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HLA Antigen Distribution in Selected Gujarati Subcaste from Mumbai, Maharastra, India

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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 178 unrelated Gujarati speaking individuals, belonging to Lohanas, Banyas and Gujarati Brahmins caste groups. We present here the HLA- A, B, C and DR locus antigen distribution of these endogamous caste groups compared with each other. The HLA antigens were identified by using the standard complement mediated NIH microlymphocytotoxicity assay. The phenotypic frequencies of HLA- A2, A9, B5, B35, B40, DR2, DR3 in Banyas, A10, A19, B8, B17, Cw3, DR7 in Lohanas and A1, B7, B22, Cw5, DR1 in Gujarati Brahmins were found to be significantly increased. The phenotype frequencies of A10, B13, DR6 in Banyas, B15, B22, DR4 in Lohanas and A2, A10, B8, B13, B37, Cw7, DR6 in Gujarati Brahmins were found to be significantly decreased among the HLA antigens tested. Haplotype analysis revealed that A33-B44-DR7 haplotype were present in all the three caste groups while, A1-B17 in Brahmins, A11-B35, A2-B5, A3-B18 in Lohanas and A11-B62, A3-B40 in Banyas were unique among the caste groups. Haplotype A24-B5 was identified among Lohanas and Banyas. The observed antigen frequencies and linkage disequilibrium among the three Gujarati caste groups suggest the influence of genetic drift caused by selection, geography and culture. The study also reveals that the caste groups in India cannot be considered as a single panmictic population with reference to 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). The Brahmins are considered the upper caste Hindus in India. Gujarati Brahmins are a group of Brahmins who practice strict endogamy within Gujarati speaking community and are mainly situated in Maharashtra and Gujarat State. They are priests, scholars or cooks referred as Maharaj. The Banyas are known as Vania in Gujarati is a conglomeration of people from different caste namely Visa, Dasha and Pancha bunched in a single group because of their profession. Lohanas are principally found in Sind, Gujarat and Kutch. They believe that they were originally soldiers and statesmen, when their power declined, they took to trade. Lohanas probably belong to the lohanis who formerly held the communities between the Sulliman Hills and the Indus. Lohanas have a number of exogamous divisions called Nukhs. Marriages are prohibited between members of the same Nukh (Einthnoven 1990).

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 implication (Charron 1997). 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 and Cancer (Charron 1996). It has also provided unique contributions to Anthropology and Population genetics (Charron 2000). 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; Shankarkumar et al. 1999, 2000, 2001, 2002a; Chhaya and Shankarkumar 2001).

In the present study we investigated the distribution of HLA antigens in Gujarati speaking Brahmins, Banyas and Lohana caste groups.

MATERIALS AND METHODS

Blood samples from random 178 healthy unrelated Gujarati speaking individuals belonging to Lohanas (n=46), Banyas (n=78) and Gujarati Brahmins (n=54) from Mumbai were studied for HLA -A, -B, -C and -DR 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, C and DR locus antigens were identified by NIH two - stage microlymphocytotoxicity assay (Terasaki and Mc Clelland 1964) using T cells for class I typing and B cells isolated by a miniature nylon wool column for class II with a longer incubation period (Manikasundari et al. 1984). A total of 190 antiserum were used for defining 17 specificities for HLA- A locus, 29 for HLA- B locus, 8 for HLA- C locus and 10 for HLA- DR 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 phenotype frequency (PF), genotype frequency (GF), standard error of gene frequency (SEGF), haplotype frequency (HF), Co efficient of linkage disequilibrium (Delta) and "t" values were calculated following the method described by Baur and Daniloves (1980).

RESULTS

The results on HLA- A, B, C and DR antigen frequencies of the three Gujarati caste groups are compared in Table 1. The phenotypic frequencies of HLA- A2, A9, B5, B35, B40, DR2, DR3 in Banyas, A10, A19, B8, B17, Cw3, DR7 in Lohanas and A1, B7, B22, Cw5, DR1 in Gujarati Brahmins were found to be significantly increased. The phenotype frequencies of A10, B13, DR6 in Banyas, B15, B22, DR4 in Lohanas and A2, A10, B8, B13, B37, Cw7, DR6 in Gujarati Brahmins were found to be significantly decreased among the HLA antigens tested. Further HLA- A28, B18, B27, Cw1, Cw6, DR6 were found to be decreased, while B48, DR8, DR9, DR10 were not identified among all the three caste groups. Haplotype analysis reveled that A33-B44-DR7 haplotype were present in all the three caste groups while, A1-B17 in Brahmins, A11-B35, A2-B5, A3-B18 in Lohanas and A11-B62, A3-B40 in Banyas were unique among the caste groups. Haplotype A24-B5 was identified among Lohanas and Banyas (Table 2). Most of the newly identified and defined WHO Nomenclature for HLA antigens 2002 (Marsh et al. 2002) have not been tested in these populations.

Table1: Percentage frequencies among different Gujarati caste groups studied

HLA	*Gujarati caste*		
	Banya N-78	*Lohana N-46*	*Brahmin N-54*
A1	24.40	21.70	46.30
A2	35.90	23.90	16.70
A3	21.80	26.10	22.20
A9	33.30	28.30	24.10
A10	9.00	23.90	11.10
A11	20.50	19.60	24.10
A19	10.30	26.10	14.80
A28	12.80	13.00	9.30
B5	41.00	23.90	38.90
B7	7.70	13.00	22.20
B8	10.30	10.90	3.70
B12	17.90	21.70	16.70
B13	1.30	13.00	1.90
B14	0.00	4.30	1.90
B15	10.30	4.30	9.30
B16	1.30	0.00	0.00
B17	17.90	30.40	18.50
B18	3.80	8.70	5.60
B21	10.30	6.50	7.40
B22	5.10	4.30	14.80
B27	3.80	4.30	1.90
B35	21.80	19.60	14.80
B37	0.00	2.20	1.90
B40	29.50	13.00	20.40
B48	0.00	0.00	0.00
Cw1	2.60	2.20	3.70
Cw2	2.60	6.50	0.00
Cw3	10.30	19.60	7.40
Cw4	30.80	34.80	25.90
Cw5	0.00	6.50	7.40
Cw6	3.80	4.30	3.70
Cw7	2.60	0.00	1.90
DR1	0.00	0.00	10.30
DR2	51.40	22.20	37.90
DR3	32.40	27.80	31.00
DR4	21.60	11.10	24.10
DR5	27.00	27.80	27.60
DR6	5.40	0.00	6.90
DR7	29.70	44.40	24.10
DR8	0.00	0.00	0.00
DR9	0.00	0.00	0.00
DR10	0.00	0.00	0.00

Table 2: Common Haplotypes observed among the Gujarati caste groups studied.

Haplotypes	*HF/1000*	*LD/1000*	*chi-square*	*T value*
Lohanas				
A2-B5	23.50	16.00	12.52	2.93
A3-B18	11.20	9.10	12.67	2.43
A11-B35	45.20	29.20	11.74	3.09
A33-B44	27.40	18.60	14.88	3.23
A24-B5	44.90	31.20	29.14	4.53
A33-B44-DR7	12.30	10.30	9.57	2.03
A11-B35-DR4	45.20	35.90	59.03	5.48
Banyas				
A11-B62	15.60	11.30	7.75	2.28
A3-B40	17.70	10.30	5.75	2.18
A24-B5	36.50	23.60	27.82	4.55
A33-B44	14.80	12.40	16.14	2.58
A24-B5-DR2	160.00	79.90	7.95	3.35
A33-B44-DR7	51.80	38.10	7.36	2.44
Brahmins				
A1-B17	84.60	58.60	7.39	3.00
A33-B44	37.70	33.70	12.00	2.12
A33-B44-DR7	27.40	22.20	13.82	2.68

HF = Haplotype frequency per 1000
Delta = Linkage disequilibrium per 1000.
T value > 2 indicates positive for Delta.
Chi-square with Yates correction.

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 et al. 2002a,b; Rozemuller et al. 2002; Shankarkumar 2002; Kankonkar et al. 2003; Shankarkumar 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. 2002a). 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 to identify newly arisen favorable variant alleles coexisting 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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