized vitiligo. B: Stable phase, localized vitiligo. C: Acrofacial vitiligo. The eyelashes present white. D: Acrofacial vitiligo. Some hair becomes white.

Clinical characteristics	HLA-DRB1*0303 Genotyping		P-value	OR(95% CI)
	Positive (n = 181)	Negative (n = 127)		
Onset				
Median age of onset (±Q)	21.44 (±13.35)	20.30 (±13.67)	0.134	0.70 (0.44–1.12)
Early-onset	100	81		
Late-onset	81	46		
Family history				
With family history	22 (12.16%)	17 (13.39%)	0.707	0.88 (0.43-1.76)
Without family history	159 (87.85%)	110 (86.61%)		
Clinical types				
Localized vitiligo	52 (28.73%)	44 (34.65%)	--	--
Generalizedvitiligo	129 (71.27%)	79 (62.21%)	0.195	0.72 (0.44-1.18)
Segmental vitiligo	19 (10.50%)	14 (11.02%)	--	--
Focal vitiligo	33 (18.23%)	34 (26.77%)	--	--
Vitiligo vulgaris	81 (44.75%)	59 (46.46%)	--	--
Universal vitiligo	9 (4.97%)	1 (0.79%)	--	--
Acrofacial vitiligo	39 (21.54%)	19 (14.96%)	0.081	--
Stable phase	67 (37.02%)	71 (55.91%)	--	--
Progressive phase	114 (62.98%)	56 (44.09%)	0.212	0.75 (0.47-1.18)

Table 5: Clinical comparison of clinical features of HLA-DQB1*0303-positive and -negative patients.

Clinical characteristics	HLA-DRB1*07/01 genotyping		P-value	OR (95% CI)
	Positive (n = 139)	Negative (n =169)		
Onset				
Median age of onset (±Q)	20.97 (±13.18)	20.96 (±13.75)	0.942	1.02 (0.65–1.61)
Early-onset	82 (58.99%)	99 (58.59%)		
Late-onset	57 (41.01%)	70 (41.42%)		
Family history				
With family history	20 (14.39%)	19 (11.24%)	0.707	0.88 (0.43-1.76)
Without family history	119 (85.61%)	15 0(88.76%)		
Clinical types				
Localized vitiligo	40 (28.78%)	60 (35.50%)	--	--
Generalized vitiligo	99 (71.22%)	109 (64.50%)	1.210	0.73 (0.45-1.19)
Segmental vitiligo	12 (8.63%)	21 (12.43%)	--	--
Focal vitiligo	28 (20.14%)	39 (23.08%)	--	--
Vitiligo vulgaris	67 (48.20%)	73 (43.20%)	--	--
Universal vitiligo	8 (5.76%)	2 (1.18%)	--	--
Acrofacial vitiligo	24 (17.27%)	34 (20.12%)	--	--
Stable phase	61 (43.89%)	62 (36.69%)	--	--
Progressive phase	78 (56.12%)	107 (63.31%)	0.199	1.35 (0.85-2.13)
Chi-squared test for categorical variables; Q means interquartile range.				
HLA: Human Leucocyte Antigen; OR: Odds Ratio; CI: Confidence Interval				

Table 6: Clinical comparison of clinical features of HLA-DRB1*0701/02-positive and -negative patients.

Clinical characteristics	HLA-DQA1*0302 genotyping		P-value	OR(95% CI)
	Positive (n = 119)	Negative (n = 189)		
Onset				
Median age of onset(±Q)	20.06 (±13.00)	21.54 (±13.77)	0.333	1.26 (0.79–2.01)
Early-onset	74 (62.19%)	107 (56.61%)		
Late-onset	45 (37.82%)	82 (43.39%)		
Family history				
With family history	14 (1.77%)	25 (13.23%)	0.707	0.88 (0.45–1.76)
Without family history	105 (88.24%)	164 (86.77%)		
Clinical types				
Localized vitiligo	34 (28.57%)	66 (34.92%)	--	--
Generalized vitiligo	85 (71.43%))	123 (65.08%)	0.247	1.34 (0.82–2.21)
Segmental vitiligo	13 (10.92%)	20 (10.58%)	--	--
Focal vitiligo	21 (17.65%)	46 (24.34%)	--	--
Vitiligo vulgaris	56 (47.06%)	84 (44.44%)	--	--
Universal vitiligo	2 (1.68%)	8 (4.23%)	--	--
Acrofacial vitiligo	27 (22.68%)	31 (16.40%)	0.329	--
Stable phase	73 (61.35%)	112 (59.26%)	--	--
Progressive phase	46 (38.66%)	77 (40.74%)	0.716	0.92 (0.59–1.44)
Chi-squared test for categorical variables; Q means interquartile range; HLA: Human Leucocyte Antigen; OR: Odds Ratio; CI: Confidence Interval				

Table 7: Clinical comparison of clinical features of HLA-DQA1*0302-positive and -negative patients.

negative group (HLA-DRB1*1201:9.88% vs. 13.66%, P = 0.707, OR = 0.88, 95% CI: 0.43–1.76; HLA-DQA1*0302:1.77% vs. 13.23%, P = 0.707, OR = 0.88, 95% CI: 0.45–1.76; HLA-DQB1*0303:12.16% vs. 13.39%, P = 0.707, OR = 0.88, 95% CI: 0.43–1.76) (Tables 4, 5,7). The HLA-DRB1*0701/02-positive group displayed an increasing frequency of family history compared to the negative group (14.39% vs. 11.24%, P = 0.707, OR = 0.88, 95% CI: 0.43–1.76) (Table 6). However, the difference did not reach a significant level.

Discussion

Different human leukocyte antigens (HLAs) are associated with the incidence of vitiligo in different ethnic groups, and obvious clinical differences in generalized vitiligo have been related to genotypic variation. In our study, the frequency of the HLA-DQA1*0302, DQB1*0303, DRB1*1201/02, and HLA-DRB1*0701/02 alleles in vitiligo patients was significantly higher than that in unaffected individuals, which suggests that HLA-DQA1*0302, DQB1*0303, DRB1*1201/02, and HLA-DRB1*0701/02 are also associated with vitiligo susceptibility in the Chinese Uygur population. Interestingly, we also found that the progressive phase of vitiligo was more common in DRB1*1201-positive patients than in HLA-DRB1*1201/02-negative patients.

The treatment of vitiligo is difficult and usually requires a longer time. The extent of the lesions and the subtype should be considered during the treatment period. The patients of stable and non segmental vitiligo have better response to surgery and drug therapy, whereas the treatment of the patients with active stage, non segmental vitiligo

and generalized vitiligo are not satisfactory. Moreover, such patients always live in fear of further progression of the disease. To prevent the progression of the disease, systemic steroids and photo-therapy are considered the treatment of choice [12]. However, studies on the role of systemic steroids are currently performed only in open-label and high doses of steroids can cause serious adverse effects [13]. The progression of nonsegmental vitiligo is impossible to predict. Generally speaking, the disease begins with focal patches of leukoderma over the hands and feet. Subsequently, it may either stabilize, leading to a less advanced disease, or spread explosively or increasingly evolved into generalized vitiligo. Liu *et al.* estimated that in 75% of the patients, the disease starts as localized vitiligo, and almost half of these open the door to generalized vitiligo [14].

Hence, Kanwar *et al.*[13] supposed that earlier and active treatment may stablize the development of the disease and prevent the total cutaneous involvement. They also found that low-dose, oral mini-pulse dexamethasone therapy is a good choice for controlling the development, unstable vitiligo with fewest adverse effects. Thus, HLA-DRB1*1202/02 might be used as a reference when choosing a treatment for vitiligo to achieve the best therapeutic effect.

Xia et al. [15] found that extended haplotypes were interrelated with all types of vitiligo in Chinese Hans, whereas there has been a marked increase in the frequency of HLA-A25-Cw*0602-DQA1*0302 in universal vitiligo, but not in focal vitiligo. Furthermore, these findingds borne out the presupposition that gene polymorphism is relate to the occurence of different types of vitiligo, the risk has increased markedly among patients with a family history of generalized vitiligo. Fain et al. [16] reported that HLA class II haplotype DRB1*04-DQB1*0301 contributes to the risk of familial generalized vitiligo.The subgroup analysis of Liu et al.[17] also found a significant correlation between the genotypic variation of rs9468925 and the clinical types of generalized vitiligo (Pgenotype = 0.03, Pcombined = 0.005), including focal vitiligo (32.02%), vitiligo vulgaris (57.02%), universal vitiligo (4.37%), and acrofacial vitiligo (6.59%). A study from North India found that the alleles associated with different manifestations of vitiligo were HLA-A*02:01, B*37:01, B*57:01, DRB1*04:03, and DRB1*10:01, which were significantly increased, and A*31:01, B*58:01, C*04:01, DRB1*01:01, DRB1*11:01, and DRB1*15:02, which were dramatically decreased in generalized vitiligo cases but not in localized ones [18]. Interestingly enough, it also revealed that besides the differences in the frequencies of other alleles, both generalized and localized vitiligo had the same predisposing MHC alleles, that is, B*44:03 and DRB1*07:01, in both populations studied, suggesting that localized vitiligo may also be an autoimmune disorder. In our study, we established a significant reduction in the frequency distribution of DRB1*1201/02 in both localized and generalized vitiligo patients ($P < 0.05$), which has some consistency with previous studies. This may be explained by the fact that generalized vitiligo is considered an autoimmune disease, whereas the localized form is not [18]. It may be illustrate that generalized vitiligo is regarded as an autoimmune disease). However, there was no significant genotypic variation in DRB1*1201/02 between focal vitiligo (32.02%), vitiligo vulgaris (57.02%), segmental vitiligo, universal vitiligo (4.37%), and acrofacial vitiligo (6.59%), which may be an explanation that the small size of samples collected from different regions.

In a recent study, Hu et al.[7], found a significant association of DRB1*07 allele with early-onset and familial vitiligo, which was partially consistent with the findings of previous studies. They also discovered that the DRB1*07-positive group showed an increased frequency of age of onset, family history, and vitiligo-associated autoimmune diseases compared to the DRB1*07-negative group. In Moroccan patients, it has been found that the difference in HLA haplotype distuibution may be relate to varying family history and anti-TPO profile [19].

In our study, in contrast to the cases of negative patients, HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, and DQB1*0303-positive patients did not have an earlier disease onset. However, there was neither statistically significant genotypic difference between patients with early-onset and late-onset vitiligo nor for positive and negative familial history, which suggests that no different heritability of gene polymorphism exists either between early-onset vitiligo and late-onset generalized vitiligo or for the positive and negative familial form of the disease in the Chinese Uygur population.

Our findings suggest that HLA-DRB1*1201/02, DRB1*0701/02, DQA1*0302, and DQB1*0303 are associated with vitiligo susceptibility, and they have confirmed that DRB1*1202/02-positive patients had obvious differenence of clinical manifestaions from DRB1*1202/02-negative patients in the Chinese Uygur population.

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