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Haptoglobin Polymorphism among Brahmins of Solan District Himachal Pradesh

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ABSTRACT Haptoglobin is a plasma glycoprotein that binds free hemoglobin with high affinity and prevents the loss of iron. In the present study 83 unrelated individuals from the Brahmin community of Solan District of Himachal Pradesh, were screened for haptoglobin polymorphism. Haptoglobin was found to be polymorphic in the selected population but the system was not found to be in Hardy Weinberg Equilibrium ($\chi^2 = 10.83$) due to the over representation of Hp2-2 type in the population. A very high frequency of *HP*2* allele (0.97) was found in the presently studied population.

INTRODUCTION

Haptoglobin is an acute-phase glycoprotein present in plasma of humans and other mammals that binds irreversibly with free hemoglobin released from destructed red blood cells with high affinity preventing renal damage (Polonovsky and Jayle 1938). It has different biochemical characteristics and functional efficiencies that account for their distinct antioxidant and immunomodulatory capacities (Guetta et al. 2007). Haptoglobin consists of carbohydrate (about 20%), comprising of hexoses, glucosanine, fucose and silic acid (Jayle and Moretti 1962). It is tetrameric protein containing two α and two β chains. In haptoglobin, hemoglobin binds to the β chain only and α chain does not directly participate in the binding (Gordon and Bearn 1966). Deoxyhemoglobin does not combine with haptoglobin, it only binds with oxyhemoglobin in Hbα1 and β2 contact region which is the haptoglobin binding site on the hemoglobin molecule (Benesch et al. 1977). Hatptoglobin is probably synthesized in the liver and synthesis for an average person with 3.2 *l* of plasma is about 0.6-1.0 *l* per day, of which about 50% is utilized to bind intravascular hemoglobin from erythrocyte breakdown.

Haptoglobin is inherited by two co-dominant autosomal alleles *HP*1*(wild type) and *HP*2* (mutant type) forming Hp1-1, Hp2-1 and Hp2-2 types (Smithies and Walker 1955). This polymorphism exists only in human beings and its locus lies on the distal part of the long arm of chromosome number 16 (16q22.1) (Robson et al. 1969). The haptoglobin polymorphism has been reported throughout the world populations, although the allele frequency varies widely. *HP*2* is distributed in a high frequency in India reaching upto 0.93 among the Irulas of India (Kirk and Lai 1961). Haptoglobin is a clinically significant marker and it is reported to be associated with various human pathologies (Wobeto et al. 2008). For example, Hp1-1 genotype is found to be associated with susceptibility to falciparum malaria and development of severe complications (Elagib et al. 1998; Quaye et al. 2000; Minang et al. 2004) and Hp2-2 genotype is also found to be associated with atherosclerosis and cardiovascular diseases, diabetes mellitus etc. (Chapelle et al. 1982; Delanghe et al. 1997; Nakhoul et al. 2001; Bessa et al. 2007). The present study was conducted with the primary objective to estimate the extent of haptoglobin polymorphism among the Brahmins of Solan district of Himachal Pradesh.

MATERIALS AND METHODS

The study was conducted among the Brahmins of Solan district, living in the mountainous region of Garkhal and Junga villages. The Brahmins of this region are believed to be migrated from the neighbouring plain areas of north India from time to time. They speak '*pahari*' which comes under the major linguistic group Indo-Aryan and '*devangi*' is used as the script. They practice caste endogamy and *gotra* exogamy.

Personal details such as name, age, sex, caste, father's birth place, mother's birth place, name of village, maternal uncle's caste etc. are collected using prelisted interview schedule. Utmost care is taken to maintain the randomness of the sample by avoiding relations up to first cousin. Blood samples by finger prick method were collected from 83 unrelated first individuals in EDTA coated 1.5 ml micro centrifuge tubes. Serum was separated by centrifugation of the blood samples for 2-3 min at 2000 rpm. Haptoglobin phenotyping was done by polyacrylamide gel electrophoresis (Raymond 1959). The allele frequencies were calculated using gene counting method. Hardy Weinberg Equilibrium test was performed and χ^2 goodness of test was used to compare the various population data with the present data.

RESULTS AND DISCUSSION

All the possible three common phenotypes of haptoglobin polymorphism were found in the Brahmins of Solan district. The HP 2-2 type was found to be the most prevalent (95.18%), followed by HP2-1 (3.61%) and HP1-1 (1.2%). The *HP*2* allele was found with a very high (0.97) frequency (Table 1).

In India, Hp*2 allele is found to be distributed in a very high frequency in various populations located in different geographical regions. A high frequency of Hp*2 allele was found among the Warli tribes (0.96) of Dadra Nagar Haveli, Kabuis (0.924), Muslims (0.918) and Meitei Brahmins (0.836) of Manipur (Shilpi et al. 2008; Asghar et al. 2009). But, this allele frequency is found to be somewhat lower among the Koyadoras (0.72) and Nayakpods (0.75) of Andhra Pradesh (Saraswathy et al. 2008). The present population was found to deviate from Hardy-Weinberg Equilibrium with respect to haptoglobin polymorphism ($\chi^2 = 10.83$, $p < 0.001$) which may be because of higher representation of homozygote HP 2 in it. As observed from Figure 1 that the Brahmins of Solan district were found to be significantly different from some other populations inhabiting Himachal Pradesh namely the Gaddi Brahmins ($\chi^2 = 32.1$, $p < 0.001$),

Table 1: Distribution of Haptoglobin (Hp) phenotypes and allele frequencies among the Brahmins of Solan District, Himachal Pradesh.

	Phenotypes			*Allele frequencies*	
	1-1	*2-1*	*2-2*	*HP*1*	*HP*2*
Absolute number	1	3	79	0.03	0.97
Percentage (%)	1.2	3.61	95.18		

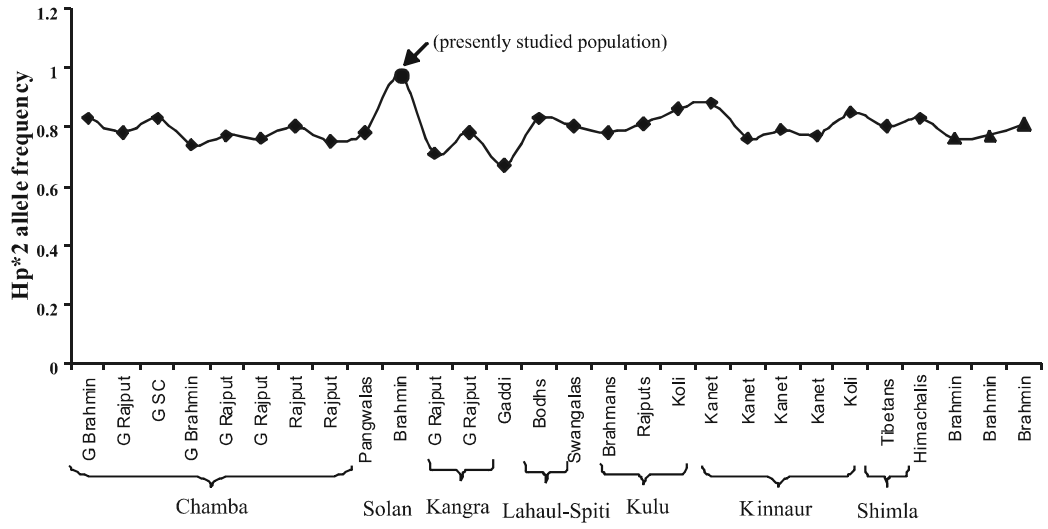

Fig.1. Distribution of Hp*2 allele frequency in different populations of north India.
(G – Gaddi, SC – Scheduled Caste)

Gaddi Rajputs ($\chi^2 = 26.3$, $p < 0.001$), Gaddi ($\chi^2 = 50.5$, $p < 0.001$), Rajputs ($\chi^2 = 30.7$, $p = 0.002$), Brahmins ($\chi^2 = 25.3$, $p < 0.001$), Koli ($\chi^2 = 12.9$, $p = 0.002$), Kanet ($\chi^2 = 33.4$, $p < 0.001$) etc. (Bhasin et al. 1992) with respect to haptoglobin polymorphism.

The presently reported frequency of *Hp*2* allele (97%) is found to be the highest among that reported in the north Indian populations (Bhasin et al. 1992). This very high frequency of the Hp*2 allele among Brahmins of Solan district could possibly be attributed to higher hemoglobin retaining capacity of HP2-HB complex (Berggard et al. 1962), besides the small sample size. The other possibility could be due to its association with other genes located on the same chromosome which have been selectively favoured (Norum K et al. 1989). However, Hp*2 allele is reported to be originated in India around 2 million years back (Schultze et al. 1966). This could be one of the reasons for such high frequency of Hp*2 allele in Indian context, apart from the selective advantage of this allele against life threatening human diseases (Schultze et al. 1966). The present study supports the hypothesis of transient polymorphism status of haptoglobin which acts as a clinically significant marker (Asghar et al. 2009). Further exploration at molecular genetic level with respect to interaction of Hp-Hb and certain complex diseases may lead to better understanding of the distribution of Hp alleles among the studied population.

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