Genetics of Castes and Tribes of India:
Glucose-6-Phosphate Dehydrogenase Deficiency and Abnormal Haemoglobins (HbS and HbE)

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ABSTRACT The discipline of Biological Anthropology (or Human Biology) incorporates study of biology and environmental factors, as well as the forces of micro-evolution leading to macro-evolution, which ultimately influences the structure of human populations. In the present paper and attempt has been made to study the distribution of Glucose-6-Phosphate Dehydrogenase Deficiency and Abnormal Haemoglobins (HBS and HBE) frequencies among the people of India, which are analysed in relation to ecological, socio-economic and linguistic factors.

INTRODUCTION

Biological Anthropology deals with the comparative biogenetics of man. Within the various fields of research of the present Biological Anthropology the study of human evolution as well as the study of genetic variation in modern man hold an eminent place. An important branch of Biological Anthropology is therefore Population Genetics, which deals on the one hand with exact genetic descriptions of human population, but which on the other hand tries to find out the reasons for genetic differences among them. To study these genetic differentiation processes in man, which are obviously still ongoing, reliable population data are necessary. As far as the various genetic markers of the human blood are concerned such comprehensive reviews have been given *e.g.* by Mourant et al. (1976), Steinberg and Cook (1981), Tills et al. (1983), Roychoudhury and Nei (1988) and Walter (1988). The existence of genetic variation in man is caused by many factors, among which selection, migration and gene flow, genetic drift and founder effects are the most important ones. By means of many examples, Vogel and Motulsky (1997) have shown the importance of these factors for the understanding of genetic variation in man. Mourant et al. (1978) have reviewed the associations between genetic markers of the blood and diseases, which are of considerable interest in this connection.

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The unit of study is genetic variation in man is a "breeding population", also referred to as a "Mendelian population". Following Harrison (1988) one can point out that "the collective unit of evolution is the population and it is in populations that all the forces we have considered operate" (p. 326). Thus selection, gene flow, genetic drift, founder effects etc. are acting on and in populations and shape their specific genetic profiles in the course of time. The "breeding population" is the minimal integrated unit of evolutionary changes. As far as delineating evolutionary factors are concerned, the "breeding populations" as a unit of study meet almost every logical requirement unit and any change in its genetic profile from one generation to the next will constitute an evolutionary change.

The impact of the population approach on the study of genetic variation in man has been to focus attention on "breeding populations" as biological or evolutionary units in man and to describe them in terms of gene frequencies or if this is not possible (anthropometric, morphological, dermatoglyphic, etc. traits) in terms of phenotype frequencies and mean values, respectively. Such exact and comprehensive descriptions are the basic requirements for the understanding of genetic variation in man and thus for the analysis of the various evolutionary factors, which caused this variation in the course of time.

The populations of India and other South Asian countries offer great opportunities to study

genetic variability. Perhaps, nowhere in the world people in a small geographic area are distributed as such a large number of ethnic, caste, religious and linguistic groups as in India and other South Asian countries. All these groups are not entirely independent, people belong concurrently to two or more of these groups. People of different groups living side by side for hundreds or even thousands of year try to retain their separate entities by practising endogamy.

The aim of the study is to have a satisfactory knowledge of micro-evolutionary processes as they are reflected in genetic and morphological traits in human populations. This variability has been studied in terms of natural regions, climatic factors, climatic regions, political division of India, ethnic groups, traditional occupations and linguistic groups (For details see Bhasin 1988; Bhasin et al. 1992, 1994; Bhasin and Walter 2001). In this paper an attempt has been made to report the Glucose-6-Phosphate Dehydrogenase Deficiency and haemoglobin variants among the people of India and factors responsible to operate in favour of these traits.

IDENTIFY AND DISTINGUISH THE PEOPLE

For the biogenetical study of the people of India, researchers have generally used the following criteria to identify and distinguish the people: 1. Regional Groups, 2. Ethnic Groups, 3. Linguistic Groups, and 4. Religious Groups.

It should, however, be kept in mind that these are the convenient units of study, although there are significant levels of overlapping between them. For example, an occupational group pursuing traditional job inhabits a region, shares religion with other categories, belongs to one or the other language group and has an aggregation of ethnic properties. But in the human population genetic studies, out of these criteria one is chosen (Bhasin 1988).

In the present study an attempt has been made to analyse the above mentioned biogenetical traits into 1. Regional Groups, 2. Ethnic Groups, 3. Traditional Occupational Groups and 4. Linguistic Groups.

I. REGIONAL GROUPS

These can be divided into the following groups:

1. Natural Regions of India
2. Climatological Factors and Climatic Regions of India
3. Political Division of India

Each region has its own characteristics and a brief description of each one will give an idea of what it constitutes of.

1. Natural Regions of India

The natural regions have broad uniformity in their characteristics, such as relief, geomorphological history, drainage, climate, soil, natural vegetation and wild life. Broadly speaking the Indian sub-continent may be divided in the following natural regions:
1. The Himalayan Mountain Complex
2. The Indus-Ganga-Brahmaputra Plain
3. The Peninsular Plateau and
4. The Islands

2. Climatological Factors and Climatic Regions of India

Various climatological factors (Rainfall, Humidity, Temperature) and Altitude have been considered to study correlations with different biological traits. The values for the climatological factors are after "Climatological Tables of Observations in 1931-1960" Meteorological Department, Government of India, New Delhi.

A climatic region generally possesses a broad uniformity in climatic conditions produced by combined effects of climatic factors. India can be divided into the following climatic regions after Köppen's method, based on the monthly values of temperature and precipitation:

(1) Tropical Savannah Type, (2) Monsoon Type with Short Dry Season, (3) Monsoon Type with Dry Season in High Sun Period, (4) Semiarid and Steppe Climate, (5) Hot Desert Type, (6) Monsoon Type with Dry Winters, (7) Cold Humid Winters Type with Shorter Summer, and (8) Polar Type.

3. Political Division of India

India is a Union of States. Comprising 25 States[1] and 7 Union Territories, according to the Census 1991, there are 4689 towns and 587,226 inhabited and 47,095 uninhabited villages in the country. The country had 466 districts in 1991.

India Political and Ethnic Zones: The weighted mean values of various biological traits

have been classified into 25 States and 7 Union Territories (U.T.) which have been categorised as follows (after Bhasin, 1988):

I. North India, II. West India, III. East India, IV. Central India, V. South India, and VI. Islands. Himalayan Region may be divided into three divisions, *i.e.,* A) Western Himalaya, B) Central Himalaya, and C) Eastern Himalaya as follows:

I. North India:

(A) Western Himalaya (S. No. 1, 2):

(1) Jammu and Kashmir, (2) Himachal Pradesh, (3) Punjab, (4) Chandigarh (U.T.), (5) Haryana, (6) Delhi (U.T.), (7) Uttar Pradesh

(B) Central Himalaya (S.No.7, Eight Districts of Uttar Pradesh)
[(i) Almora, (ii) Chamoli, (iii) Dehra Dun, (iv) Garhwal (Pauri), (v) Naini Tal, (vi) Pithoragarh, (vii) Tehri Garhwal, and (viii) Uttarkashi.] and 8. Rajasthan

II. *West India:*

(1) Gujarat, (2) Maharashtra, (3) Goa[2], (4) Daman and Diu[2] (U.T.) and (5) Dadra and Nagar Haveli (U.T.)

III. *East India:*

C) Eastern Himalaya: (S. No.1 to 8 and Darjeeling District of West Bengal)

(1) Arunachal Pradesh, (2) Assam, (3) Nagaland, (4) Manipur, (5) Mizoram, (6) Tripura, (7) Meghalaya, (8) Sikkim, (9) West Bengal, (10) Bihar, and (11) Orissa

IV. *Central India:*

(1) Madhya Pradesh

V. *South India:*

(1) Karnataka, (2) Andhra Pradesh, (3) Tamil Nadu, (4) Kerala and (5) Pondicherry (U.T.).

VI. *Islands:*

(1) Lakshadweep (U.T.) and (2) Andaman and Nicobar Islands (U.T.).

II. ETHNIC GROUPS

An aggregation of biological and socio-cultural characteristics constitutes an ethnic group. Within the category of Ethnic Group, we include Castes, Scheduled Castes, Scheduled Tribes and Communities (the names of Scheduled Castes and Scheduled Tribes after Manual of Election Law 1982, Government of India, New Delhi). Biological anthropological studies of such ethnic groups as well as "Communities" have been reported in India. By Community we generally refer to a group of people who may have occupational, linguistic, religious or regional characteristics (Bhasin 1988).

III. TRADITIONAL OCCUPATIONAL GROUPS

In the traditional society, there were occupational guilds. The *Chaturvarna* system with its division into *Brahman* (priestly caste), *Kshatriya* (warrior caste), *Vaishya* (land owners and traders) and *Sudra* (labouring caste) was based on occupational differentiation. The occupations are grade manual labour is looked down upon, and those dealing with swine-herding, scavenging, butchery, removal of night soil are regarded as polluting (Bhasin 1988). The caste based division of occupation is 1. Priesthood, 2. Warfare, 3. Trade and Commerce, 4. Agriculture, 5. Animal Husbandry, 6. Artisan, and 7. Menial Workers.

IV. LINGUISTIC GROUPS

Although the Schedule VIII recognizes fifteen languages in India, there are innumerable dialects which change after few scores of kilometers. Linguistic diversity is an important factor in the formation of regional groups, and it also reflects the regional differentiation. The four-fold regional division can be seen for the major languages, *i.e.,* (i) the Dravidian region of the south; (ii) the Indo-Aryan regions of the north and north-west; (iii) the Mon Khmer and the Tibeto-Burman region of the north-east and the Himalayan region; and (iv) the Austric region of the Aravalli-Vindhya-Chota Nagpur complex. These languages are again divided into sub-families and groups as follows:

Language Classification-Indian Languages

The family, branch, group and language of India are as follows:

I. AUSTRO-ASIATIC FAMILY
  Mon-Khmer Group (Mon-Khmer Branch)
  Munda Group (Munda Branch)
II. TIBETO-CHINESE FAMILY
  SIAMESE-CHINESE SUB-FAMILY
  Tai Group
  TIBETO-BURMAN SUB-FAMILY
  Tibeto-Himalayan Branch
  Bhotia Group (Tibetan Group)
  Himalayan Group (Pronominalized/Non-

Pronominalized Himalayan Group)
    North-East Frontier Group (North Assam Branch)
    Assam-Burmese Branch
    Bodo Group (Bara or Bodo Group)
    Naga Group
    Kachin Group
    Kuki-Chin Group
    Burma Group
III. DRAVIDIAN FAMILY
    South Dravidian Group
    Central Dravidian Group
    North Dravidian Group
IV. INDO-EUROPEAN FAMILY ARYAN SUB-FAMILY
    Dradic (or Pisacha) Branch
    Kafir Group
    Khowar Group
    Dard Group
    Indo-Aryan Branch:
    Outer Sub-Branch
    North-Western Group
    Southern Group
    Eastern Group
    Bihari Group (Bhojpuri, Maithili & Magahi Sub-Group)
    Mediate Sub-Branch/Inner Sub-Branch:
    Mediate Group/Central Group/Pahari Group
    Mediate Group/Central Group
    Pahari Group
    Eastern Pahari
    Central Pahari
    Western Pahari

MEAN WEIGHTED VALUES

To discern the pattern of regional groups, ethnic groups, traditional occupational groups and linguistic groups using the frequency data, the mean weighted values of the biological traits have been calculated and estimates for the various groups are presented.

GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G-6-PD) SYSTEM (E.C.1.1.1.49)

Glucose-6-phosphate dehydrogenase (G-6-PD) enzyme is necessary as a catalyst in a biological oxidation-reduction reaction of glucose-6-phosphate—one of the stages in the metabolism of carbohydrates. The G-6-PD deficiency disease was discovered when a number of Americans of African and Asian descent were treated with certain antimalarial drugs particularly primaquine, which produced a mild haemolysis in these individuals (Carson et al. 1956). Investigations showed them to be deficient in the red cell enzyme G-6-PD. A number of other drugs chemically related to primaquine produce haemolysis when given to individuals deficient in G-6-PD (WHO 1967). Favism, a haemolytic condition produced by eating fava beans (*Vicia fava*) is observed among populations living in the Mediterranean area and is believed to be connected with G-6-PD deficiency. The G-6-PD deficiency in red cells is inherited as an X-linked trait (chromosome location Xq28). Heterozygous females are usually intermediate between normal individuals and those clearly G-6-PD deficient.

Two common types referred to as A and B could be demon strated by electrophoresis. The commonest allele in all populations is *G6PD*B*. In Africans two other alleles *G6PD*A+* and *G6PD*A–* are also relatively common each with allele frequencies between 0.01 and 0.25 in different populations. In Mediterranean countries and the Middle East another allele *G6PD*Mediterranean* is relatively common. Certain electrophoretic variants also occur in Southeast Asia (*G6PD*Canton*) and in Greece (*G6PD*Athens*).

Investigations of enzyme in different human populations have shown many variants—more than 300 different variants have been described on the basis of their biochemical properties (Luzzatto and Mehta 1989; Beutler 1990) and most of them are relatively rare, but some have appreciable frequencies in certain localised populations. So far seven different G-6-PD variants namely—*G6PD* Andhra Pradesh* (Rattazzi 1966), *G6PD*Cutch* (Goshar 1979), *G6PD* Jammu* (Beutler 1975), *G6PD* Kalayan* (Ishwad and Naik 1984), *G6PD*Kerala* (Azevedo et al. 1968), *G6PD*Porbandar* (Cayani et al. 1977; Goshar 1979) and *G6PD*West Bengal* (Azevedo et al. 1968) have been reported from India. With the cloning and sequencing of G-6-PD the variants that were thought to be different have proven to be identical, and those that were thought to be the same are now seen to be heterogenous (Martini et al. 1986; Persico et al. 1986a, b; Takizawa et al. 1986 and Yoshida and Takizawa 1986).

Most of the studies on G-6-PD published prior

to the WHO Report (1967) were based on investigations carried out on patients in hospitals, manifesting clinical conditions such as haemoglobinuria, neonatal jaundice, drug-induced haemolytic anaemia etc. It has been estimated that approximately hundred million people suffer from G-6-PD deficiency in different parts of world (Azevedo et al. 1968; WHO 1967).

The Rhesus and ABO blood groups have been analysed in G-6-PD deficient and non-deficient samples. The frequency of Rhesus negatives was observed low among Sardinians and Congolese Bantus, both of whom show very high frequency of primaquine sensitivity (Sonnet and Michaux 1960). In the distribution of B and O groups, Tarlov et al. (1962) observed relative rarity of B group in deficients. However, Baxi et al. (1963) and Jolly et al. (1972) failed to observe such differences.

Prenatal selection and foetal development disturbances are reported in carriers of G-6-PD deficiency by Toncheva and Tzoneva (1985) and they observed that the incidence of spontaneous abortions in first trimester is higher (21.7 per cent) in the women of heterozygous carriers of G-6-PD deficiency as compared to control group (9.3 per cent).

Limited information on the distribution of G-6-PD phenotypes is available among the population groups reported from different areas. It is believed that red cell G-6-PD deficiency is one of the important markers to explore the eco- and pharmacogenetic aspects of a population, due to its association with past malarial incidence.

G-6-PD deficiency was mainly found in populations originating from tropical and sub-tropical areas of the world. The geographic distribution was similar to that of falciparum malaria and suggested that G-6-PD deficiency similar to the sickling trait owed its distribution to selection by this malarial organism. Evidence related to a correlation of the frequencies of the sickling gene and that of A-type of G-6-PD deficiency exists in African countries and that between β-Thalassemia and the Mediterranean type of G-6-PD deficiency in Sardinia.

The deficiency of G-6-PD is found in a belt extending from Mediterranean area through Southwest Asia and India to South east Asia. The *G6PD*def* is very much prevalent in Saudi Arabia (varies from 0.07 to 0.44). Perhaps the highest frequency of deficiency recorded is among Shia of Al Qatif, Saudi Arabia (0.44),

whereas the incidence in other Southwest Asian countries ranges from 0 to 0.21. From East Asian populations the frequency of *G6PD*def* is low (0.01 to 0.05). Among Khmer population from Vietnam (South east Asia) the frequency of *G6PD*def* is highest (0.15 to 0.35) and in Central and North-East Thailand the incidence is 0.11 to 0.17, but in most populations of Southeast Asian region the frequencies are less than 0.10. In the Indian region, it is around 0.19 (Mourant et al. 1976).

According to WHO Report (1966), the frequency of *G6PD*def* in India ranges between 0.04 and 0.19. Since most of the studies published prior to this report were based on investigations carried out on patients in hospitals, studies on well defined populations are too few to allow a fair estimate of regional variations in the enzyme deficiency.

From a total of 224 studies reported among Indian populations the frequency of *G6PD*def* is 0.045 (varies from complete absence to 0.271 among Angami Nagas studied by Seth and Seth 1971). The frequency is higher in East India zone (0.067 from 24 studies) as compared to other zones (Central India from 3 studies - 0.061; North Indian from 34 studies - 0.058; West India from 110 studies - 0.032 and South India from 53 studies - 0.032). From Himalayan region the frequency of *G6PD*def* is high (0.087) as compared to non-Himalayan region (0.043) from where only 15 studies are reported. Among scheduled tribes the frequency is highest (0.055) from 53 studies as compared to other ethnic groups (community from 93 studies - 0.049; caste from 49 studies - 0.036 and scheduled caste from 29 studies - 0.027). It has been observed that the number of studies available from different zones, regions and ethnic groups are not well distributed, therefore it is not possible to evaluate the distribution of this trait precisely (Table 1).

The frequency of *G6PD*def* is quite high from the Himalayan mountain complex [(0.095, varies from 0.030 to 0.271 among Nagas of Nagaland, in whom highest frequency is reported, albeit, recently Saha et al. (1990a) observed near absence of the allele among Nagas)] as compared to other natural regions. The frequency of deficients is 0.060 and 0.042 from monsoon type with dry winters and tropical savannah type climatic regions, respectively from where maximum number of studies have been conducted (Bhasin et al. 1994; Bhasin and Walter 2001).

Table 1: Glucose 6 Phosphate dehydrogenase system (Allele frequencies)

Particulars	Subjects studied	No. of studies	Frequency G6PD*def Mean	Min	Max
1. NATURAL REGION					
Himalayan Mountain Complex	836	7	**0.095**	0.030	0.271
Indus-Ganga-Brahmaputra Plains	11478	48	**0.057**	0.017	0.179
Peninsular Plateau	27169	169	**0.039**	0.000	0.196
Islands	-	0	-	-	-
2. CLIMATIC REGION					
Monsoon Type with Short Dry Season	2207	11	**0.011**	0.000	0.050
Monsoon Type with Dry Season	647	6	**0.016**	0.000	0.090
Tropical Savannah Type	23898	146	**0.042**	0.000	0.196
Semi Arid Steppe Type	260	4	**0.038**	0.000	0.125
Hot Desert Type	-	0	-	-	-
Monsoon Type with Dry Winters	12471	57	**0.060**	0.017	0.271
Cold Humid Winters with Short Summers	-	0	-	-	-
Polar Type	-	0	-	-	-
3. POLITICAL DIVISION OF INDIA					
I. NORTH INDIA					
A. Western Himalaya (S. No. 1, 2)					
1. Jammu and Kashmir	124	2	**0.057**	0.049	0.064
2. Himachal Pradesh	170	1	**0.095**	0.095	0.095
3. Punjab	5148	16	**0.048**	0.017	0.135
4. Chandigrah UT	1528	3	**0.075**	0.052	0.096
5. Haryana	49	1	**0.020**	0.020	0.020
6. Delhi UT	600	2	**0.025**	0.021	0.028
B. Central Himalaya (S. No. 7, Eight Districts of Uttar Pradesh)					
7. Uttar Pradesh	209	9	**0.079**	0.022	0.185
8. Rajasthan	-	0	-	-	-
II. WEST INDIA					
9. Gujarat	1473	14	**0.042**	0.000	0.138
10. Maharashtra	15446	88	**0.040**	0.000	0.190
11. Goa, Daman and Diu UT	418	5	**0.005**	0.000	0.011
12. Dadra and Nagar Haveli UT	238	3	**0.130**	0.064	0.196
III. EAST INDIA					
C. Eastern Himalaya (S. No. 13 to 20 and Darjeeling District of West Bengal)					
13. Arunachal Pradesh	-	0	-	-	-
14. Assam	558	5	**0.088**	0.043	0.158
15. Nagaland	85	1	**0.271**	0.271	0.271
16. Manipur	-	0	-	-	-
17. Mizoram	-	0	-	-	-
18. Tripura	-	0	-	-	-
19. Meghalaya	257	3	**0.062**	0.037	0.079
20. Sikkim	-	0	-	-	-
21. West Bengal	1799	14	**0.048**	0.017	0.140
22. Bihar	-	0	-	-	-
23. Orissa	200	1	**0.110**	0.110	0.110
IV. CENTRAL INDIA					
24. Madhya Pradesh	329	3	**0.061**	0.039	0.075
V. SOUTH INDIA					
25. Karnataka	87	1	**0.000**	0.000	0.000
26. Andhra Pradesh	6732	40	**0.036**	0.000	0.120
27. Tamil Nadu	280	6	**0.071**	0.000	0.125
28. Kerala	1809	6	**0.012**	0.000	0.050
29. Pondicherry UT	-	0	-	-	-
VI. ISLANDS					
30. Lakshadweep UT	-	0	-	-	-
31. Andman Islands and Nicobar Islands UT	-	0	-	-	-
3A. ZONES OF INDIA					
I. North India	9772	34	**0.058**	0.017	0.185
II. West India	17575	110	**0.041**	0.000	0.196
III. East India	2899	24	**0.067**	0.017	0.271
IV. Central India	329	3	**0.061**	0.039	0.075
V. South India	8908	53	**0.032**	0.000	0.125
VI. Islands	-	0	-	-	-
INDIA (TOTAL)	39483	224	**0.045**	0.000	0.271
3B. REGIONS OF HIMALAYA					
A. Western Himalaya	294	3	**0.079**	0.049	0.095
B. Central Himalaya	457	3	**0.072**	0.030	0.185
C. Eastern Himalaya	900	9	**0.098**	0.037	0.271
HIMALAYA (TOTAL)	1651	15	**0.087**	0.030	0.271
NON-HIMALAYAN REGIONS	37832	209	**0.043**	0.000	0.196
4. ETHNIC GROUP					
A. ZONES OF INDIA					
I. NORTH INDIA					
Caste	1813	10	**0.066**	0.022	0.185
Scheduled Caste	-	0	-	-	-
Scheduled Tribe	518	3	**0.056**	0.030	0.095
Community	7441	21	**0.057**	0.017	0.179
II. WEST INDIA					
Caste	2340	25	**0.017**	0.000	0.081
Scheduled Caste	4492	20	**0.030**	0.000	0.100
Scheduled Tribe	1805	17	**0.065**	0.000	0.196

Table 1: Contd.....

Particulars	Subjects studied	No. of studies	Frequency G6PD*def		
			Mean	Min	Max
Community	8939	48	**0.048**	0.000	0.190
III. EAST INDIA					
Caste	464	5	**0.040**	0.030	0.050
Scheduled Caste	103	1	**0.117**	0.117	0.117
Scheduled Tribe	776	8	**0.117**	0.037	0.271
Community	1556	10	**0.047**	0.017	0.110
IV. CENTRAL INDIA					
Caste	-	0	-	-	-
Scheduled Caste	-	0	-	-	-
Scheduled Tribe	120	1	**0.067**	0.067	0.067
Community	209	2	**0.057**	0.039	0.075
V. SOUTH INDIA					
Caste	686	9	**0.020**	0.000	0.052
Scheduled Caste	1327	8	**0.011**	0.000	0.042
Scheduled Tribe	2249	24	**0.026**	0.000	0.125
Community	4646	12	**0.042**	0.000	0.095
VI. ISLANDS					
Caste	-	0	-	-	-
Scheduled Caste	-	0	-	-	-
Scheduled Tribe	-	0	-	-	-
Community	-	0	-	-	-
INDIA					
Caste	5303	49	**0.036**	0.000	0.185
Scheduled Caste	5922	29	**0.027**	0.000	0.117
Scheduled Tribe	5468	53	**0.055**	0.000	0.271
Community	22790	93	**0.049**	0.000	0.190
B. REGIONS OF HIMALAYA					
A. Western Himalaya					
Caste	61	1	**0.049**	0.049	0.049
Scheduled Caste	-	0	-	-	-
Scheduled Tribe	170	1	**0.095**	0.095	0.095
Community	63	2	**0.064**	0.064	0.064
B. Central Himalaya					
Caste	109	1	**0.185**	0.185	0.185
Scheduled Caste	-	0	-	-	-
Scheduled Tribe	348	2	**0.037**	0.030	0.044
Community	-	0	-	-	-
C. Eastern Himalaya					
Caste	-	0	-	-	-
Scheduled Caste	103	1	**0.117**	0.117	0.117
Scheduled Tribe	612	7	**0.111**	0.037	0.271
Community	185	1	**0.043**	0.043	0.043
5. TRADITIONAL OCCUPATION					
Priesthood	3350	27	**0.025**	0.000	0.074

Particulars	Subjects studied	No. of studies	Frequency G6PD*def		
			Mean	Min	Max
Warfare	170	2	**0.136**	0.049	0.185
Trade and Commerce	1560	14	**0.049**	0.000	0.081
Agriculture	3356	22	**0.012**	0.000	0.067
Animal Husbandry	319	1	**0.000**	0.000	0.000
Artisans	17	1	**0.000**	0.000	0.000
Menial Workers	2991	12	**0.047**	0.000	0.117
No Information	27720	145	**0.051**	0.000	0.271
6. LANGUAGE GROUP					
I. AUSTRO-ASIATIC FAMILY					
Mon Khmer Group	100	1	**0.070**	0.070	0.070
Munda Group	164	1	**0.140**	0.140	0.140
II. TIBETO-CHINESE FAMILY					
(i) Siamese-Chinese Sub-Family					
Tai Group	-	0	-	-	-
(ii) Tibeto-Burman Sub-Family					
Bhotia Group	348	2	**0.037**	0.030	0.044
Himalayan Group	-	0	-	-	-
North East Frontier Group	130	1	**0.054**	0.054	0.054
Bodo Group	297	4	**0.105**	0.037	0.158
Naga Group	85	1	**0.271**	0.271	0.271
Kachin Group	-	0	-	-	-
Kuki Chin Group	-	0	-	-	-
III. DRAVIDIAN FAMILY					
South Dravidian Group	7268	37	**0.033**	0.000	0.125
Central Dravidian Group	1631	15	**0.029**	0.000	0.120
North Dravidian Group	-	0	-	-	-
IV. INDO-EUROPEAN FAMILY					
Dard Group	124	2	**0.057**	0.049	0.064
North Western Group	-	0	-	-	-
Southern Group	13385	76	**0.034**	0.000	0.196
Eastern Group	200	1	**0.110**	0.110	0.110
Bihari	1923	15	**0.043**	0.017	0.117
Central Group	12868	58	**0.060**	0.000	0.190
Pahari Group	170	1	**0.095**	0.095	0.095
Unspecified	-	0	-	-	-
Other Languages	412	4	**0.024**	0.013	0.035
No Information	378	5	**0.045**	0.031	0.061
6A. LANGUAGE FAMILY					
I. Austro Asiatic Family	264	2	**0.113**	0.070	0.140
II. Tibeto Chinese Family	860	8	**0.086**	0.030	0.271
III. Dravidian Family	8899	52	**0.033**	0.000	0.125
IV. Indo European Family	28670	153	**0.047**	0.000	0.196
Other Languages	412	4	**0.024**	0.013	0.035
No Information	378	5	**0.045**	0.031	0.061

The frequencies of *G6PD*def* allele in different zones and regions of India present a heterogeneous picture. From North India, the frequency of *G6PD*def* is comparatively high from all the States and Union Territories as observed from the states of Jammu and Kashmir (0.057 among Pandits and Muslims) and Himachal Pradesh (0.095 among Gaddis) from Western Himalayan region; Punjab (0.048, from where highest frequency is reported among Punjabis), Chandigarh (0.075, among Jat Sikhs - 0.096, Brahmins - 0.074 and Banias - 0.052) and Uttar Pradesh (0.079) and from Central Himalayan region (0.072), whereas from Harayana and Delhi low frequencies are observed (0.020 and 0.025, respectively). Similarly in West India, from the states of Gujarat and Maharashtra the frequencies of *G6PD*def* are high (0.042 and 0.040, respectively), Dadra and Nagar Haveli (0.130, Dhodia - 0.063 and Warlis - 0.196 tribal groups), whereas it is almost absent in Goa, Daman and Diu (Saraswat groups). From Bombay (Maharashtra) among Parsis frequency of *G6PD*def* is quite higher than their neighbours, the indigenous Indians. The Parsis came from Persia due to religious persecution after the fall of Zoroastrian Empire in A.D. 651. They settled down around Surat (Gujarat) and later Bombay city became one of their main clusters. Parsis are having a clear-cut genetic profile with a high frequency of *ry (RH*cDE)* in the Rhesus complex, G-6-PD deficiency and a previously unknown *GM*1,3,21* haplotype at a frequency of 0.03, very low *KM*1,* occasional presence of the HbAS trait and high frequency of *GC*1F* (0.48) and this shows that the Parsis as a result of migration, genetic drift, limited admixture and selection have changed their gene pool during the course of their 1300 years stay in their new location which is quite different from their ancestral one (Undevia 1973; Undevia et al. 1972, 1973; Steinberg et al. 1973; Undevia and Saha 1987). For the high frequency of *G6PD*def* explanation is that Parsis, mostly wealthy, had open 'tanks' in the centre of their dwelling compounds and in these mosquitoes were breeding and maintaining a very local endemicity of malaria (Mourant 1983).

From Central India, only one study is available on Bhil tribals among whom the frequency is high (0.067).

From South India, the frequency of *G6PD*def* is comparatively low (0.032) as observed from Karnataka (absent) and Kerala (0.012) except in Andhra Pradesh (0.036) and Tamil Nadu (0.071, high frequency may be due to a small sample of Kurumba tribal among whom quite high frequency is reported 0.125). From East India, the studies available from different areas are either none or a few. From the states of Assam and Meghalaya (Eastern Himalayan region) among the populations with Mongoloid affinities the frequencies are high (0.088 and 0.062, respectively) whereas from the state of West Bengal the frequency is 0.048 (where among all the studies, the allele *G6PD*def* is present and the frequency is highest among Santhal tribals - 0.140) and from Orissa in one study among general population the frequency is 0.110.

In general, the frequencies of *G6PD*def* are high in North and West India as compared to South India where the frequencies are uniformly low except in Andhra Pradesh and Tamil Nadu, whereas in East India the studies are not sufficient. However, it is observed that among the populations with Mongoloid affinities from Eastern Himalayan region the frequency is high and among all studies reported from West Bengal, the *G6PD*def* allele is present (Fig. 1).

The allele frequency of *G6PD*def* correlation with various climatic factors and altitude by different ethnic groups though showing significant differences are not high (Table 4).

Among all the different traditional occupational groups, *G6PD*def* allele is present and the similar frequencies are found among trade and commerce (0.049) and menial worker (0.047) groups, which indicates gene flow among them as also observed from the study of genetic markers already discussed (Bhasin et al. 1994; Bhasin and Walter 2001).

The frequency of *G6PD*def* is high among speakers of Pahari group (0.095), Dard group (0.057) of Indo-European; North East Frontier group (0.054), Bodo group (0.105) of Tibeto-Chinese; and Mon Khmer group (0.070) of Austro-Asiatic languages from Himalayan region. The frequency is high among the speakers of Central group of Indo-European languages (0.060) whereas among the speakers of Dravidian languages the frequencies are low (0.033 among South Dravidian group and 0.029 in Central Dravidian group). In Munda group, only one study is available, where the frequency is high (0.140).
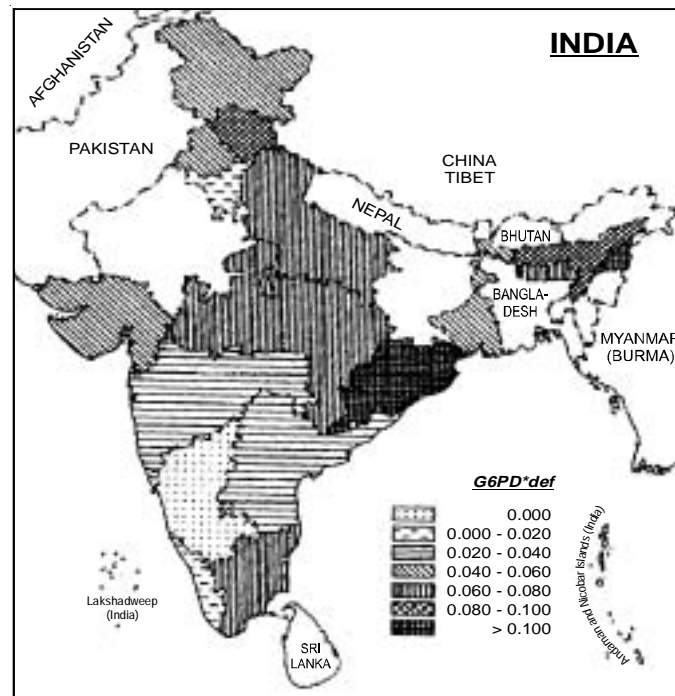
The origin of *G6PD*Mediterranean* allele in

Fig. 1. Allele *G6PD*def* of Glucose-6-Phosphate Dehydronenase System in different regions of India

India and its spread out throughout the region and possibility of malaria exerting pressure for its maintenance in Indian populations pose complicated problems.

About the origin of *G6PD*Mediterranean* allele Baxi (1974) reported that it appears this gene had its passage through the North and then spread throughout the adjoining regions as history records several contacts between the Mediterranean people and Indians. Hence there may be an ancient genetic link between the Greeks, Persians and other non-Semetic Near East inhabitants and the people of Northwest India. As a result, one might expect same similarities in the G-6-PD variants found in this area. It has been observed that in the distribution of *G6PD*def* allele among Indian populations, comparatively higher frequencies in the North and West indicate that considerable stability of the *G6PD*def* allele has been attained in these areas. On the other hand, frequencies in South India are uniformaly low except in Andhra Pradesh and Tamil Nadu and in Eastern India, it is difficult to comment as the studies available are few.

With regard to the possibility of malaria exerting selective pressure for the maintenance of the *G6PD*def* allele in Indian populations, it has been found that the distribution of G-6-PD is not closely related to that of malaria Table 3, (Fig. 4). Saha et al. (1990a) observed a very low frequency of *G6PD*def* among Naga, Hmar, Lepcha and Adi populations in the region of high malarial endemicity and reported this may be due to the fact that these people live at high altitude which probably caused relaxation of selection by malaria. On the other hand, the results of clinical and cellular studies seeking more direct evidence of resistance to malaria among G-6-PD deficient subjects have been somewhat contradictory. Thus it appears that the mechanism of protection afforded by variants of the G-6-PD gene may be complex. Further, the distribution of *G6PD*def* allele among Indian populations is difficult to interpret due to very wide range of environmental conditions to which they are exposed, their diversity in ethnic composition (consisting of racial elements of autochthonous, Caucasoid and Mongoloid) and existence of caste and tribal system among them.

The frequency of *G6PD*def* is 0.045 (varies from complete absence to 0.271) among Indian populations and it is high among scheduled tribes (0.055) as compared to other ethnic groups. The frequency is comparatively higher in North and West India zones, which indicates considerable stability of this allele in these areas, whereas in South India it is uniformly low except in Andhra Pradesh and Tamil Nadu and from East India the studies are too few to evaluate. Among the speakers of different languages, the frequencies are high in Mon Khmer group, North East Frontier group, Bodo group and Pahari group from Himalayan region and low among the speakers of Dravidian languages. The studies available from different ecological settings are not sufficient as yet to evaluate the distribution of this genetic marker in India, especially in connection with prevalence of malaria.

HAEMOGLOBIN

Haemoglobin is a tetramer that consists of two α-like and two β-like globin subunits. These subunits are encoded by two clusters of genes each of which is expressed sequentially during development. The earliest embryonic haemo-globin tetramer, Gower 1, consists of ϵ (β-like) and ζ (α-like) polypeptide chains. Beginning at approximately eight weeks of gestation the embryonic chains are gradually replaced by the adult α-globlin chain and two different foetal b-like chains, designated $^{G}\gamma$ and $^{A}\gamma$. During the transition period between embryonic and foetal development, HB Gower 2 ($\alpha_2 \epsilon_2$) and HB Portland ($\zeta_2 \gamma_2$) are detected. HB F($\alpha_2 \gamma_2$) eventually becomes the predominant HB tetramer throughout the remainder foetal life. Beginning just prior to birth, the γ-globin chains are gradually replaced by the adult β-and δ-globin poly-peptides. At six months after birth 97-98 per cent of the haemoglobin is $A_1(\alpha_2\beta_2)$, while $A_2(\alpha_2\delta_2)$, accounts for approximately 2 per cent. Small amounts of HB F (1 per cent) are also found in adult peripheral blood (Deisseroth et al. 1978; Embury et al. 1980; Maniatis et al. 1980). The loci for HB are assigned for haemoglobin alpha to chromosome 16 (16p13.3) and for haemoglobin beta, haemoglobin delta, haemoglobin gamma to chromosome 11 (11p.15.5).

Haemoglobin Variants

Normal adult human haemoglobin is composed of two different portions which can be separated by electrophoresis techniques; the major portion is called haemoglobin A_1 and the minor portion haemoglobin A_2. The difference between haemoglobin A and a number of aberrant human haemoglobins is a single amino acid sub-stitution in the α or β or γ or δ chain. Most of the mutant haemoglobins have been demonstrated to be under simple genetic control. A number of haemoglobins variant are associated with or produce clinical signs. Over 470 abnormal forms of haemoglobin have been described in the literature. Of them, one third are on the alpha (α) chain, the remaining being mostly on the beta (β) chain and a few on the gamma (γ) and delta (δ) chains. The term 'haemoglobinopathies' covers the group of hereditary abnormalities in which the structure (e.g. HB S, HB C, HB D, HB E) or the rate of synthesis (thalassaemia) of normal haemoglobin is altered.

A close concordance between the geographic distribution of endemic malaria and that of high frequency haemoglobin variants, thalassaemias and other red cell defects have been observed which represents one of the principal factors leading to the general acceptance of the malaria hypothesis *i.e.,* in a malarial environment, selective forces have acted to preserve hetero-zygotes of haemoglobin variants because of their advantage against malarial infection (Allison 1954 a,b, 1964; Livingstone 1957, 1967, 1971, 1983; Rucknagel and Neel 1961; Motulsky 1964; Durham 1983). The selective resistance of the heterozygote illustrates the concept of balanced polymorphism and may be contributory to the maintenance of high allele frequency in a parti-cular area. It is possible that there are still other factors that maintain this genetic equilibrium.

The general incidence of haemoglobin variants has been observed about 0.5 per cent from the Indian region. The abnormal haemo-globins observed among various population groups are HBS, HB E and HB D. The relatively rare abnormal haemoglobins reported from this region are HB J, HB K, HB L, HB M, HB Q, HB Lepore, HB Norfolk and the hereditary persistence of HB F. There are two principal types of thalassaemia namely alpha and beta. Beta thalassaemia is of two types: (i) Beta-thala-ssaemia major on which studies are available from all over India and (ii) Beta-thalassaemia minor, which is mostly reported from north and east India. Alpha thalassaemia is present in two forms: (i) Haemoglobin Barts and (ii) Haemoglobin H.

1. Haemoglobin S

One of the most interesting human haemoglobin mutant has been designated S, $Hb\alpha_2^A\beta_2^S$. The notation signifies that the mutation has affected the β-chain. In homozygous individuals $Hb\alpha_2^A\beta_2^S$ and small amount of $Hb\alpha_2^A\delta_2^{A2}$ are found. In heterozygous individuals three components are found $Hb\alpha_2^A\beta_2^A$, $Hb\alpha_2^A\beta_2^S$ and $Hb\alpha_2^A\delta_2^{A2}$. Haemoglobin S may be separated from haemoglobin A by electrophoresis or by performing sickling test on fresh blood. The sickling of red cells of homozygotes (Hb SS– *HB*S/HB*S*) is more severe than that of heterozygotes (HB AS–*HB*A/HB*S*).

Genetic load of sickle cell anemia is indeed very high affecting not only the health and physical performance but poses also a challenge to the health services. It is estimated that 186096 cases of sickle cell anemia are present in the Indian sub-continent. Each patient is not only burden on the health services but also affects normal family life (Bhatia, 1987).

The sickle cell trait occurs with highest frequency in tropical Africa (0.100 to 0.400), with high frequency in India, Greece and Southern Turkey (0.050 to 0.100) and less than 0.100 among the population groups living around the Mediterranean Sea (Palestine, Tunisia, Algeria and Sicily) and shows a distribution continuous throughout these areas.

Among the problems which the abnormal haemoglobins present is the one of interaction of alleles for the b-chain variants. Haemoglobin S is also known to occur with other abnormal haemoglobins. They are: Sickle cell HB C (*HB*S/ HB*C*), Sickle cell HB D (*HB*S/HB*D*), Sickle cell HB E (*HB*S/HB*E*), Sickle cell Thalassaemia (*HB*S/b*THAL*), Sickle cell associated with foetal haemoglobin other than during infancy.

With regard to the origin of sickle cell gene, there has been much debate whether the extensive geographical occurrence of sickle-cell disease can be explained by a single origin of the mutation with subsequent large scale migration in prehistoric times or whether it relates to multicentric origins (Lehmann 1953; 1954a,b, 1956-57; Lehmann and Cutbush 1952 a,b; Lehmann et al. 1956; Livingstone 1967). These queries have been examined by an analysis of restriction site polymorphisms (RFLPs) linked to *HB*S* globin gene; Kan and Dozy (1980) observed differences in the association of sickle cell gene which constituted a base for the hypothesis of multiple mutation origin of *HB*S*. Subsequently studies of an array of RFLPs linked to the *HB*S* mutation in Jamaicans (Wainscoat et al. 1983; Antonarakis et al. 1984), U.S. Americans (Antonarakis et al. 1984) and African Blacks (Pagnier et al. 1984) strongly supported the hypothesis that the *HB*S* mutation has arisen independently on several occasions in Africa. The distribution of the different *HB*S* haplotypes among six different population groups of Africa and Asia by Kalozik et al. (1986) provided strong evidence for an independent Asian origin of mutation. Migration of West African population carrying *HB*S* Mutation to North Africa, the Mediterranean and West Saudi Arabia is suggested from the analysis but no haplotype has been found by them in their Indian and East Saudi Arabian samples that predominantly showed the major Asian *HB*S* mutation. They further added that whether the Asian *HB*S* mutation originated in East Saudi Arabia and spread to India possibly with the Arab expansion in the first millennium A.D. (Bowles 1977) as suggested previously (Lehmann et al. 1963) or vice versa, possibly carried by Indian Arabic trade routes (Bowles 1977) is not known. They concluded that the geographical distribution of Asian *HB*S* haplotype as observed by them corresponds to the reported distribution of mild homozygous SS *(HB*S/ HB*S)* disease associated with high levels of HB F (Ali 1970; Haghsenass et al. 1977; Pembrey et al. 1978; Perrine et al. 1978; Brittenham et al. 1979; Weatherall and Clegg 1981; Acquaye et al. 1985; Bakioglu et al. 1985).

The HB S trait is prevalent in Africa with lesser frequencies in the Mediterranean basin, Saudi Arabia and also in India where average frequency *HB*S* is 0.031. Geographic and climatic factors have been suggested as determinants for the understanding the observed variations (Charmot and Lefevre-Witier 1978; Lefevre-Witier 1985). The frequency of *HB*S* is highest in the peninsular plateau (0.039), whereas in other natural regions, it is either absent or present in a very low frequency (Table 2). The frequency of *HB*S* is quite high in semiarid steppe type region (0.071) followed by tropical savannah type region (0.039) as compared to monsoon type with dry winters region (0.003) (Bhasin et al. 1994; Bhasin and Walter 2001).

It was in the Nilgiri Hills that sickle cell trait

was first detected in India (Lehmann and Cutbush 1952a, b, c) and among Indian populations the frequency of this trait is 0.031 (varies from complete absence to 0.410). It is present in high frequency among the scheduled tribes (0.054) as compared to other ethnic groups -caste (negligible), scheduled caste (0.024) and community (0.011). The trait is reported to be present among scheduled castes and communities, who are living in close proximity with tribal populations. Therefore the trait has been transmitted among these groups due to admixture with tribal groups. In North India, the trait is absent, except sporadic incidences, which may be due to admixture or traces of the past populations who have migrated or displaced by other populations.

The numerous tribal populations inhabiting Rajasthan and West India zone are known by the generic term 'Bhil'. Sickle cell trait is present among all of them, but the regional variation in the frequencies of the trait is very large (varies from complete absence to 0.167). The presence of sickle cell trait in the Parsis of Bombay indicates admixture with the neighbouring tribes of Gujarat and Maharashtra (Undevia et al. 1972). This observation is consistent with the presence of *GM*1,5,13,14* haplotype and G-6-PD deficiency among Parsis.

From Central India (Madhya Pradesh) among 'Gond' group of tribal populations the frequency of sickle cell trait in general varies from 0.10 to 0.14. Eastern India inhabited by the Kol/Munda group of populations (Kol, Munda, Ho, Bhuniya, Kharia, Santal, Khairwar, Chero, Bhumij etc.) is characterised by general absence of sickle cell trait. In addition to Kol/Munda group of populations Eastern India is also inhabited by Gond/Khond in Orissa among whom the trait is present; the trait is present in quite high frequency among the tribals from Koraput district of Orissa. From the Eastern Himalayan region sickle cell trait is almost absent except in the state of Assam where *HB*S* incidence is reported amongst the tea garden workers (Batabyal and Wilson 1958; Dunlop and Mozumdar 1952). It has been ascribed to the origin of these population groups mainly in Orissa, where *HB*S* is not uncommon followed by migration to Assam (Roy and Roy Chaudhuri 1967). Flatz et al. (1972) have suggested that the *HB*S* allele is being introduced into the general Assamese population due to the current lowering of social barriers.

Unlike the Bhil, Gond and Kol/Munda groups of Western, Central and Eastern India, there is no such embracing generic term to signify the tribals of Southern India, though this area is inhabited by a large number of small tribal populations. In between the areas of Nilgiri Hills and Wynad plateau, among the tribal populations—Kurumba, Irula, Paniyan, Yerava, Soliga, Adiyan etc., the frequency of sickle cell trait is quite high (varies from 0.18 to 0.32) as compared to Jenu Kurumba, Betta Kurumba, Muduga, Malasaar, Badagas and Todas among whom the frequencies are quite low (varies from 0.03 to 0.08), while the allele is almost absent among Kotas of Nilgiri and Paliyar and Paliyan of Palni, Kadar of Anamalai and Kanikar, Malapantram, Kuruvan, Ulladan of Cardamon Hills although these areas were hyperendemic for malaria. The HbS trait is present among Siddis of African desent, whereas it is absent among Andamanese (Negrito) of Andaman Islands. Among Nicobarese with Mongoloid affinity of Nicobar Islands the trait is also absent.

The sickling allele is, therefore, spread over the Central Belt from Gujarat through Madhya Pradesh to Orissa in East and over the Western tract from Gujarat through Maharashtra to South of Kerala. Gene flow for *HB*S*, however, showed a decline from South to North, but not from East to West (Fig. 2).

The correlations of frequencies of sickle cell with various climatic factors and altitude by different ethnic groups show significant differences but these are not high (Table 4).

Among the occupational groups the sickle cell trait is absent among the warfare, trade and commerce, and priesthood groups, *i.e.,* among higher caste groups, whereas the frequency of *HB*S* is high among the menial workers—scheduled castes (0.037); the trait has been transmitted among them due to admixture with tribal groups, who were living in close proximity (Bhasin et al. 1994; Bhasin and Walter 2001).

The *HB*S* allele is absent among the speakers of Mon Khmer group of Austro-Asiatic, different groups of Indo-European and Pahari group of Indo-European langauges from the Himalayan region, most of which are having Mongoloid affinities. The trait is either absent (Bihari group of Indo-European family) or present in very low frequency (0.010) among Munda group of Austro-Asiatic speakers as compared to Indo-European and Dravidian languages speakers (0.027 and 0.047, respectively).

Table 2: Haemoglobin system (Allele Frequencies)

Particulars	Subjects studied	No. of studies	Frequency HB*A			Frequency HB*S			Frequency HB*E		
			Mean	Min	Max	Mean	Min	Max	Mean	Min	Max
1. NATURAL REGION											
Himalayan Mountain Complex	2778	25	**0.987**	0.909	1.000	**0.000**	0.000	0.000	**0.013**	0.000	0.091
Indus-Ganga-Brahmaputra Plains	9578	48	**0.883**	0.354	1.000	**0.004**	0.000	0.113	**0.114**	0.000	0.646
Peninsular Plateau	47999	296	**0.956**	0.465	1.000	**0.039**	0.000	0.410	**0.005**	0.000	0.535
Islands	181	2	**1.000**	1.000	1.000	**0.000**	0.000	0.000	**0.000**	0.000	0.000
2. CLIMATIC REGION											
Monsoon Type with Short Dry Season	2683	21	**0.970**	0.806	1.000	**0.030**	0.000	0.194	**0.000**	0.000	0.000
Monsoon Type with Dry Season	3827	16	**0.988**	0.815	1.000	**0.012**	0.000	0.185	**0.000**	0.000	0.000
Tropical Savannah Type	35957	218	**0.961**	0.590	1.000	**0.039**	0.000	0.410	**0.000**	0.000	0.000
Semi Arid Steppe Type	4968	35	**0.929**	0.600	1.000	**0.071**	0.000	0.400	**0.000**	0.000	0.000
Hot Desert Type	-	0	-	-	-	-	-	-	-	-	-
Monsoon Type with Dry Winters	13101	81	**0.892**	0.354	1.000	**0.003**	0.000	0.113	**0.105**	0.000	0.646
Cold Humid Winters with Short Summers	-	0	-	-	-	-	-	-	-	-	-
Polar Type	-	0	-	-	-	-	-	-	-	-	-
3. POLITICAL DIVISION OF INDIA											
I. NORTH INDIA											
A. Western Himalaya (S. No. 1, 2)											
1. Jammu and Kashmir	-	0	-	-	-	-	-	-	-	-	-
2. Himachal Pradesh	-	0	-	-	-	-	-	-	-	-	-
3. Punjab	494	3	**1.000**	1.000	1.000	**0.000**	0.000	0.000	**0.000**	0.000	0.000
4. Chandigrah UT	114	1	**0.989**	0.989	0.989	**0.011**	0.011	0.011	**0.000**	0.000	0.000
5. Haryana	-	0	-	-	-	-	-	-	-	-	-
6. Delhi UT	-	0	-	-	-	-	-	-	-	-	-
B. Central Himalaya (S. No. 7, Eight Districts of Uttar Pradesh)											
7. Uttar Pradesh	3237	8	**0.989**	0.887	1.000	**0.010**	0.000	0.113	**0.001**	0.000	0.005
8. Rajasthan	343	3	**0.917**	0.882	0.951	**0.083**	0.049	0.118	**0.000**	0.000	0.000
II. WEST INDIA											
9. Gujarat	4281	30	**0.935**	0.833	1.000	**0.065**	0.000	0.167	**0.000**	0.000	0.000
10. Maharashtra	17342	84	**0.977**	0.857	1.000	**0.023**	0.000	0.143	**0.000**	0.000	0.000
11. Goa, Daman and Diu UT	601	2	**0.999**	0.999	1.000	**0.001**	0.000	0.001	**0.000**	0.000	0.000
12. Dadra and Nagar Haveli UT	276	3	**0.920**	0.886	0.982	**0.080**	0.018	0.014	**0.000**	0.000	0.000
III. EAST INDIA											
C. Eastern Himalaya (S. No. 13 to 20 and Darjeeling District of West Bengal)											
13. Arunachal Pradesh	-	0	-	-	-	-	-	-	-	-	-
14. Assam	3506	23	**0.697**	0.354	0.949	**0.000**	0.000	0.005	**0.303**	0.051	0.646
15. Nagaland	-	0	-	-	-	-	-	-	-	-	-
16. Manipur	417	3	**0.934**	0.909	0.968	**0.000**	0.000	0.000	**0.066**	0.032	0.091
17. Mizoram	-	0	-	-	-	-	-	-	-	-	-
18. Tripura	-	0	-	-	-	-	-	-	-	-	-
19. Meghalaya	708	6	**0.637**	0.465	0.802	**0.000**	0.000	0.000	**0.363**	0.198	0.535
20. Sikkim	1080	20	**0.994**	0.953	1.000	**0.000**	0.000	0.000	**0.006**	0.000	0.047
21. West Bengal	3508	15	**0.992**	0.981	1.000	**0.001**	0.000	0.006	**0.007**	0.000	0.019
22. Bihar	1321	12	**0.999**	0.992	1.000	**0.001**	0.000	0.008	**0.000**	0.000	0.000
23. Orissa	1506	10	**0.954**	0.860	1.000	**0.046**	0.000	0.140	**0.000**	0.000	0.000
IV. CENTRAL INDIA											
24. Madhya Pradesh	4514	39	**0.939**	0.800	1.000	**0.061**	0.000	0.200	**0.000**	0.000	0.000
V. SOUTH INDIA											
25. Karnataka	1398	9	**0.918**	0.590	1.000	**0.082**	0.000	0.410	**0.000**	0.000	0.000
26. Andhra Pradesh	6399	36	**0.962**	0.817	1.000	**0.038**	0.000	0.183	**0.000**	0.000	0.000
27. Tamil Nadu	6282	36	**0.953**	0.815	1.000	**0.047**	0.000	0.185	**0.000**	0.000	0.000
28. Kerala	3028	26	**0.955**	0.806	1.000	**0.045**	0.000	0.194	**0.000**	0.000	0.000
29. Pondicherry UT	-	0	-	-	-	-	-	-	-	-	-
VI. ISLANDS											
30. Lakshadweep UT	-	0	-	-	-	-	-	-	-	-	-
31. Andman Islands and	68	1	**1.000**	1.000	1.000	**0.000**	0.000	0.000	**0.000**	0.000	0.000
Nicobar Islands UT	113	1	**1.000**	1.000	1.000	**0.000**	0.000	0.000	**0.000**	0.000	0.000
3A. ZONES OF INDIA											
I. North India	4188	15	**0.985**	0.882	1.000	**0.015**	0.000	0.118	**0.001**	0.000	0.005
II. West India	22500	119	**0.989**	0.833	1.000	**0.031**	0.000	0.167	**0.000**	0.000	0.000
III. East India	12046	89	**0.880**	0.354	1.000	**0.006**	0.000	0.140	**0.114**	0.000	0.646
IV. Central India	4514	39	**0.939**	0.800	1.000	**0.061**	0.000	0.200	**0.000**	0.000	0.000
V. South India	17107	107	**0.954**	0.590	1.000	**0.046**	0.000	0.410	**0.000**	0.000	0.000
VI. Islands	181	2	**1.000**	1.000	1.000	**0.000**	0.000	0.000	**0.000**	0.000	0.000
INDIA (TOTAL)	60536	371	**0.946**	0.354	1.000	**0.031**	0.000	0.410	**0.023**	0.000	0.646

Table 2: Contd.......

Particulars	Subjects studied	No. of studies	Frequency HB*A			Frequency HB*S			Frequency HB*E		
			Mean	*Min*	*Max*	*Mean*	*Min*	*Max*	*Mean*	*Min*	*Max*
3B. REGIONS OF HIMALAYA											
A. Western Himalaya	-	0	-	-	-	-	-	-	-	-	-
B. Central Himalaya	1281	2	0.999	**0.999**	1.000	**0.000**	0.000	0.000	**0.001**	0.000	0.001
C. Eastern Himalaya	5711	52	0.763	**0.354**	1.000	**0.000**	0.000	0.005	**0.237**	0.000	0.646
HIMALAYA (TOTAL)	6992	54	0.806	**0.354**	1.000	**0.000**	0.000	0.005	**0.193**	0.000	0.646
NON-HIMALAYAN REGIONS	53544	317	0.964	**0.590**	1.000	**0.035**	0.000	0.410	**0.000**	0.000	0.019
4. ETHNIC GROUP											
A. ZONES OF INDIA											
I. NORTH INDIA											
Caste	976	4	0.999	0.995	**1.000**	0.000	**0.000**	0.000	0.001	**0.000**	0.005
Scheduled Caste	1112	3	0.970	**0.887**	0.999	0.029	0.000	0.113	**0.001**	0.000	0.001
Scheduled Tribe	274	3	0.920	**0.882**	1.000	0.080	0.000	0.118	0.000	0.000	0.000
Community	1826	5	0.995	**0.951**	1.000	**0.004**	0.000	0.049	**0.001**	0.000	0.001
II. WEST INDIA											
Caste	1499	12	1.000	0.999	**1.000**	0.000	**0.000**	0.001	0.000	**0.000**	0.000
Scheduled Caste	6160	34	0.978	**0.880**	1.000	**0.022**	0.000	0.120	**0.000**	0.000	0.000
Scheduled Tribe	7569	46	0.941	**0.833**	1.000	**0.059**	0.000	0.167	**0.000**	0.000	0.000
Community	7272	27	0.984	**0.857**	1.000	**0.016**	0.000	0.143	**0.000**	0.000	0.000
III. EAST INDIA											
Caste	992	11	0.988	**0.949**	1.000	**0.000**	0.000	0.000	**0.012**	0.000	0.051
Scheduled Caste	1048	9	0.898	**0.650**	1.000	**0.000**	0.000	0.000	**0.102**	0.000	0.350
Scheduled Tribe	5809	43	0.853	**0.354**	1.000	**0.013**	0.000	0.140	**0.134**	0.000	0.646
Community	4197	26	0.886	**0.597**	1.000	**0.000**	0.000	0.005	**0.114**	0.000	0.403
IV. CENTRAL INDIA											
Caste	350	3	1.000	1.000	**1.000**	0.000	**0.000**	0.000	0.000	**0.000**	0.000
Scheduled Caste	511	7	0.902	**0.800**	0.981	**0.098**	0.019	0.200	**0.000**	0.000	0.000
Scheduled Tribe	3068	24	0.931	**0.857**	1.000	**0.069**	0.000	0.143	**0.000**	0.000	0.000
Community	585	5	0.975	**0.877**	1.000	**0.025**	0.000	0.123	**0.000**	0.000	0.000
V. SOUTH INDIA											
Caste	2094	10	0.999	0.990	**1.000**	0.001	**0.000**	0.010	0.000	**0.000**	0.000
Scheduled Caste	3029	13	0.997	**0.858**	1.000	**0.023**	0.000	0.142	**0.000**	0.000	0.000
Scheduled Tribe	9850	70	0.930	**0.590**	1.000	**0.070**	0.000	0.410	**0.000**	0.000	0.000
Community	2134	14	0.986	**0.952**	1.000	**0.014**	0.000	0.048	**0.000**	0.000	0.000
VI. ISLANDS											
Caste	-	0	-	-	-	-	-	-	-	-	-
Scheduled Caste	-	0	-	-	-	-	-	-	-	-	-
Scheduled Tribe	181	2	1.000	**1.000**	1.000	**0.000**	0.000	0.000	**0.000**	0.000	0.000
Community	-	0	-	-	-	-	-	-	-	-	-
INDIA											
Caste	5911	40	0.997	0.949	**1.000**	0.000	**0.000**	0.010	0.002	**0.000**	0.051
Scheduled Caste	11860	66	0.966	**0.650**	1.000	**0.024**	0.000	0.200	**0.009**	0.000	0.350
Scheduled Tribe	26751	188	0.917	**0.354**	1.000	**0.054**	0.000	0.410	**0.029**	0.000	0.646
Community	16014	77	0.959	**0.597**	1.000	**0.011**	0.000	0.143	**0.030**	0.000	0.403
B. REGIONS OF HIMALAYA											
A. Western Himalaya											
Caste	-	0	-	-	-	-	-	-	-	-	-
Scheduled Caste	-	0	-	-	-	-	-	-	-	-	-
Scheduled Tribe	-	0	-	-	-	-	-	-	-	-	-
Community	-	0	-	-	-	-	-	-	-	-	-
B. Central Himalaya											
Caste	-	0	-	-	-	-	-	-	-	-	-
Scheduled Caste	-	0	-	-	-	-	-	-	-	-	-
Scheduled Tribe	64	1	1.000	**1.000**	1.000	**0.000**	0.000	0.000	**0.000**	0.000	0.000
Community	1217	1	0.999	**0.999**	0.999	**0.000**	0.000	0.000	**0.001**	0.001	0.001
C. Eastern Himalaya											
Caste	474	7	0.982	0.949	**1.000**	0.000	**0.000**	0.000	0.018	**0.000**	0.051
Scheduled Caste	505	5	0.789	**0.650**	1.000	**0.000**	0.000	0.000	**0.211**	0.000	0.350
Scheduled Tribe	2380	19	0.673	**0.354**	1.000	**0.000**	0.000	0.000	**0.327**	0.000	0.646
Community	2352	21	0.805	**0.597**	1.000	**0.000**	0.000	0.005	**0.195**	0.000	0.403
5. TRADITIONAL OCCUPATION											
Priesthood	3239	22	0.997	**0.949**	1.000	**0.000**	0.000	0.004	**0.003**	0.000	0.051
Warfare	100	1	1.000	**1.000**	1.000	**0.000**	0.000	0.000	**0.000**	0.000	0.000
Trade and Commerce	1290	10	0.997	**0.987**	1.000	**0.000**	0.000	0.000	**0.003**	0.000	0.013

Table 2: Contd.......

Particulars	Subjects studied	No. of studies	Frequency HB*A			Frequency HB*S			Frequency HB*E		
			Mean	*Min*	*Max*	*Mean*	*Min*	*Max*	*Mean*	*Min*	*Max*
Agriculture	4085	26	**0.997**	0.885	1.000	**0.000**	0.000	0.010	**0.003**	0.000	0.115
Animal Husbandry	307	1	**1.000**	1.000	1.000	**0.000**	0.000	0.000	**0.000**	0.000	0.000
Artisans	-	0	-	-	-	-	-	-	-	-	-
Menial Workers	7772	41	**0.951**	0.650	1.000	**0.037**	0.000	0.200	**0.012**	0.000	0.350
No Information	43733	270	**0.934**	0.354	1.000	**0.037**	0.000	0.410	**0.029**	0.000	0.646
6. LANGUAGE GROUP											
I. AUSTRO-ASIATIC FAMILY											
Mon Khmer Group	313	3	**0.858**	0.775	1.000	**0.000**	0.000	0.000	**0.142**	0.000	0.225
Munda Group	2662	18	**0.989**	0.938	1.000	**0.010**	0.000	0.062	**0.000**	0.000	0.005
II. TIBETO-CHINESE FAMILY											
(i) Siamese-Chinese Sub-Family											
Tai Group	-	0	-	-	-	-	-	-	-	-	-
(ii) Tibeto-Burman Sub-Family											
Bhotia Group	214	3	**0.990**	0.987	1.000	**0.000**	0.000	0.000	**0.010**	0.000	0.013
Himalayan Group	741	14	**0.995**	0.953	1.000	**0.000**	0.000	0.000	**0.005**	0.000	0.047
North East Frontier Group	662	6	**0.658**	0.597	0.736	**0.000**	0.000	0.000	**0.342**	0.264	0.403
Bodo Group	1520	9	**0.536**	0.354	0.802	**0.000**	0.000	0.000	**0.464**	0.198	0.646
Naga Group	-	0	-	-	-	-	-	-	-	-	-
Kachin Group	-	0	-	-	-	-	-	-	-	-	-
Kuki Chin Group	308	2	**0.922**	0.909	0.929	**0.000**	0.000	0.000	**0.078**	0.071	0.091
III. DRAVIDIAN FAMILY											
South Dravidian Group	13928	86	**0.960**	0.590	1.000	**0.040**	0.000	0.410	**0.000**	0.000	0.000
Central Dravidian Group	5104	33	**0.933**	0.817	1.000	**0.067**	0.000	0.183	**0.000**	0.000	0.000
North Dravidian Group	647	5	**0.948**	0.860	1.000	**0.052**	0.000	0.140	**0.000**	0.000	0.000
IV. INDO-EUROPEAN FAMILY											
Dard Group	-	0	-	-	-	-	-	-	-	-	-
North Western Group	177	2	**0.907**	0.860	0.973	**0.093**	0.027	0.140	**0.000**	0.000	0.000
Southern Group	13589	70	**0.976**	0.800	1.000	**0.024**	0.000	0.200	**0.000**	0.000	0.000
Eastern Group	1027	10	**0.908**	0.858	1.000	**0.092**	0.000	0.142	**0.000**	0.000	0.000
Bihari	4806	25	**0.923**	0.650	1.000	**0.000**	0.000	0.005	**0.077**	0.000	0.350
Central Group	14266	77	**0.965**	0.833	1.000	**0.034**	0.000	0.167	**0.000**	0.000	0.005
Pahari Group	189	4	**0.997**	0.990	1.000	**0.000**	0.000	0.000	**0.003**	0.000	0.010
Unspecified	-	0	-	-	-	-	-	-	-	-	-
Other Languages	283	3	**0.988**	0.975	1.000	**0.012**	0.000	0.025	**0.000**	0.000	0.000
No Information	100	1	**0.917**	0.917	0.917	**0.083**	0.083	0.083	**0.000**	0.000	0.000
6A. LANGUAGE FAMILY											
I. Austro Asiatic Family	2975	21	**0.975**	0.775	1.000	**0.009**	0.000	0.062	**0.015**	0.000	0.225
II. Tibeto Chinese Family	3445	34	**0.721**	0.354	1.000	**0.000**	0.000	0.000	**0.279**	0.000	0.646
III. Dravidian Family	19679	124	**0.953**	0.590	1.000	**0.047**	0.000	0.410	**0.000**	0.000	0.000
IV. Indo European Family	34054	188	**0.962**	0.650	1.000	**0.027**	0.000	0.200	**0.011**	0.000	0.350
Other Languages	283	3	**0.988**	0.975	1.000	**0.012**	0.000	0.025	**0.000**	0.000	0.000
No Information	100	1	**0.917**	0.917	0.917	**0.083**	0.083	0.083	**0.000**	0.000	0.000

2. Haemoglobin E

Unlike haemoglobin S, both the homozygote and heterozygote of haemoglobin E (β chain variant) are found in healthy individuals. Similarly, those individuals which have a combination of sickle cell and HB E (*HB*S/HB*E*) also seem to be healthy.

The HBE, first reported in a child whose father was partly of Indian origin, has since then been found in Thailand, Burma, North Eastern Malaya, Indonesia, Assam, Bengal, Nepal, Ceylon and in an Eti-Turk.

The β^E-globin gene is quite common in Southeast Asia (gene frequencies approaching as high as 0.20 to 0.30) and presumably it produces mild form of β-thalassaemia (Orkin et al. 1982) and thereby is under a positive selection in areas in which malaria is endemic. Using restriction analysis multiple origins of β^E mutation have been pointed out. In fact, β^E mutation has been observed in five different haplotypes (restriction endonucleases), three in Southeast Asians (Antonarakis et al., 1982) and two in Europeans (Kazaziani et al., 1984). These haploytpes may be found in association with two different β-globin gene frameworks in Southeast Asians, and a third framework in Europeans. Using restriction analysis at eight restriction sites, Hundrieser et al. (1988a) studied Bodo group - Kachari of Tibeto-Burman languages in Assam among whom highest known prevalence of haemoglobin
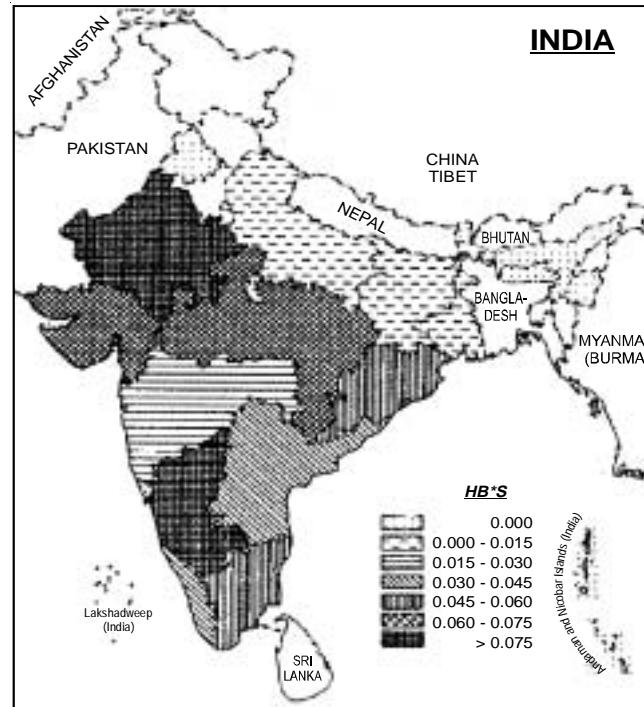
Fig. 2. Allele *HB*S* of Hemoglobin variants in different regions of India

E has been reported (Das et al. 1988) and found a common origin of the *HB*E* gene in Southeast Asia and Assam. This was surprising since main area of the distribution of *HB*E* is Southeast Asia and in contrast other Assamese populations *e.g.* Ahom and Khasi, the Tibeto-Burman groups have no direct links with Southeast Asians.

The pattern of distribution of *HB*E* and malarial infection in Southeast Asia and North East India suggests the introduction of *HB*E* from Southeast Asia and attainment of higher frequencies in certain populations, probably because of continued selective pressure of malarial infection (Saha 1990).

Haemoglobin E, one of the most frequent haemoglobin variants, occurs principally in populations of Southeast Asia. Within this region *HB*E* has been found with a frequency of nearly 0.60 in some isolated areas (Flatz 1967; Na-Nakorn et al. 1956; Na-Nakorn and Wasi 1978; Wasi et al. 1967; Wasi 1983); the highest incidence occurs at the junction of Laos, Thailand and Cambodia in what has been referred to the the "*HB*E* Triangle" (Na-Nakron and Wasi 1978). Among Filipinos *HB*E* is almost absent. In general, all

over Indonesia the frequency of *HB*E* varies from 0.01 to 0.05 and in Malayan population it ranges in between 0.05 and 0.10 with a few exceptions. Among Burmese the overall incidence is around 0.25 to 0.30. From East Asia, the frequency *HB*E* is reported 0.01 to 0.02. It is absent among Tibetans. Among the populations of Southwest Asian region the *HB*E* has not been observed, except among Iranian, where it is reported about 0.01. From Indian region, the frequency of *HB*E* is reported from 0.004 to 0.040 among Nepalies. Its frequency is around 0.01 to 0.05 from Bhutan. The frequency *HB*E* is less than 0.01 in the populations from Pakistan and it is also observed among Bengali Muslims of Bangladesh. *HB*E* is present in Bengal and in high frequency in Assam; in other parts of India sporadic cases have been reported. Livingstone (1964) stated that there appears to be a stronger neighbourhood of Calcutta with *HB*E* predo-minating in the east and *HB*S* in the west. *HB*E* was suggested as a marker for the Mongoloid element in Northeast Indian populations (Flatz 1978).

A low frequency of *HB*E* has been observed among Sinhalese, Tamils and Muslims of

Sri Lanka by Saha (1988a). Whereas Veddahs in Sri Lanka have been reported to have a high frequency of *HB*E* (Kirk et al. 1962; Wickremasinghe et al. 1963), Wickremasinghe and Ponnuswamy (1963) found no *HB*E* in more than 1000 samples of Sinhalese, while De Silva et al. (1959) had reported a high frequency in one locality of Sri Lanka apparently due to admixture with Veddahs in that area. An important feature to note is that the incidence of *HB*E* is very low and is present in both the Sinhalese and the Tamils of Sri Lanka. Saha stated that this suggests that *HB*E* has originated with the Veddahs rather than being introduced from Southeast Asia, in which case the incidence should have bene greater in the Sinhalese, contrary to Kirk's (1976) suggestion. *HB*E* has also occasionally been reported among Europeans (Fairbanks et al. 1979).

In Thailand a reduced fertility of HB E homozygotes (*HB*E/HB*E)* compared to that of heterozygotes has been demonstrated (Flatz et al. 1965; Hoflinger 1971). But no differential fertility or mortality in respect of *HB*E* genotypes among the Kacharis of Upper Assam is observed by Deka (1976). The adaptive advantage of *HB*E* alleles in areas of endemic malaria in Thailand (Flatz 1967; Kruatrachue et al. 1969) are not detected in Assam (Deka 1976), in spite of wide prevalence of falciparum malaria. Das et al. (1980) observed that these findings appear to corroborate their earlier suggestion (Das et al. 1975; Deka 1976) that the *HB*E* polymorphism in Bodo populations of lower Assam is of transient nature as *HB*E* allele tends to replace both HB T and HB A.

The frequency of *HB*E* in Indian populations varies from complete absence to as high as 0.646 among Boro Kachari of Assam with average frequency of 0.023. Among caste groups the frequency is low (0.002) as compared to other groups—scheduled caste (0.009), scheduled tribe (0.029) and community (0.030). The highest frequency *HB*E* is observed from Indus-Ganga-Brahmaputra plains region (0.114) as compared to other regions. From the climatic regions, the *HB*E* is present only in the monsoon type with dry winters region (0.105) (Bhasin et al. 1994; Bhasin and Walter 2001). The *HB*E* is observed mainly from East India zone, where frequency is highest among the populations from the state of Meghalaya (0.363, varies from 0.198 to 0.535) followed by Assam (0.303, ranges from 0.051 to 0.646) as compared to Manipur (0.066, varies

between 0.032 and 0.091), Sikkim (0.006, ranges from nil to 0.047) and West Bengal (0.007). A few sporadic cases of *HB*E* are observed from other areas also (*e.g.* Uttar Pradesh). In general, *HB*E* allele is confined to Eastern India, particularly to the Eastern Himalayan populations with Mongoloid affinities in which the frequency is highest among scheduled tribes (0.327), followed by scheduled castes (0.211) and communities (0.195) which shows extensive admixture among these groups as compared to castes among whom the frequency is very low (0.018) (Fig. 3).

Different ethnic groups show correlations of *HB*E* with mean annual rainfall and mean annual humidity (Table 4). The reasons may be that since these climatic factors are responsible for breeding of vector anopheles responsible for malaria and if *HB*E* is favoured by selection against malaria, it may attain a high frequency.

The frequency of *HB*E* allele is high among menial workers (0.012) as compared to other occupational groups among whom the frequency is very low. The presence of allele *HB*E* among higher occupational groups may be due to admixture (Bhasin et al. 1994; Bhasin and Walter 2001).

The frequency of allele *HB*E* is observed high in Mon-Khmer group of Austro-Asiatic language family which comprises Cambodia, Vietnam, Mon in Lower Burma, Thailand, Burma, Southern China and East India (Assam and Bengal). *HB*E* may have emerged in an original Austro-Asiatic group and alongwith the Austro-Asiatic language may gradually have diffused throughout mainland South-eastern Asia. However, a quite high frequency of *HB*E* observed among the speakers of Tibeto-Chinese languages (0.279) from Bodo group (0.464) and North East Frontier group (0.342) in Eastern Himalayan region cannot merely be explained away being introduced into them by Austro-Asiatic speakers.

Further heterogeneity of the *HB*E* allele has recently been observed both in South-East Asia and North-East India (Antonarakis et al. 1982; Hundrieser et al. 1988b).

Although attempts have been made to eradicate malaria from all over the world, yet these have not been successful, especially in India. Whole of the Indian subcontinent is endemic for the malignant falciparum malaria. In India, the vast tracts of land, particularly in Peninsular India, Eastern India (Bihar, Orissa, West Bengal, Assam) and the entire Terai Belt, at the foothills of the
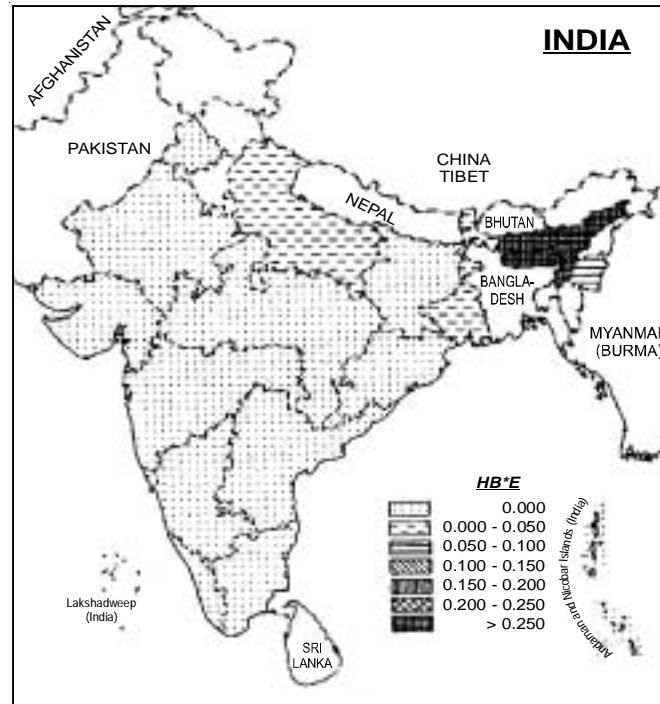
Fig. 3. Allele *HB*E* of Hemoglobin variants in different regions of India

Himalayan mountain system, had malaria in hyperendemic or endemic conditions Table 3, (Fig. 4). Evidently, sickle cell trait is not found to be present in all these regions. Furthermore, it is also significant that the caste populations all over the country, including highly malarial regions, are also free from this trait. To explain the occurrence of sickle cell trait in West Africa, Livingstone (1958) has marshalled archaeo-logical, linguistic epidemiological and genetic evidences in support of his reconstruction, with the basic premise that malaria is the principle factor which confers resistance on sickle cell heterozygotes. But in India such a reconstruction to explain the maintenance of comparatively high frequencies is not possible, due to great degree of variations in the incidence of the trait among populations sharing the same highly malarious habitat.

A selective advantage of *HB*E* against malaria in Southeast Asia has been suggested, but could not be corroborated in the Northeast Indian populations so far studied (Deka 1981).

Cruz-Coke (1978) report that no abnormal haemoglobin has been found among the high altitude populations. Is it due to the fact that abnormal haemoglobins carry less oxygen and so they just cannot survive or is it due to absence of malarial parasite in high altitude areas and that the abnormal haemoglobin genes have no selective advantage. Saha (1990) observed a low frequency of *HB*E* (about 0.02) among Khasis of Cherrapunji district (Meghalaya) as compared to Khasis of Shillong (0.22) and reported that this may be due to relaxation of selection in the absence of malarial infection at high altitude. Saha et al. (1987) have also found a low frequency of *HB*E* among Lepchas of Darjeeling Hills.

CONCLUSION

The information available on the abnormal haemoglobins, their frequencies, geographical locations, ethnic groups etc. are not sufficient and complete as observed, therefore it is rather difficult to study the relationship among different factors. That the incidence of G-6-PD deficiency in different populations shows a positive correla-tion with incidence of abnormal haemoglobin alleles, has been recorded in Southeast Asia and

Table 3: Species distribution of positive cases encountered state-wise breakup (provisional) alongwith haemoglobins S and E and glucose-6-phosphate dehydrogenase deficiency

S. No.	Name of the Zone/Region State & Union Territory (U.T.)	PV	PF Cases		Others	Total	HB*AS	Hb*E	G6PD*def
			R+	Rg+					
I.	NORTH INDIA								
A.	Western Himalaya (S. No. 1, 2)								
1.	Jammu and Kashmir	0.005	-	-	-	0.004	-	-	0.057
2.	Himachal Pradesh	0.018	-	-	-	0.015	-	-	0.095
3.	Punjab	0.131	0.005	0.001	0.003	0.112	0.000	0.000	0.048
4.	Chandigrah UT	0.016	-	-	-	0.013	0.011	0.000	0.075
5.	Haryana	0.174	0.003	0.088	0.017	0.149	-	-	0.020
6.	Delhi UT	0.043	0.0002	-	-	0.037	-	-	0.025
B.	Central Himalaya (S. No. 7, Eight Districts of Uttar Pradesh)								
7.	Uttar Pradesh	0.058	0.004	0.029	0.014	0.050	0.010	0.001	0.079
8.	Rajasthan	0.034	0.007	0.017	0.011	0.030	0.083	0.000	-
II.	WEST INDIA								
9.	Gujarat	0.136	0.020	0.105	0.011	0.119	0.065	0.000	0.042
10.	Maharashtra	0.072	0.062	0.089	0.036	0.070	0.023	0.000	0.040
11.	Goa, Daman and Diu UT	0.001	-	-	-	0.001	0.001	0.000	0.005
12.	Dadra and Nagar Haveli UT	-	-	-	-	-	0.080	0.000	0.130
III.	EAST INDIA								
C.	Eastern Himalaya (S. No. 13 to 20 and Darjeeling District of West Bengal)								
13.	Arunachal Pradesh	0.008	0.020	0.037	0.138	0.010	-	-	-
14.	Assam	0.013	0.100	0.005	0.046	0.024	0.000	0.303	0.088
15.	Nagaland	0.002	0.009	0.027	0.0014	0.0044	-	-	0.271
16.	Manipur	0.001	0.003	0.050	0.106	0.002	0.000	0.066	-
17.	Mizoram	0.003	0.026	0.019	0.015	0.007	-	-	-
18.	Tripura	0.0011	0.021	0.004	-	0.004	-	-	-
19.	Meghalaya	0.0013	0.035	0.004	0.008	0.006	0.000	0.363	0.062
20.	Sikkim	0.00002	-	-	-	0.00002	0.000	0.006	-
21.	West Bengal	0.002	0.0003	-	-	0.0014	0.001	0.007	0.048
22.	Bihar	0.014	0.60	0.023	0.010	0.020	0.001	0.000	-
23.	Orissa	0.042	0.429	0.148	0.137	0.098	0.046	0.000	0.110
IV.	CENTRAL INDIA								
24.	Madhya Pradesh	0.070	0.143	-	0.085	0.080	0.061	0.000	0.061
V.	SOUTH INDIA								
25.	Karnataka	0.098	0.020	0.166	0.201	0.088	0.082	0.000	0.000
26.	Andhra Pradesh	0.018	0.019	0.076	0.067	0.019	0.038	0.000	0.036
27.	Tamil Nadu	0.037	0.002	0.098	0.069	0.033	0.047	0.000	0.071
28.	Kerala	0.002	0.00001	0.0001	0.001	0.0013	0.045	0.000	0.012
29.	Pondicherry UT	0.0002	-	0.0002	-	0.0001	-	-	-
VI.	ISLANDS								
30.	Lakshadweep UT	-	-	-	-	-	-	-	-
31.	Andman Islands and Nicobar Islands UT	0.003	0.002	0.002	0.023	0.003	0.000	0.000	-
	INDIA (TOTAL)						0.031	0.023	0.045

PV = *Plasmodium vivax*   PF = *Plasmodium falciparum*   R+ = Rings and Gametocytes

Mediterranean populations (Siniscalco et al. 1961; Allison et al. 1963; Flatz et al. 1965). The data from India are as yet insufficient for any generalization, however, high incidence of *HB*S* as well as *G6PD*def* have been observed among scheduled tribes from West, Central and South India (Sukumaran et al. 1956; Vyas et al. 1962; Das et al. 1967; Negi 1968; Kate et al. 1984; Bhatia 1987). Since *G6PD*def* is prevalent in adult population nearly all over India in frequencies varying from less than 0.01 to 0.16, no significant correlation has been established with any particular haemoglobin variant as yet.

Samuel et al. (1986) observed that the red cell *G6PD*def* allele was significantly associated with the sickle cell gene (*HB*S*) in both males and females and thalassaemias (in males α- and β-thalassaemias and in females β-thalassaemia) and concluded that the three commonly occuring inherited red cell defects—G-6-PD, sickle cell and thalassaemia genes—have probably originated as a result of the same selection factor *i.e.* malarial

infection. But a selective advantage of *G6PD*def*, *HB*E* and *HB*S* could not be corroborated in the Indian populations so far studied.

The effect of and relation with various environment factors are as yet uncertain, since the studies wherever available are fragmentary and ambiguous. The interaction of an abnormal gene with other genes and with climate, nutrition, geographical and other environment parameters requires a thorough analysis. Future studies should therefore be conducted with carefully planned sampling techniques, with an understanding of historical, demographic and genealogical relationship of people living in different environmental conditions.

Among Indian populations the incidence of haemoglobin variants is about 0.005.*HB*S* allele with a frequency ranging from complete absence to 0.410 is present among them with a general frequency of 0.031. It is prevalent among the scheduled tribe followed by scheduled caste groups but is almost absent in the caste groups. Its frequency is high in semi arid steppe type of climatic region (0.071) as compared to others. It is present in high frequency in Central India

followed by South, West and North India. The frequency is quite low in East India and the allele is absent in Islands zone. *HB*S* frequency is high in Dravidian language family (0.047) but it is lacking in Tibeto-Chinese language family. With regard to the origin of sickle cell gene, Kan and Dozy (1980) proposed the view that Indian and West African sickle cell gene mutations arose by separate events. The *HB*E* is observed in high frequency among the population groups of East India particularly from Eastern Himalayan region where the frequency is 0.237. The frequency of *HB*E* is high in speakers of Mon Khmer group of Austro-Asiatic language family, as well as among the speakers of Tibeto-Chinese language family from Eastern Himalayan region. Heterogeneity of the *HB*E* allele has been recently observed both in Southeast Asia and North-east India. A selective advantage of *HB*S* and *HB*E* against malaria could not be corroborated in the Indian populations. The low frequency of *HB*E* at high altitude is suggested to be due to relaxation of selection.

It has been observed that most of the studies reported in the literature involve case studies
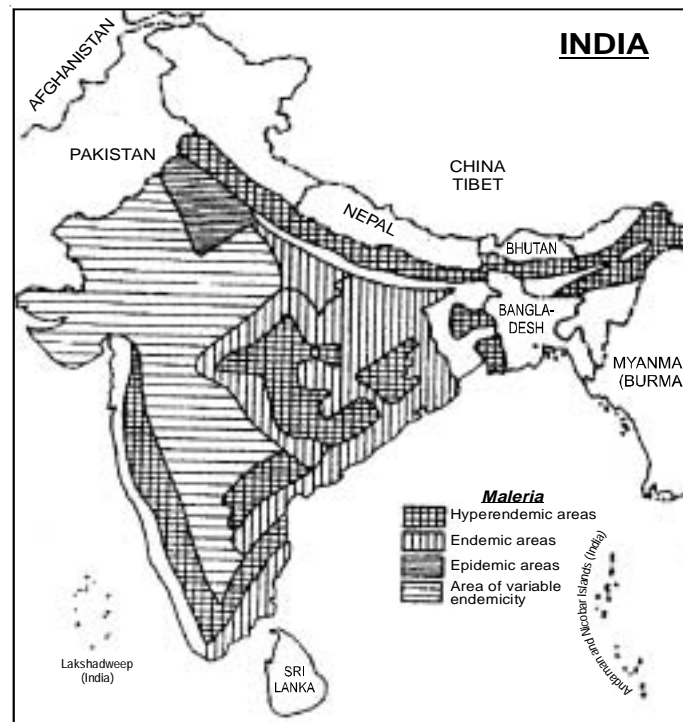

Fig. 3. Maleria in India

Table 4: Correlation with climatic factors and ethnic groups

Ethnic groups	G-6-PD	Haemoglobin		
	G6PD*def	HB*A	HB*S	HB*E
Mean Annual Temperature				
Caste	0.445[2]	0.139	0.078	-0.209
Scheduled Caste	0.028	0.331[2]	-0.079	-0.400[3]
Scheduled Tribe	0.423[2]	0.075	0.152	-0.319[3]
Community	0.063	0.315[2]	0.233[1]	-0.515[3]
Total	0.295[3]	0.170[2]	0.110[2]	-0.365[3]
Mean Annual Rainfall				
Caste	0.207	-0.042	-0.059	0.085
Scheduled Caste	-0.099	0.156	-0.074	0.312[1]
Scheduled Tribe	-0.385[2]	0.077	-0.244[3]	0.436[3]
Community	-0.076	-0.301[2]	-0.262[1]	0.502[3]
Total	-0.095	-0.134[2]	-0.195[3]	0.408[3]
Mean Annual Humidity				
Caste	0.207	-0.035	0.126	-0.056
Scheduled Caste	-0.115	-0.216	-0.011	0.339[2]
Scheduled Tribe	-0.317[1]	-0.006	-0.238[2]	0.350[3]
Community	0.110	-0.371[3]	-0.226[1]	0.556[3]
Total	-0.046	-0.097	-0.194[3]	0.370[3]
Mean Altitude				
Caste	-0.114	0.075	-0.056	-0.044
Scheduled Caste	0.097	0.069	0.153	-0.338[2]
Scheduled Tribe	0.203	-0.019	-0.035	0.104
Community	0.045	0.195	-0.050	-0.169
Total	0.017	-0.023	0.069	-0.063

1. Significant at P < 0.05   2. Significant at P < 0.01   3. Significant at P < 0.001

and reports from hospital, which cannot be regarded to represent population surveys, as samples studied are heterogeneous. Further, most of the studies have not given any details about the ethnic group, social and environmental factors etc. Therefore it was rather difficult to study the relationship of abnormal haemoglobins with different factors. Carefully designed studies should therefore be planned in the future.

NOTES

1. Three more states have come into existence recently. Now Bihar has been divided into Bihar and *Jharkhanda;* from Madhya Pradesh have resulted the states of Madhya Pradesh and *Chattisgarh;* the earlier state of of Uttar Pradesh is now divided into Uttar Pradesh and *Uttaranchal*. The states in italics are newer ones. India at present comprises 28 states.
2. The frequency distributions for the State of Goa and Union Teritory of Daman and Diu have been listed under Goa, Daman and Diu.

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