Haptoglobin polymorphism among three populations of Manipur, India: a critical analysis

M Asghar, N Achoubi, S Meitei, K Meitei, B Murry, M Sachdeva, K Saraswathy

Citation

M Asghar, N Achoubi, S Meitei, K Meitei, B Murry, M Sachdeva, K Saraswathy. *Haptoglobin polymorphism among three populations of Manipur, India: a critical analysis*. The Internet Journal of Biological Anthropology. 2008 Volume 3 Number 2.

Abstract

Haptogloin is a plasma protein that binds free hemoglobin, thereby inhibiting hemoglobin induced oxidative damage. The distribution of haptoglobin alleles varies according to the geographical location and ethnicity. The present study is carried out to study the frequency distribution of haptoglobin in three endogamous populations of Manipur, India. Serum was separated from blood samples collected from 335 Muslims, 262 Meitei Brahmins and 121 Kabuis. HP*2 is found to be highest among Kabuis (0.924) followed by Muslims (0.918) and Meitei Brahmins (0.836). Muslims are found to deviate from the Hardy-Weinberg equilibrium (p=0.006). Comparison between the populations show a significant difference between Muslims and Meitei Brahmins (p=0.00) and Meitei Brahmins and Kabuis (p=0.005). The frequency of HP*2 is also found to have increased significantly in comparison to earlier reported data, supporting the hypothesis that haptoglobin polymorphism is still in transient form.

INTRODUCTION

Haptoglobin is a plasma protein that binds free hemoglobin, thereby inhibiting hemoglobin-induced oxidative damage. During intravascular hemolysis, free hemoglobin in the circulation passes through the glomerular filter and renal damage may occur [1] . The binding of HP with HB prevents both iron loss and kidney damage [1] . HP was first detected by Polonovski and Jayle [2] in serum. Smithies [3] identified three major variants of Haptoglobin in humans using starch gel electrophoresis. These three phenotypes are determined by two co-dominant alleles HP*1 and HP*2. Although HP*1 is found in serum of all mammals, this polymorphism exists only in humans [4] and it is believed to have originated by a partial intergenic duplication of HP*1 during the course of human evolution [5, 6, 4] .

The distribution of haptoglobin alleles varies according to the geographical location. An increasing trend of HP*1 frequency is observed from Southeast Asia towards Europe and Africa with the highest frequency (0.87) being reported from Palikour Amazonian Indians of South America [7] . Correspondingly, HP*2 is found to be highest in Southeast Asia - as high as 1.0 has been reported among Bhumij of India [8] . HP*2 is estimated to have originated in India [5] . At present, the human species is in a state of transient haptoglobin polymorphism [5] . HP*2 has spread over the world under a strong genetic pressure, gradually displacing the other allele. It has been hypothesized that the ability of the HP*2 allele to spread so rapidly in man was due to its ability to provide a selective advantage against life threatening infectious diseases which were the dominant driving forces early in human evolution [5] . Studies have shown the association between HP with various clinical disorders [9] . Thus, HP is an important marker in the study of human evolution and diversity as well as from the clinical point of view.

In the last five decades a large number of studies have been conducted on the distribution of haptoglobin polymorphism from various populations throughout the world. Various authors have summarized these frequency distributions in their respective times [10, 11, 12] . In Indian subcontinent, Bhasin and Walter [13] had compiled almost all the published frequency reports up to 1990. The present study aims at studying the frequency distribution of this marker in three populations inhabiting the Manipur state of India. There are very few reported studies available on haptoglobin in this malarial endemic region. The three population groups studied are Kabui, (a tribe), Meitei Brahmins, (a caste group) and Muslim, (a religious group). All the three populations inhabit the plain regions of Manipur and follow strict

endogamy thereby maintaining their own gene pools.

MATERIALS AND METHODS

Blood samples were collected from 335 Muslims, 262 Meitei Brahmins and 131 Kabuis. Two to three drops of blood were collected in EDTA coated micro-centrifuge tubes (1.5ml) by finger pricking after taking due informed written consent. Plasma was separated by centrifuging the tubes on the same day. The separated plasma was used for genotyping by polyacrylamide disc gel electrophoresis [14] .

Allele frequencies were calculated by gene counting method. Heterozygosities were obtained using the software POPGENE [15] . Hardy-Weinberg equilibrium was calculated using chi-square goodness of fit test. Inbreeding co-efficient was calculated following Sewall Wright formula.

RESULTS

The HP*2 allele frequency is much higher than that of HP*1 in all the three populations and the highest is found among Kabuis (0.924) followed by Muslims (0.918) and Meitei Brahmins (0.836). On testing for Hardy-Weinberg equilibrium, Muslims are found to deviate from the equilibrium (p=0.006). Comparisons between the populations show a significant difference between Muslims and Meitei Brahmins (p = 0.000) and Meitei Brahmins and Kabuis (p = 0.005). However, between Muslims and Kabuis the difference is statistically non-significant (p=0.697).

Figure 1

Table 1: Distribution of Haptoglobin alleles among the three studied populations

Population	**HP1**		**HP2-1**		**HP2**		*Total*	*Allele frequency*	
	N	%	N	%	N	%		***HP*2***	***HP*1***
Muslims	6	2.09	43	12.83	286	85.37	335	0.918	0.082
Meitei Brahmins	10	3.82	66	25.19	186	70.99	262	0.836	0.164
Kabuis	1	0.76	18	13.74	112	85.50	131	0.924	0.076

The Nei [16] mean heterozygosity was calculated for all the populations using POPGENE. Heterozygosity is found to be comparatively very low (lower than 0.5) in all the three populations, Meitei Brahmins being the highest with 0.274 followed by Muslims and Kabuis (0.151 and 0.141, respectively). The inbreeding co-efficient was found to be highest among Muslims with 0.149 followed by Meitei Brahmins and Kabuis (0.084 and 0.030, respectively)

Muslims in Manipur are believed to have migrated from Assam and Bengal in around 1600 AD and started to settle there after marrying with the Meitei women [17] . The present data was compared with Muslims of Assam, Bangladesh and West Bengal and also with Meiteis of Manipur which had been reported two decades before to see the changes in the allele frequency, if any. In all the cases except with West Bengal (WB) Muslims (p=0.067) [18] , it shows significant differences with Assam Muslims (p= 0.000) [19] , with Bengali Muslims (p = 0.003) [20] ; with Calcutta Muslims (p= 0.006) [21] and with Meiteis (p= 0.000) [22] .

When we compare the present data of Meitei Brahmins with earlier reported data in the same population and also with Meitei population of the same state, statistically significant differences are observed; p-value being 0.000 when comparing between Meitei Brahmins of present study and earlier reported data [22] , p= 0.001 between Meiteis [22] . The same is observed in case of Kabuis also. In comparison with the earlier Meitei data, Kabuis show significant difference (p= 0.000) [22] .

DISCUSSION

Even though the frequency distribution of HP follows the trend as observed in other Indian populations, there is a significant statistical difference in its distribution among the studied populations. This could be because of the strict endogamy being practiced by the three studied populations. The deviation from Hardy-Weinberg equilibrium observed in case of Muslims could be explained by the observed comparatively higher positive inbreeding coefficient among them.

Though the Muslims of Manipur are believed to have migrated from Sylhet (now in Bangladesh), the HP*2 frequency shows a significant difference when compared with earlier reported frequencies in the neighbouring populations. In case of Meitei Brahmins, the HP*2 frequency is not in agreement with the earlier reported data. All the populations studied also show a significant difference with the Meiteis (a population in the same geographical region). This shows that haptoglobin phenotype frequencies have changed in these populations in the last two decades mainly due to the increase in HP*2 frequency (Table 2).

Figure 2

Table 2: Haptoglobin frequency for some of the neighboring populations.

Population	N	HP1	HP2-1	HP2	*HP*2*	*HP*1*	Reference
Muslims	335	2.09	12.83	85.37	0.918	0.082	Present study
M Brahmins[a]	262	3.82	25.19	70.99	0.836	0.164	Present study
Kabuis	131	0.76	13.74	85.50	0.924	0.076	Present study
B Muslim[b]	121	2.48	24.79	67.77	0.830	0.170	20
A Muslim[c]	104	3.85	27.88	68.27	0.822	0.178	19
A Brahmin[d]	97	3.84	28.85	67.31	0.747	0.253	19
E M Brahmin[e]	109	0	19.83	80.17	0.725	0.275	22
Meiteis	102	8.25	34.02	57.73	0.770	0.230	22
C Muslim[f]	52	14.96	46.78	38.26	0.817	0.183	21
WB Muslim[g]	121	7.76	37.69	54.54	0.901	0.099	18

[a]Meitei Brahmin, [b] Bengali Muslims of Bangladesh, [c]Assam Muslims, [d]Assam Brahmin, [e]Earlier Manipuri Brahmin, [f]Calcutta Muslims, [g]West Bengal Muslims

HP*2 is thought to have originated in India [5] . The frequency of HP*2 is found to be highest in India ranging from 0.594 among Dawoodi Bohras [23] to 1.000 among Bhumij [8] . This high frequency of HP*2 is explained by its ability to provide a selective advantage against life threatening infectious diseases [5] . But in case of the present study the increase in the frequency of HP*2 seems to be because of inbreeding rather then the selective pressure as all the three population inhabit the same geographical region but have significant differences in the distribution of HP*2 frequency. Or alternatively, HP*2 allele has a positive selection in the population further accentuated by the inbreeding. This is supported by the significant increased frequency in these populations as compared to the earlier reported data and the observed positive inbreeding coefficient. This observation also supports the hypothesis that haptoglobin polymorphism is still in transient form.

References

1. Giblet ER. The haptoglobin system. Ser. Haemato. 1968; 1: 3-20.
2. Polonovski M and Jayle MF. Existence dans le plasma sanguine d'une substance activant l'action peroxydasique de l'haptoglobine. C.R.Soc.Biol. 1938; 129: 457-460.
3. Smithies O. Zone electrophoresis in starch gels: group variations in the serum proteins of normal human adults. Biochem. J. 1955; 61: 629-641.
4. Bowman BH. Haptoglobin. - In: Bowman B.H., (ed), Hepatic Plasma Proteins. Academic Press, San Diego. 1993; pp. 159-167.
5. Schultze HE and Heremans JF. Molecular biology of human proteins. Volume 1: nature and metabolism of extrcellular proteins. Elsevier, Amsterdam. 1966.
6. Bowman BH and Kurosky A. Haptoglobin: The evolutionary product of duplication, unequal crossing over and point mutation. Adv. Hum Genet.1982; 12: 189-261.
7. Santos SEB, Ribeiro-dos-Santos AKC, Guerreiro JF, Santos EJM, Weimer TA, Callegari-Jacquest SM, Mestriner MA, Franco MHLP, Hutz MH and Salzano FM. New protein genetic studies in six Amazonian Indian Populations. Ann. Hum. Biol. 1998; 25: 505-522.
8. Giri AK, Data S, Gajra B, Ray Chaudhury A, Talukder G and Sharma A. Some Genetic Markers in Tribals of Eastern India. Acta Anthropogenet. 1982; 6: 99-106.
9. Langlois MR and Delanghe JR. Biological and Clinical significance of haptoglobin polymorphism in humans. Clin. Chem. 1996; 42: 1589-1600.
10. Planas J. Los tipos de haptoglobinas en el hombre. Datos Sobre una poblacion Castellanan. Genet. Iber. 1963; 15: 103-133.
11. Giblet ER. Genetic Markers in Human Blood. Blackwell Scientific Publication. Oxford & Edenburgh. 1969.
12. Wobeto VA, Zaccariotto TR and Sonati M F. Polymorphism of human haptoglobin and its clinical importance. Genet. Mol. Biol. 2008; 31: 602-620.
13. Bashin MK, Walter H and Danker-Hopfe H. The distribution of genetical, morphological and behavioural traits among the peoples of India region. Kamla Raj Enterprises, Delhi. 1992.
14. Raymond S and Weintraub L. Acrylamide gel as a supporting medium for zone electrophoresis. Science. 1959; 130: 711.
15. Yeh FC, Yang RC and Boyle T. POPGENE version 1.32. - A joint project development for Molecular Biology and Biotechnology Center, University of Alberta and center for International Forestry Research. 1999.
16. Nei M. Analysis of gene diversity in subdivided populations. – PNAS. 1973; 70: 3321-3323.
17. Parratt SNA. (translated) The Cheitharon Kumpapa: the Count Chronicle of the Kings of Manipur. Routledge, London and New York. 2005.
18. Study of some serum group systems in Mahishyas and Muslims in 24-Parganas district, West Bengal. Humangenetik: 1974; 21: 27-32.
19. Walter H, Mukherjee BN, Gilbert K, Lindenberg P, Dannewitz A, Malhotra KC, Das BM and Deka R. Investigation on the variability of haptoglobin, Transferrin and GC Polymorphism in Assam, India. Hum. Hered. 1986; 36: 388-396.
20. Saha N. Blood Genetic Marker in Bengali Muslims of Bangladesh. Hum Hered. 1987; 37: 86-93.
21. Mukherjee BN and Das SK. The Haptoglobin and Transferrin types in West Bengal and a case of Haptoglobin 'Johnson'. Hum. Hered. 1970; 20: 209-214.
22. Singh KS, Mukherjee BN, Walter H, Lindenberg P, Gilbert K, Danewitz A, Malhotra KC, Banerjee S, Roy M and Dey B. Genetic markers among Meities and Brahmin of Manipur, India. Hum.Hered. 1986; 36: 177-187.
23. Jindal A and Basu SK. A genetic profile of Dawoodi Bohras of Udaipur (Rajasthan). Ind. J. Phys. Anthrop. Hum. Genet. 1982; 8: 163-169.

Author Information

Mohammad Asghar, M.Sc.
Biochemical and Molecular Lab, Department of Anthropology, University of Delhi, Delhi 110007

Nongthombam Achoubi, MSc
Biochemical and Molecular Lab, Department of Anthropology, University of Delhi, Delhi 110007

Sanjenbam Yaiphaba Meitei, MSc
Biochemical and Molecular Lab, Department of Anthropology, University of Delhi, Delhi 110007

Khangembam Somibabu Meitei, MSc
Biochemical and Molecular Lab, Department of Anthropology, University of Delhi, Delhi 110007

Benrithung Murry, PhD
Biochemical and Molecular Lab, Department of Anthropology, University of Delhi, Delhi 110007

MP Sachdeva, PhD
Biochemical and Molecular Lab, Department of Anthropology, University of Delhi, Delhi 110007

KN Saraswathy, PhD
Biochemical and Molecular Lab, Department of Anthropology, University of Delhi, Delhi 110007