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HLA Antigen Distribution in Selected Population Groups from Maharashtra

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ABSTRACT Indian population is well known for its genetic diversity. Among the numerous endogamous communities, which are restricted very much by custom, marriage and occupation we have collected 195 unrelated individuals, belonging to Marathi, Gujarathi, Punjabi, South Indian, Christian and Muslim population groups. We present here the HLA- A, B, and C locus antigen distribution of these population groups compared with each other. The HLA antigens were identified by using the standard complement mediated NIH microlymphocytotoxicity assay. The results revealed that HLA A1, A2, A3, A11, A24, B5, B35, B40, B44, Cw4 and Cw7 were the most frequent alleles while HLA A28, A36, A69, B14, B16, B38, Cw2 and Cw8 were the less frequent alleles represented in all the populations studied. Further, HLAA30, A36, A69, B50 and B55 alleles were observed among the Punjabis, A29 and B62 among the Gujarathi population, High frequencies of HLAB5 and Cw4 among the South Indians as well as rare allelic splits like A23 among the amalgamated Christians were also observed. The study reveals that the population or caste groups in India cannot be considered as a single panmictic population with reference to HLA genetic characteristics, which may have a clinical relevance in unrelated donor selection for allogenic bone marrow transplantation in India.

INTRODUCTION

The population of India has been subjected to successive waves of immigration and invasions from the Middle East, Central Asia and Mongolia, contributing to the present day gene pool (Bhasin et al. 1994). Risely (1969) was the first to study the racial types in Indian population. The population exhibits not only a wide variety of ethnic but also great cultural and linguistic diversity with regard to the linguistic map, the greater India (before 1947 partition) was divided into five major linguistic families viz.: Iranian, Indo-Aryan, Austro-Asiatic, Tibeto-Burman and Dravidian languages (Shankarkumar et al. 1999). Further the social structure is governed by a large number of religious groups. Eighty-two percent of the Indian population is Hindus, while the other minor religions include Christians, Sikhs, Buddhists, Jains and Muslims. The Brahmins are considered the upper caste Hindus in India.

Several workers have conducted numerous studies on the genetics of various populations in India. Literature has been reported on blood groups, red cell enzymes and serum protein polymorphisms (Bhatia and Rao 1986). The HLA complex is the most diverse and polymorphic genetic system with major functional and medical implications. Our initial knowledge of this highly complex system which has developed over the second half of the 20th century allowed us to understand its role in the immune response and thereby, its impact in Transplantation Medicine, Autoimmunity, Infectious Disease, Allergy, Cancer and also unique contributions to Anthropology and Population genetics (Charron 1997). Distribution of HLA antigens in various ethnic groups of the world and India have been reported (Imanishi et al. 1992; Mittal et al. 1982; Pitchappan et al. 1984; Mehra et al. 1986; Chhaya and Shankarkumar 2001; Shankarkumar et al. 1999, 2000, 2001, 2002). In the present study, we investigated the distribution of HLA antigens in selected population groups.

MATERIALS AND METHODS

Blood samples from random 195 healthy unrelated individuals belonging to Maharashtra (n=48), Gujarat (n=45), South India (n=25), Punjab (n=23), Christians (n=32) and Muslims (n=22) referred for HLA tissue typing were studied for HLA -A, -B, and -C locus antigen profiles. Ten to fifteen milliliters of venous blood (in heparin 50 IU/ml) was collected in a sterile tube from each individual. The lymphocytes were isolated by density gradient centrifugation on Histopaque. HLA- A, B, and C locus antigens were identified by NIH two - stage microlymphocytotoxicity

assay (Terasaki and McClelland 1964). A total of 190 antiserum were used for defining 17 specificities for HLA- A locus, 29 for HLA- B locus, 8 and for HLA- C locus antigens. The antisera were commercial (Biotest, Germany; Behring, Germany; Pelfreez, USA) in origin. The typing tray included a minimum of three antisera for each supertypic specificity. The allele frequency (AF%) was calculated as AF = n+/ Nx2; where n+ is total number of individuals having the allele, N is the total number of Individuals studied.

RESULTS

The results on HLA- A, B, and C allele frequencies of the selected population groups are presented in Table 1. The results revealed that HLA A1, A2, A3, A11, A24, B5, B35, B40, B44, Cw4 and Cw7 were the most frequent alleles while HLA A28, A36, A69, B14, B16, B38, Cw2 and Cw8 were the less frequent alleles

Table: 1 HLA allele frequencies (AF%) in selected population groups studied

HLA	*Populations*					
	Maharashtrian N = 48	*Punjabi N = 23*	*Gujarathi N = 45*	*South Indian N = 25*	*Christian N = 32*	*Muslim N = 22*
A1	9.37	8.69	13.33	**16**	1.56	9.09
A2	12.5	6.52	10	6	12.5	**25**
A3	10.41	4.34	5.55	10	3.12	9.09
A11	13.54	10.86	**18.88**	16	4.68	6.81
A23	0	0	0	0	1.56	0
A24	11.45	**17.39**	8.8	10	6.25	4.54
A26	6.25	8.69	8.8	6	**10.93**	2.27
A28	6.25	0	4.44	4	10.93	6.81
A29	1.04	0	3.33	0	3.12	2.27
A30	0	6.52	2.22	0	0	0
A31	6.25	0	1.11	2	12.5	6.81
A32	1.04	0	4.44	0	0	4.54
A33	3.12	4.34	0	12	0	2.27
A36	0	4.34	0	0	0	0
A69	0	6.52	0	0	0	0
B5	15.62	6.52	16.66	**20**	4.68	18.18
B7	7.29	0	5.55	10	**14.06**	4.54
B8	5.2	4.34	7.77	4	3.12	6.81
B13	6.25	0	4.44	0	0	2.27
B14	0	0	1.11	0	0	0
B15	2.08	0	1.11	**10**	3.12	11.36
B16	2.08	0	0	0	0	0
B17	8.33	13.04	6.66	6	**18.75**	4.54
B18	1.04	2.17	3.33	0	1.56	0
B21	0	0	0	0	3.12	2.27
B22	3.12	4.34	0	0	1.56	2.27
B27	0	0	4.44	0	0	4.54
B35	10.41	15.21	13.33	14	18.75	11.36
B37	4.16	**10.86**	5.55	4	0	6.81
B38	0	0	1.11	0	1.56	2.27
B40	8.33	10.86	**15.55**	6	3.12	0
B44	4.16	8.69	2.22	6	**10.93**	6.81
B49	1.04	0	0	0	0	2.27
B50	2.08	**8.69**	2.22	0	0	0
B55	3.12	4.34	0	0	0	2.27
B62	2.08	0	1.11	8	0	11.36
Cw1	3.12	0	**3.3**	0	1.56	0
Cw2	0	0	1.11	0	0	0
Cw3	5.2	4.34	2.22	0	7.81	6.81
Cw4	15.62	17.39	17.77	**20**	15.62	9.09
Cw6	12.5	6.52	11.11	12	0	**13.63**
Cw7	11.45	2.17	10	12	**18.75**	15.9
Cw8	0	0	0	0	0	2.27
Cw17	0	0	0	0	3.12	0

represented in all the populations studied. Further, HLAA30, A36, A69, B50 and B55 alleles were observed among the Punjabis, A29 and B62 among the Gujarathi population, High frequencies of HLAB5 and Cw4 among the South Indians as well as rare allelic splits like A23 among the amalgamated Christians were also observed. Most of the newly identified and defined WHO Nomenclature for HLA antigens 2002 (Marsh et al. 2002) have not been tested in these populations.

DISCUSSION

Studies of various human populations using PCR based typing have revealed the extent of allelic diversity in HLA (Apple and Erlich 1996). Theoretically, high polymorphism of a gene can occur due to mutation rate, selection, genetic hitchhiking or a combination of all the three (Kaufmann 1996). In addition, these data have been used to generate hypothesis about the nature of selective forces operating on the HLA loci to elucidate the pattern of human evolution and migration. Earlier population studies have indicated that there are many alleles and haplotypes that appear to be specific for a given population group. Indigenous populations or caste groups show a very restricted diversity of alleles at a particular HLA loci consistent within a population (Trachtenberg et al. 1995). Moreover specific alleles found uniquely in a particular indigenous group may have been generated by point mutation or gene conversion from the ancestral allele after the group separated from the other groups (Titus-Trachtenberg et al. 1994). Multiple polymorphic alleles in a population are maintained at appreciable frequencies due to either overdominance (heterozygous advantage), frequency dependent selection or other selective force (Erlich and Gyllenten 1991). Both selective forces and a high rate of germline diversification are involved in the evolution of HLA allelic diversity. Thus a newly arisen favorable variant allele might co-exist with the parental allele rather than replacing it when selective forces favoring diversity is operating. Recently in the Indian population newer HLA alleles like A*0211, A*3303, A*3306, B*1405, B*2708, B*2714, DRB1*1506, DRB1*1508 have been identified to co-exist with other alleles (Shankarkumar 2002; Shankarkumar et al. 2002a, b, 2003; Rozemuller et al. 2002; Kankonkar et al. 2003). One of the characteristic properties of HLA diversity in human population is the phenomenon of linkage disequilibrium, the non-random association of particular alleles at HLA loci. Certain haplotypes are very much more frequent than any other combination of alleles (Shankarkumar et al. 2002). Strong linkage disequilibrium between closely linked loci may be due to lack of cross - over between the loci and more likely selection for a particular combination of allele (Apple and Erlich 1996). In principle, population admixture may also create linkage disequilibrium patterns but that is unlikely to account for extensive disequilibrium observed in human populations. Thus, elucidation of the extended haplotypes in these caste groups by molecular typing for newly identified antigens will reveal the HLA allelic diversity and enable one to identify newly arisen favorable variant alleles co-existing in the population. Further, it will help in identifying the allelic mismatches in the allogenic bone marrow transplantation with unrelated donors.

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