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Heterozygosity and Fixation Index for ABO Gene in Barak Valley Populations *vis-a-vis* a Few Exotic Populations

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Abstract

In a genetic study of 26 human populations including 2 major endogamous populations (Hindus and Muslims) of Barak Valley in Assam and 24 exotic populations, observed heterozygosity (Ho), fixation index (F) and Panmictic index (P) for ABO gene were estimated from gene frequency data to reveal the extent of inbreeding that has taken place in each population during evolution. Observed heterozygosity, a measure of genetic variation, ranged from 0.3254 to 0.6086 in these populations. Expected Hardy-Weinberg heterozygosity of ABO gene was estimated as 0.6666 assuming the occurrence of all the three alleles in equal frequency. Fixation index was the highest in the population of Sudan (51.18%) followed by Australia (48.51%) and Iceland (38.28%) indicating the occurrence of high inbreeding and the presence of more homozygosity in these populations during evolution. But the fixation index was the lowest in the population of South China (8.70%) followed by Central Asia (11.82%) and Russia (12.96%). It suggested the occurrence of low inbreeding and hence more outbreeding in these populations resulting in the existence of more heterozygosity (high genetic variation) in these populations. Panmictic index, a measure of outbreeding, is the opposite of fixation index and it varied from 48.82 (Sudan) to 91.30% (South China). The population showing the highest fixation index recorded the lowest panmictic index and *vice-versa*. In evolutionary context, outbreeding in human populations would be more desirable to reduce the incidence of genetic diseases caused by recessive genes and to enhance heterozygosity for those loci for better adaptation of future generations, possibly at the cost of gradually increasing genetic load in the population.

Keywords: ABO gene, fixation index, panmictic index

Introduction

Human populations across the globe originated from one ancestral population in Central Africa which spread over time and space to form the present day nations. Due to the significant role having been played by the evolutionary forces like selection, mutation, recombination and genetic drift, the existing human populations all over the globe differ in their genetic make-up. Using the approach of population genetics it is possible to quantify the extent of genetic variation in a population. Fixation index (F) is a good measure of inbreeding and can be easily estimated from the allele frequencies of a gene. F estimates for different populations for one or more genes help us compare the populations for the extent of inbreeding that has taken place in each population during evolution. Panmictic index (P), on the other hand, is the opposite of fixation index (F) and is a good measure of the extent of outbreeding for a locus in a population.

Human beings are naturally outbreeding organisms. Outbreeding favors heterozygosity for individual loci and thereby suppresses the expression of deleterious recessive alleles by the dominant desirable alleles.

But inbreeding in human populations, arising primarily from marriages between individuals related by ancestry and within ethnic groups, makes recessive allele to express in diploid homozygous condition following Mendelian segregation. Inbreeding is the mating between individuals related by ancestry. Inbreeding causes negative health effects due to the expression of rare, recessive deleterious genes that are inherited from common ancestors or a single shared ancestor.

Several studies on populations in which inbreeding is common have shown increased levels of mortality and morbidity due to a variety of genetic defects. The negative health effect of inbreeding was evident in the Royal families of Europe from the widespread number of cases of hemophilia starting with Queen Victoria of England. Hemophilia is caused by a recessive X-linked gene. Queen Victoria is thought to be the original carrier of recessive hemophilic gene and from her it spread through her children and grandchildren to the royal families in Europe, Russia and Spain (Stevens, 1999). From the study of adult women in the Hutterites population of Canada and Dakotas, Ober *et al.* (1999) observed that deleterious recessive alleles received from inbreeding lowered the fertility rates of women. Dorsten *et al.* (1999) studied the effect of inbreeding in the Amish population of Lancaster, Pennsylvania and observed an increase in infant mortality under one-year-age due to a recessive genetic disorder called Ellis-van Creveld disease. This disease is associated with dwarfism in the extremities and a malformation in

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the heart's atrium. In Japan, shortly after the United States dropped atom bombs in World War II, there was an increase in the number of consanguineous marriages, mostly at first-cousin level, in the Japanese population surrounding Hiroshima and Nagasaki. The study of the effects of inbreeding on the offspring of consanguineous marriages in Japan revealed an increase in childhood mortality, morbidity, and birth of handicapped babies along with late onset of talking and walking in children (Schull and Neel, 1965).

But inbreeding can also result in the production of perfectly healthy offspring (Bittles *et al.*, 1991). A study was performed by Al-Abdulkareen (1998) on the population of Dammam, a city of Saudi Arabia, where the first cousin consanguineous marriages dominate all other forms of marriage. No significant difference was found between the children of consanguineous and non-consanguineous marriages for number of stillbirths, childhood death and mean birth weight. This study revealed that inbreeding is not always harmful and can produce perfectly normal offspring. Some investigators believe that long-term practice of inbreeding can actually benefit a population and its health by reducing deleterious harmful gene through selection if ample time is given for selection to act on the harmful gene (Hedrick, 1991).

ABO blood group typing nowadays is one of the routine lab tests performed not only for medical treatment but also for identification of an individual for official purpose (life insurance policy, driving license etc.) in several countries of the world. Blood group is a good genetic marker. ABO blood group phenotype is governed by a single gene with three alleles where O is the recessive allele and A and B alleles are dominant over O but codominant to each other. ABO blood group phenotyping data of individuals in a population can be used to estimate the frequencies of three alleles (O, A and B) and for further estimating other genetic parameters to characterize the population.

The present study was undertaken to obtain information on the level of inbreeding that has taken place during evolution through the estimation of fixation index and panmictic index for ABO gene in 26 populations including 2 major endogamous populations (Hindus and Muslims) of Barak Valley residing in the State of Assam in North East India *vis-à-vis* 24 exotic populations.

Materials and methods

The present study comprised of 26 populations including two major endogamous populations (Hindus and Muslims) of Barak Valley in Assam and 24 other exotic populations/nations along the route of journey of mankind from Africa as depicted by Stephen Oppenheimer (www.bradshawfoundation.com).

In this study, ABO blood group distribution data of 24 exotic populations were obtained from the published literature and websites (Tab. 1). The ABO blood group distribution data in Barak Valley Hindus and Muslims were estimated by the author (Chakraborty, 2010). The frequencies of O, A and B alleles belonging to ABO blood group system for each population were estimated from ABO blood group phenotyping data using the formulae suggested by Hedrick (2005) as given below:

$$A = 1 - \sqrt{\frac{N_{22} + N_{23} + N_{33}}{N}}$$

$$B = 1 - \sqrt{\frac{N_{11} + N_{13} + N_{33}}{N}}$$

$$O = \sqrt{\frac{N_{33}}{N}}$$

Where N= Total individuals
$N_{11}+N_{13}$= Individuals having "A" blood group
$N_{22}+N_{23}$= Individuals having "B" blood group
N_{33}= Individuals having "O' blood group

Observed heterozygosity (Ho) for ABO gene was calculated on the basis of estimated allele frequencies as:

$$Ho = 1 - \sum_{i=1}^{n} p_i^2$$

where p_i^2 = genotype frequency of observed heterozygotes.

Expected heterozygosity (He) at Hardy-Weinberg Equilibrium was calculated assuming the occurrence of all the three alleles of ABO gene in equal frequency (q=1/k where k is the number of alleles). It was estimated as 0.6666 for ABO gene considering 3 alleles.

Fixation index (F) for ABO gene in each population was estimated according to Hedrick (2005) as

$$F = \frac{He - Ho}{He}$$

and F was expressed in percentage. Panmictic index (P) was calculated as (1- F) and expressed in percentage.

Results and discussion

Hindus and Muslims are two major endogamous populations of Barak Valley zone, named after the mighty river Barak, located in southern part of Assam State in North East India. Barak Valley is geographically located between 24°15'and 25°9'N latitudes and between 92°16'and 93°15'E longitudes with subtropical, warm, humid climate. The region receives an average annual rainfall of about 318 cm with 146 rainy days per annum. The region inhabits a population of nearly 3.21 million and characterized by undulating topography with wide plain area, low lying water logged tracts and hillocks. Nearly 80% of the total population depends on agriculture for livelihood.

The frequencies of O, A and B alleles of ABO gene were estimated as 0.60, 0.19 and 0.21 in Hindus and as 0.63, 0.18 and 0.19 (Tab. 1) in Muslims, respectively in an earlier study (Chakraborty, 2010). The estimates of allele frequencies of other 24 exotic populations along the route of journey of mankind from Africa were collected or estimated from the genotype frequencies using standard formulae from diverse sources (Tab. 1).

Heterozygosity

The most widespread measure of genetic variation in a population is the amount of heterozygosity. Since individuals in diploid species are either heterozygous or homozygous at a given locus, the measure of heterozygosity represents a biologically useful quantity. Measures of heterozygosity are not very sensitive to additional variation because the upper limit, unity, is the same for any number of alleles (Hedrick, 2005).

In the present study the observed heterozygosity (Ho) for ABO gene ranged from 0.3254 to 0.6086 (Tab. 2). It was the highest in the population of South China (0.6086) followed by Central Asia (0.5878) and Russia (0.5802) indicating large genetic variations in these populations. Lowest Ho was found in Sudan (0.3254) followed by Australia (0.3432) and Iceland (0.4114) revealing low genetic variation in these populations. Barak Valley Hindus (0.5598) revealed higher genetic variation for ABO gene than Muslims (0.5364).

Expected Hardy-Weinberg heterozygosity (He) was same (0.6666) for all the populations as it was calculated assuming the occurrence of all the three alleles in equal frequency (q=1/k where k is the number of alleles). Nei (1987) called this measure as gene diversity and suggested that it is particularly useful as it is applicable for genes of different ploidy levels and in organisms with different reproductive systems.

Fixation Index (F) vs. Panmictic Index (P)

Fixation index (F) for ABO gene ranged from 8.70 to 51.18% in the populations under study (Tab. 2). F for ABO gene was the highest in Sudan (51.18%) followed by Australia (48.51%) and Iceland (38.28%) which indicated high inbreeding and hence more homozygosity in these populations. Panmictic index (P) is the opposite of fixation index (F) and therefore, F plus P equals to unity. Consequently, the panmictic index (P) was the lowest in

Tab. 1. Estimates of allele frequency of ABO gene in Barak Valley populations *vis-a-vis* other exotic nations enroute the journey of mankind from Africa

Sl. No.	Population	ABO Allele Frequency				Reference*
		O	A	B	Total	
1	Kenya	0.69	0.17	0.14	1.00	Anees and Mirza (2005)
2	Sudan	0.81	0.11	0.08	1.00	www.bloodbook.com
3	Saudi Arabia	0.58	0.21	0.21	1.00	- do -
4	India (Overall)	0.62	0.16	0.22	1.00	- do -
5	Sri Lanka	0.69	0.16	0.15	1.00	- do -
6	West Indonesia	0.69	0.10	0.21	1.00	Breguet *et al.* (1986)
7	Borneo (Malaysia)	0.62	0.22	0.16	1.00	Kamil *et al.* (2010)
8	South China	0.53	0.23	0.24	1.00	www.bloodbook.com
9	Australia	0.78	0.22	-	1.00	- do -
10	Bulgaria	0.57	0.31	0.12	1.00	- do -
11	Hungary	0.60	0.27	0.13	1.00	- do -
12	Austria	0.60	0.30	0.10	1.00	- do -
13	Pakistan	0.74	0.12	0.14	1.00	- do -
14	Central Asia (Uzbekistan)	0.56	0.25	0.19	1.00	Revavov *et al.* (1983)
15	Eastern Europe(Poland)	0.57	0.28	0.15	1.00	www.bloodbook.com
16	Siberia	0.57	0.16	0.27	1.00	- do -
17	Russia	0.57	0.25	0.18	1.00	- do -
18	Alaska	0.62	0.29	0.09	1.00	- do -
19	USA (Whites)	0.67	0.25	0.08	1.00	- do -
20	Britain	0.69	0.26	0.05	1.00	- do -
21	Norway	0.62	0.32	0.06	1.00	- do -
22	Sweden	0.62	0.31	0.07	1.00	- do -
23	Iceland	0.74	0.19	0.07	1.00	- do -
24	Denmark	0.64	0.27	0.09	1.00	- do -
25	Barak Valley Hindus	0.60	0.19	0.21	1.00	Chakraborty (2010)
26	Barak Valley Muslims	0.63	0.18	0.19	1.00	- do -

*Detailed reference in text

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Tab. 2. Estimates of Fixation Index (F) and Panmictic Index (P) for ABO gene in Barak Valley populations *vis-a-vis* other nations enroute the journey of mankind from Africa

Sl. No.	Population	Obs. H (Ho)	Exp. H (He)	F	F (%)	P	P (%)
1	Kenya	0.4754	0.6666	0.2868	28.68	0.7132	71.32
2	Sudan	0.3254	0.6666	0.5118	51.18	0.4882	48.82
3	Saudi Arabia	0.5754	0.6666	0.1368	13.68	0.8632	86.32
4	India (Overall)	0.5766	0.6666	0.1350	13.50	0.8650	86.50
5	Sri Lanka	0.4758	0.6666	0.2862	28.62	0.7138	71.38
6	West Indonesia	0.4698	0.6666	0.2952	29.52	0.7048	70.48
7	Borneo (Malaysia)	0.5416	0.6666	0.1875	18.75	0.8125	81.25
8	South China	0.6086	0.6666	0.0870	8.70	0.9130	91.30
9	Australia(Aborigines)	0.3432	0.6666	0.4851	48.51	0.5149	51.49
10	Bulgaria	0.5646	0.6666	0.1530	15.30	0.8470	84.70
11	Hungary	0.5502	0.6666	0.1746	17.46	0.8254	82.54
12	Austria	0.5400	0.6666	0.1899	18.99	0.8101	81.01
13	Pakistan(Gujrat)	0.4184	0.6666	0.3723	37.23	0.6277	62.77
14	Central Asia (Uzbekistan)	0.5878	0.6666	0.1182	11.82	0.8818	88.18
15	Eastern Europe(Poland)	0.5742	0.6666	0.1386	13.86	0.8614	86.14
16	Siberia(Buryats)	0.5766	0.6666	0.1350	13.50	0.8650	86.50
17	Russia	0.5802	0.6666	0.1296	12.96	0.8704	87.04
18	Alaska(Eskimo)	0.5234	0.6666	0.2148	21.48	0.7852	78.52
19	USA (Whites)	0.4822	0.6666	0.2766	27.66	0.7234	72.34
20	Britain	0.4538	0.6666	0.3192	31.92	0.6808	68.08
21	Norway	0.5096	0.6666	0.2355	23.55	0.7645	76.45
22	Sweden	0.5146	0.6666	0.2280	22.80	0.7720	77.20
23	Iceland	0.4114	0.6666	0.3828	38.28	0.6172	61.72
24	Denmark(Danes)	0.5094	0.6666	0.2358	23.58	0.7642	76.42
25	Barak Valley Hindus	0.5598	0.6666	0.1602	16.02	0.8398	83.98
26	Barak Valley Muslims	0.5346	0.6666	0.1980	19.80	0.8020	80.20

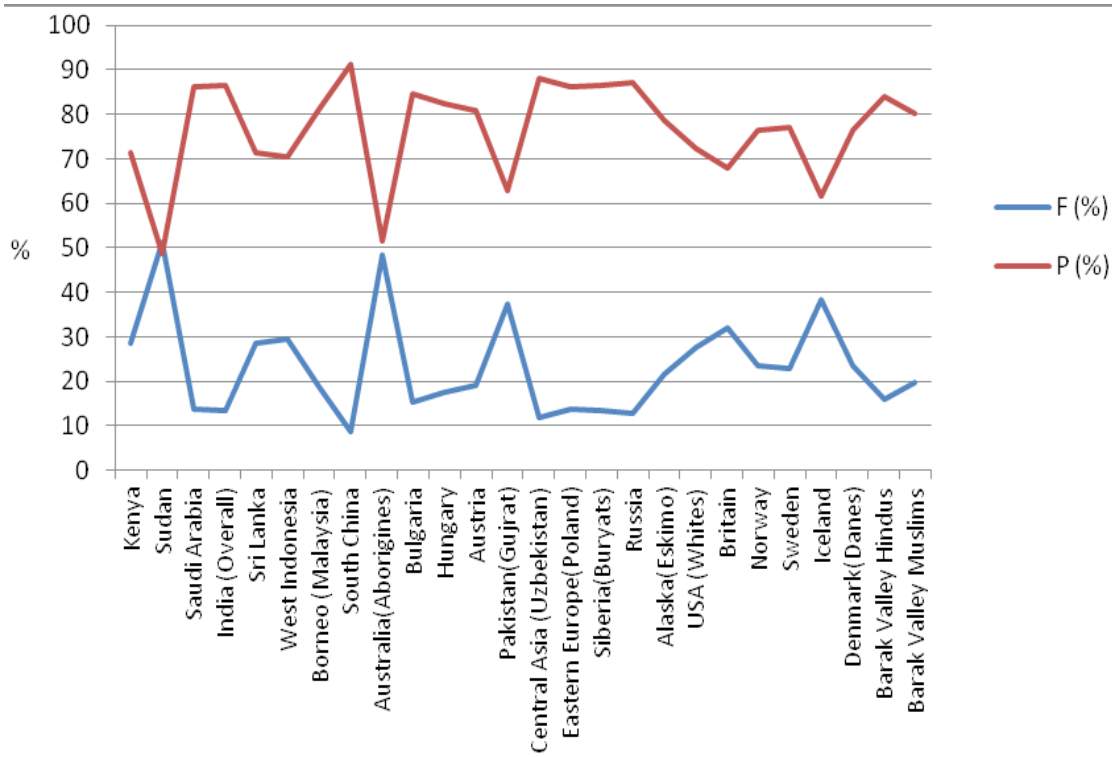

Fig. 1. Fixation Index (F) and Panmictic Index (P) of population for ABO gene

these populations which revealed lowest heterozygosity and hence lowest genetic variation for ABO gene (Fig. 1). In general the estimate of P for ABO gene varied from 48.82 (Sudan) to 91.30% (South China) in the populations under study.

But F was the lowest in South China (8.70%) followed by Central Asia (11.82%) and Russia (12.96%) revealing the occurrence of less inbreeding and hence more outbreeding in these populations during evolution. In other words these populations possessed more heterozygosity and greater genetic variation for ABO gene now.

In Barak Valley populations, F was lower in Hindus (16.02%) than Muslims (19.80%) indicating greater genetic variation in Hindus than Muslims for ABO gene. It could be due to the effect of consanguineous marriages and/or random genetic drift in the Muslims of Barak Valley. The populations showing low F possessed high P and *vice-versa*.

In evolutionary context, outbreeding in human populations is more desirable to hide the expression of deleterious recessive genes in homozygous condition and to enhance heterozygosity for those loci for better adaptation of future generations. But outbreeding at the same time is likely to increase the genetic load of the population through aggregation of harmful recessive genes in heterozygous condition.

Conclusions

The results of the present study revealed that the observed heterozygosity, a measure of genetic variation, for ABO blood group gene ranged from 0.3254 to 0.6086 in 26 human populations. Expected Hardy-Weinberg heterozygosity (He), also called gene diversity of Nei (1987), was estimated as 0.6666 for all the populations assuming the occurrence of O, A and B alleles in equal frequency (q=1/k where k is the number of alleles). Fixation index (F) for ABO blood group gene was the highest in the population of Sudan followed by Australia and Iceland indicating very high inbreeding and hence more homozygosity in these populations during evolution. But F was the lowest in the population of South China followed by Central Asia and Russia suggesting less inbreeding and hence more outbreeding in these populations during evolution. This indicated the presence of more heterozygosity (genetic variation) in the latter three populations for ABO gene. Panmictic index (P), a measure of the extent of outbreeding, ranged from 48.82 to 91.305 for ABO gene over 20 populations under study. Since fixation index and panmictic index are just like the two sides of a coin, the population showing the largest fixation index for ABO gene recorded the lowest panmictic index and vice-versa. Outbreeding is more desirable in human populations to reduce the incidence of genetic diseases caused by recessive genes and to enhance heterozygosity for better adaptation in evolutionary context, possibly at the cost of gradually increasing genetic load in the population.

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