

# Gene Frequency and Heritability of Rh Blood Group Gene in 44 Human Populations

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## Abstract

The frequency of RhD and Rhd alleles of Rh blood group gene was estimated in 44 human populations distributed all over the world from the RhD phenotypic data. The average frequency of RhD and Rhd allele over these populations was 0.70 and 0.30, respectively. Higher frequency of RhD allele than the expected estimate (0.50) in all the populations, under Hardy-Weinberg equilibrium condition assuming equal frequency of both alleles in the initial population, indicated inbreeding at RhD/d locus as well as natural selection for RhD allele. Very high heritability estimate (84.04%) of Rh allele frequency revealed that this trait was under weak selection pressure and resulted in greater genetic variation in existing populations. It is consistent with Fisher's fundamental theorem of natural selection. The results from the present study suggest that inbreeding at RhD/d locus and some other factors (possibly mutation, migration and genetic drift) other than natural selection alone played major roles in changing the Rh allele frequency in these populations.

**Keywords:** gene frequency, heritability, human populations, Rh gene

## Introduction

Rh system is one of the most complex human blood group systems and it is genetically controlled. In identification and transfusion practices, Rh blood group typing in man is routinely done. Human beings are broadly categorized as Rh +ve and Rh -ve following blood tests depending on the presence or absence of Rh-antigen or D-antigen. The term Rh was coined from the Rhesus monkey in which the blood antigen was first detected. An Rh +ve individual produces D-antigen whereas the Rh -ve individual fails to produce D-antigen on RBC. D-antigen (Rho) is clinically the most important in the Rh system because it is highly antigenic. Other common Rh antigens are C, c, E and e. These are less immunogenic than the D-antigen. D is considered to be the most potent immunogen followed by c and E. About 100 Rh antigens have been discovered so far.

The genes of the Rh system are located on chromosome 1 of human genome. The inheritance of Rh genes is highly complex. Two major theories *i.e.* Fisher-Race system and Weiner system have been put forward to explain the inheritance of Rh system. Fisher and Race postulated the theory of 3 closely linked genes C, D and E with their corresponding recessive alleles c, d and e in governing the Rh system. But the allele d has not yet been identified. Weiner system favored the multiple allelic series at one locus governing the Rh system. Neither the Fisher-Race nor the Weiner concept has any practical significance in laboratory work (Saran, 2003) and individual identification. So the phenotype of the Rh system of an individual is determined in a routine test depending on the expression of D-antigen on

RBC using anti-RhD sera. The genotype of an individual with respect to Rh system cannot be precisely predicted mainly due to the non-existence of d antigen and the difficulty in determining the arrangement of the genes in two homologues of chromosome 1 of a normal diploid.

Since the presence or absence of D-antigen on RBC is routinely tested, it is assumed for the sake of genetic analysis that a single gene with two alleles (RhD, Rhd) showing dominance governs the expression of D-antigen. Rh +ve phenotype will be exhibited by dominant homozygote (RhD/RhD) and heterozygote (RhD/Rhd) whereas Rh -ve genotype by recessive homozygote (Rhd/Rhd).

RhD phenotyping data of a population are generated to estimate the frequency of these alleles in the population to characterize it. The proportions of different alleles of a gene in a panmictic population are known as allele or gene frequency (Singh, 1990). The present study was undertaken to estimate the frequencies of two alleles (RhD and Rhd) from the RhD phenotyping data of 44 human populations collected from diverse sources to characterize these populations and to estimate the heritability (broad sense) of gene frequency of Rh system. The term gene frequency in population genetics is treated as a mean and so it is used in various genetic and biostatistical analyses.

## Materials and methods

RhD phenotyping data showing the distribution of Rh+ve and Rh-ve groups in 44 human populations/races were collected from diverse sources as shown in Tab. 1. These data sources included published papers and websites. The RhD phenotyping data of each population were

Tab. 1. Estimates of RhD and Rhd allele frequencies of Rh gene in 44 world populations

Sl. No.	Population / Ethnic Group	Allele Frequency		Total	Reference*
		RhD	Rhd		
1	Argentina	0.70	0.30	1.00	www.reference for bl type
2	Australia	0.56	0.44	1.00	- do -
3	Austria	0.56	0.44	1.00	- do -
4	Arabs (Lebanon)	0.67	0.33	1.00	Mourant <i>et al.</i> , 1976
5	Bengalis (Kolkata)	0.78	0.22	1.00	- do -
6	Belgium	0.78	0.22	1.00	www.reference for bl type
7	Baluchistan (Pak)	0.78	0.22	1.00	Khattak <i>et al.</i> , 2008
8	Britain (UK)	0.59	0.41	1.00	Khattak <i>et al.</i> , 2008
9	Barak Valley (Hindus)	0.83	0.17	1.00	Chakraborty, 2010
10	Barak Valley (Muslims)	0.86	0.14	1.00	- do -
11	Brazil	0.56	0.44	1.00	www.blood type facts
12	China (Beijing)	0.90	0.10	1.00	Mourant <i>et al.</i> , 1976
13	Canada	0.60	0.40	1.00	www.reference for bl type
14	Denmark	0.60	0.40	1.00	- do -
15	Estonia	0.64	0.36	1.00	www.blood type facts
16	Eskimo (Alaska)	1.00	-	1.00	Mourant <i>et al.</i> , 1976
17	France	0.61	0.39	1.00	www.reference for bl type
18	Finland	0.64	0.36	1.00	-do-
19	Guinea (France)	0.80	0.20	1.00	Loua <i>et al.</i> , 2007
20	Germany	0.61	0.39	1.00	www.blood type facts
21	Hong Kong	0.90	0.10	1.00	www.reference for bl type
22	Iceland	0.61	0.39	1.00	www.blood type facts
23	Ireland	0.60	0.40	1.00	- do -
24	Israel	0.68	0.32	1.00	- do -
25	India (General)	0.76	0.24	1.00	Khattak <i>et al.</i> , 2008
26	Kenya	0.81	0.19	1.00	Khattak <i>et al.</i> , 2008
27	Korea (South)	0.95	0.05	1.00	www.reference for bl type
28	Mexico	0.58	0.42	1.00	Mourant <i>et al.</i> , 1976
29	Nigeria	0.79	0.21	1.00	Khattak <i>et al.</i> , 2008
30	Netherlands	0.60	0.40	1.00	www.reference for bl type
31	Norway	0.62	0.38	1.00	www.blood type facts
32	New Zealand	0.58	0.42	1.00	- do -
33	Peswar (Pak)	0.77	0.23	1.00	Khattak <i>et al.</i> , 2008
34	Poland	0.61	0.39	1.00	www.reference for bl type
35	Portugal	0.63	0.37	1.00	www.blood type facts
36	Red Indians (Canada)	0.86	0.14	1.00	Mourant <i>et al.</i> , 1976
37	Saudi Arabia	0.74	0.26	1.00	Khattak <i>et al.</i> , 2008
38	Spain	0.57	0.43	1.00	www.blood type facts
39	Sudan	0.74	0.26	1.00	www.ncbi.nlm.nih.gov
40	Sweden	0.60	0.40	1.00	www.reference for bl type
41	Swat (Pak)	0.90	0.10	1.00	Khattak <i>et al.</i> , 2008
42	Sindh (Pak)	0.71	0.29	1.00	- do -
43	Turkey	0.67	0.33	1.00	www.blood type facts
44	USA	0.61	0.39	1.00	Khattak <i>et al.</i> , 2008
	Average	0.70	0.30	1.00	

\* Detailed reference in text

then used to estimate the frequency of two alleles (RhD, Rhd) in each population following the formulae suggested by Hedrick (2005). In the present study it was assumed that RhD antigen production in RBC is governed by a single gene with two alleles showing complete dominance.

Since gene frequency is treated as a mean in population genetics, the analysis of variance (one way) on the estimated frequencies of RhD and Rhd alleles over 44 populations was carried out as per Gupta (1991). Genotypic variance, environmental variance and phenotypic variance

of the Rh gene frequency were estimated using the expected mean squares given in Tab. 2. Heritability (broad sense) of the Rh gene frequency was calculated as per Johnson *et al.* (1955).

### Results and discussion

The estimates of RhD and Rhd alleles in 44 world populations are presented in Tab. 1. The average frequency of RhD and Rhd alleles in these populations was 0.70 and 0.30 respectively. Theoretically, the frequencies of both RhD and Rhd alleles should be equal to 0.50 in Hardy-Weinberg equilibrium assuming the occurrence of both the alleles in equal frequencies in the starting population. In the existing populations the RhD allele on an average occurred 2.33 fold more than Rhd allele indicating that inbreeding might have occurred in RhD/d locus, thereby increasing the frequency of RhD allele. This increase could also result from the natural selection for RhD allele in these populations. In the Eskimos (Alaska), the RhD allele was fixed as revealed by the allele frequency value of unity.

The analysis of variance (one way ANOVA) for the allele frequency of Rh gene (Tab. 2) revealed that the two blood groups of Rh system differed between themselves at  $p=0.01$  indicating that these two blood groups are genetically different. It was indicated by the F test value of 240.41 of "between blood groups" variation at 1, 86 degrees of freedom. Genotypic variance and phenotypic variance for Rh allele frequency (Tab. 3) were estimated using the expected mean squares shown in Tab. 2. The difference between genotypic and phenotypic variance for Rh allele frequency was very small indicating the predominant role of genes and simultaneously the insignificant role of environment in determining the Rh allele frequency.

Tab. 2. Analysis of variance for allele frequency of Rh gene in 44 populations

Source of variation	df	Mean squares	F value	Expected mean squares
Between Blood Groups (BG)	1	3.150	240.41*	$V(WG) + nV(BG)$
Within Blood Groups (WG)	86	0.015	–	$V(WG)$

\* Significant at  $p=0.01$

Heritability is the most widely used measure to determine the importance of genetic factors in determining the variation of a quantitative trait (Hedrick, 2005). Heritability measure is specific to a particular trait, organism, environment and population. Mousseau and Roff (1987) summarized data from 1120 heritability estimates in wild outbred animal populations and gave the cumulative frequency distribution of four types of traits *i.e.* those related to life history, behavior, physiology and morphology. The results suggested that the heritability for traits related to morphology are the largest followed by that for physiol-

ogy, behavior and life history. Rh allele frequency could be considered as a morpho-physiological trait for human identification. The traits that have been under stronger selection during evolution show lower heritability and lower genetic variation.

Tab. 3. Genetic parameters of allele frequency of Rh gene

Character	Env. Variance	Genotypic Variance	Heritability Variance	Phenotypic (%)
Rh allele frequency	0.015	0.079	0.094	84.04

The estimate of broad sense heritability for Rh allele frequency in the present study was very high (84.04%) indicating that the role of environment in the variation of Rh allele frequency over populations was small (15.69%). Very high heritability estimate of Rh gene frequency over the populations indicated that this trait was under weak selection pressure during the evolutionary history of mankind resulting in greater genetic variation in existing populations. It is consistent with the prediction from Fisher's fundamental theorem of natural selection (Fisher, 1958). It also revealed that selection was not the major factor in changing the allele frequency of Rh gene.

### Conclusions

The results from the present study revealed that RhD allele occurs nearly 2.33 fold more than the Rhd allele in existing human populations with an average frequency of 0.70 for RhD and 0.30 for Rhd alleles. Rh gene frequency showed a broad sense heritability estimate of 84.04% indicating the dominant role of genetic factors and the little role of environmental factors in determining the Rh allele frequency in human populations. The results further suggested that inbreeding at RhD/d locus since initial generation and some evolutionary forces (particularly mutation, migration and random drift) other than selection alone played major roles in changing the Rh allele frequency in existing populations.

### References

- Chakraborty, S. (2010). Genetic analysis on frequency of alleles for Rh and ABO blood group systems in the Barak Valley populations of Assam. *Not. Sci. Biol.* 2(2):31-34.
- Fisher, R. A. (1958). *The Genetic Theory of Natural Selection*. Dover, New York, USA, pp.133.
- Gupta, S. P. (1991). *Statistical Methods*. Sultan Chand & Sons Publishers, New Delhi, India, p. A-51-57.
- Hedrick, P. W. (2005). Measures of genetic variation. In: Jones and Bartlett (Eds.), *Genetics of Populations* (3<sup>rd</sup> Ed).

- Sudbury, Madison, USA, pp.61-112.
- Johnson, H. W., H. F. Robinson and R. E. Comstock (1955). Estimates of genetic and environmental variability in soybean. *Agron. J.* 47:314-318.
- Khattak, I. D., T. M. Khan, P. Khan, S. M. A. Shah, S. T. Khattak and A. Ali (2008). Frequency of ABO and rhesus blood groups in district Swat, Pakistan. *J. Ayub. Med. Coll.* 20(4) at <http://faculty.matcmadison.edu/mljensen/Blood Bank/lectures/Rh Blood Group System.htm>.
- Loua, A., M. R. Lamah, N. Y. Haba and M. Camara (2007). Frequency of blood groups ABO and rhesus D in Guinean population. *Transfus. Clin. Biol.* 14(5):435-439.
- Mourant, A. E., A. C. Kopec and K. Domaniewska-Sobczak (1976). *The Distribution of Human Blood Groups and Other Polymorphisms* (2<sup>nd</sup> Ed). Oxford University Press, New York, USA.
- Mousseau, T. A. and D. A. Roff (1987). Natural selection and the heritability of fitness components. *Heredity* 59:181-197.
- Saran, R. K. (2003). Rh blood group system. In: *Transfusion Medicine Technical Manual*. Ministry of Health and Family Welfare, Govt. of India, New Delhi, India. pp.75-87.
- Singh, B. D (1990). Population genetics. In: *Fundamentals of Genetics*. Kalyani Publishers, New Delhi, pp.676-704.
- [www.blood type facts, discussion forum and encyclopedia article.htm](http://www.blood type facts, discussion forum and encyclopedia article.htm).
- [www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov).
- [www.reference for blood type-search\\_com](http://www.reference for blood type-search_com).