

Haptoglobin Polymorphism among Warli Tribe of Dadra Nagar Haveli, India

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ABSTRACT Haptoglobin (HP) is a protein that is well known for its hemoglobin (HB)-binding property. Data are presented on this polymorphic marker in a sample of 100 subjects belonging to the Warli tribe inhabiting Dadra and Nagar Haveli in Western India. The incidence of the HP* 1 allele was found to be 0.04 – lowest so far reported in Western and South India. The significance of the present study is elucidated with the prevalence of malaria and cases of hemolytic anemia in this area.

INTRODUCTION

Haptoglobin (HP) is a plasma glycoprotein that binds extracorporeal hemoglobin (HB) in a tight non-covalent complex (HB-HP) thereby preventing free haemoglobin from entering the kidney. The molecular mass of hemoglobin is approximately 65 kDa, whereas the molecular mass of the simplest polymorphic form of haptoglobin (HP 1-1) found in humans is approximately 90 kDa. Thus, the Hb-Hp complex has a molecular mass of approximately 155 kDa. Free hemoglobin passes through the glomerulus of the kidney, enters the tubules, and tends to precipitate therein. However, the Hb-Hp complex is too large to pass through the glomerulus. This conserves the valuable iron present in the hemoglobin, which would otherwise be lost to the body (Murray et al., 2003).

Haptoglobin is inherited by two co-dominant autosomal alleles situated on chromosome 16 in humans, namely HP*1 and HP*2. There are three phenotypes HP1-1, HP2-1 and HP2-2. HP1-1 individuals have greater hemoglobin binding capacity when compared to those individuals with HP2-1 and HP2-2. However, in spite of the HP1 molecule having greater binding capacity, it has lesser HB retaining capacity owing to its smaller molecular size as compared to HP2 molecule thus making it more likely to pass through the glomerular membrane of the kidney.

Haptoglobin also acts as an antioxidant, has antibacterial activity and plays a role in modulating many aspects of the acute phase response. Possession of a particular phenotype has been associated with a variety of common disorders (e.g. cardiovascular disease, autoimmune disorders, malignancy), a fact which can only be explained by the idea that possession of a particular phenotype offers some protection against the development of these disorders. Knowledge of phenotype could therefore aid in the prognosis of disease and allow treatment to be better tailored to suit an individual's needs (Langlois and Delanghe, 1996). Haptoglobin is a clinically significant marker with HP1 allele being the wild type and HP2 being the mutant type. Haptoglobin polymorphism has an effect on the prevalence of many life-shortening conditions. HP2-2 type has been found to be associated with tuberculosis, HIV mortality, auto-immune disorders and coronary heart diseases while HP1-1 type has been associated with viral hepatitis, allergies, malignancies and haematological disorders (Langlois and Delanghe, 1996).

The objectives of the present study were to estimate the extent of haptoglobin polymorphism among the Warli community of Dadra Nagar Haveli and to understand the status of Warli tribe among the contemporary neighbouring populations with respect to this serum protein polymorphism.

MATERIALS AND METHODS

The Warli is a well-known tribe living in the mountainous regions of Dharampur and Vansda talukas and in the coastal region of Umbergaon

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taluks of Valsad district. The Warli speak their own language, which is a mixture of Khandeshi Bhili dialect and Marathi. They speak Gujarati and use Gujarati script. The Warlis are principally monogamous but polygyny is also practiced. Cross cousin marriages are allowed.

Fingerprick Blood samples were collected from unrelated Warli individuals with prior informed verbal consent in eppendorf tubes coated with EDTA. Serum was separated by centrifugation of the samples. The technique used to analyze haptoglobin types is Polyacrylamide gel electrophoresis (PAGE) using disc gel electrophoretic apparatus (Raymond, 1959) Electrophoresis is carried out for 2 hours at a fixed voltage of 150 volts. A small amount of bromophenol blue is added to one of the sample tubes as a marker dye to indicate the progress of separation. After electrophoresis, the gels are removed from the tubes and directly expelled into test tubes containing the Benzidine solution. Immediately, blue bands appear in the gel which in time turns brownish. The results were recorded. Allele frequencies were calculated using gene-counting method

RESULTS AND DISCUSSION

In the Warli population, HP2 phenotype was found to be very prevalent (94%) followed by HP2-1 (4%) and HP1 (2%). The population was not in Hardy-Wienberg equilibrium. HP2 frequency was very high (0.96) as compared to HP1 (0.04). Comparison with published data (Bhasin et al., 1992) reveals that the Warlis have the least HP 1 frequency reported as yet in any West or South Indian population

It is interesting to note that an allele of such a clinically significant marker has reached a frequency as high as 96% in Warli. Apart from

Table 1: Distribution of Haptoglobin (HP) phenotypes and allele frequencies in the Warli tribe of Dadra and Nagar Haveli.

	Phenotypes			Allele frequencies	
	1-1	2-1	2-2	HP*1	HP*2
Number observed	2	4	94	0.04	0.96
Number expected	0.16	7.68	92.16		
Chi-square	24.59				

genetic drift and small sample size, one can also attribute this to selective advantage of HP2 individuals in areas where high frequency of HBS & G-6PD deficiency are found. Going by the physiological role, Hp1 individuals need to be more selected with its high binding capacity. However, the variability in sizes of the HP-HB complex in Haptoglobin phenotypes gives some hint for HP2 selection, where HP (2)-HB complex being longer and heavier has a higher HB retaining capacity.

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