

HLA-DR PATTERN OF RHEUMATOID ARTHRITIS IN SAUDI ARABIA

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The association of rheumatoid arthritis (RA) with specific HLA-DR antigens in different populations has been extensively documented.¹ HLA-DR4 has been shown to be associated with RA in many previous studies,²⁻⁴ however, other studies have shown association of RA with DR1 and/or DR10.⁵⁻⁸ We sought to determine the association of HLA-DR antigens with RA among Saudis.

Patients and Methods

Ninety-two RA patients satisfying the revised American Rheumatism Association (ARA) criteria⁹ were recruited and their HLA-DR was obtained, using the Mixed Lymphocyte Reaction technique. Each patient gave a blood sample of 20 mL, which was then dispensed into four black-top citrated vacutainer bottles, with 2.4 mL sodium citrate, each containing 5 cc of whole blood. The four citrated bottles and their contents were properly sealed to avoid leakage, labeled and put into a nylon zip-lock bag. The samples were kept at room temperature, and within a few hours of collection, transported to Omnilabs Ltd. in London, U.K.

The antigen frequencies were calculated by gene counting. HLA-DR was compared to control data on HLA-DR in a Saudi population.¹⁰ Frequency comparisons for different antigens were made by chi-square analysis with Yates' correction or by Fischer's exact test when appropriate, using the Epi Info[®] statistics package.

Results

A total of 92 patients (72 females and 20 males) were studied. Their mean ages were 39.97±12.88 and 41.36±12.79 years, respectively. The distribution of HLA-DR antigens in our patient population is shown in Table 1. It shows that the most prevalent HLA antigen was HLA-DR3, constituting 33.7%. This was further specified to be HLA-DR17 in 13 patients (14.13%) and HLA-DR18 in 1 patient (1.08%). HLA-DR4 was found in 25 (27.17%), while HLA-DR2 was present in 28 (30.43%). HLA-DR10 appeared in 22 patients (23.91%). When comparison was

TABLE 1. HLA phenotype and subtypes among 92 RA patients.

HLA-DR	Total n (%)	Subtype	No. (%)
1	10 (10.87%)	-	-
2	28 (30.43)	15	23 (25)
		16	5 (5.43)
3	31 (33.7)	N.D.	17 (18.48)
		17	13 (14.13)
		18*	1 (1.08)
4	25 (27.17)	-	-
5	15 (16.3)	11	13 (14.13)
		12	2 (2.17)
6	16 (17.39)	13	14 (15.22)
		14	2 (2.17)
7	22 (23.91)	-	-
8	3 (3.26)	-	-
9	1 (1.08)	-	-
10	22 (23.91)	-	-

*Not done.

TABLE 2. HLA-DR phenotype frequency among 92 RA patients and 189 healthy controls.*

HLA-DR	RA no. (%)	Controls* n (%)	χ^2	Significance (corrected)
1	10 (10.87)	24 (12.69)	0.06	NS
2	28 (30.43)	50 (26.45)	0.31	NS
3	31 (33.69)	57 (30.16)	0.21	NS
4	25 (27.17)	61 (32.27)	0.54	NS
6	16 (17.39)	43 (22.75)	0.77	NS
7	22 (23.91)	59 (31.22)	1.27	NS
8	3 (3.26)	7 (3.7)	0.02	NS
9	1 (1.08)	1 (0.53)	0.05	NS
10	22 (23.91)	17 (8.99)	10.31	P=0.0013
11 (5)	13 (14.13)	21 (11.11)	0.2926	NS
12 (5)	2 (2.17)	7 (3.7)	0.10	NS

*Data: Khan and Sheth.¹⁰

made to the control (Table 2), we observed a significant increase in the frequency of HLA-DR10. There was a decrease in the frequencies of HLA-DR4 and DR7, however, this decrease was not significant.

Discussion

The results of our study showed that the most prevalent HLA antigen in our group was HLA-DR3, followed by DR2 and DR4, then DR7 and DR10. However, when compared to our control group, there was a significant rise in the HLA-DR10. An insignificant increase was noticed in HLA-DR2 and DR3, whereas an insignificant decrease was found in the frequencies of DR7 and DR4 in the RA

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patients. Our results of HLA-DR10 association agree with the reports on the RA patients from Pakistan¹¹ and India.¹²⁻¹³ Hameed et al. reported a statistically significant increase of HLA-DR10 frequency in RA.¹¹ They also reported an insignificant increase in the frequency of HLA-DR2 in their RA population. In their study of Indians of northern origin, Taneja et al. reported a significant rise in the frequency of HLA-DR10.¹² At the same time, they also reported a significant rise in the HLA-DR4, more specifically the allele HLA-DRB1*0405. Similarly, a study from South Africa on RA patients of South Asian origin showed the association of HLA-DR10 among Tamils and Hindis and HLA-DR4 among Muslims.¹³

Our results partly agree with the Kuwaiti study, where a low prevalence of HLA-DR5 and DR7 was indicated.¹⁴ However, the significantly increased HLA-DR3 among Kuwaitis is not in line with our results. The lowered frequencies of HLA-DR4 and DR7 were explained in the light of an experimental study carried out on transgenic mice, which showed that DRB1*1502 confers protection against collagen-induced arthritis in mice.¹⁵ These results were explained on the basis of occurrence of the alleles DRB5*0101 or DRB5*0102. Both alleles carry Asp at position 70 as reported for DRB1 first domain of DRB1*0402, which is known to be protective or negatively associated with RA.¹⁵ The other alleles that are reported to carry amino acid Asp at position 70 included DRB1*0103, DR13, *1403, *0701, 1101/02 and *08. Taneja et al. suggested that the presence of Asp at position 70 in the DRB1 chain of the alleles might be conferring the protection to RA.¹² Our reported results of decrease in HLA-DR4 and DR7 could be explained in the light of the above study.

In conclusion, our study showed an association of RA with HLA-DR10 in our group of patients.

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