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Distribution of Glucose-6-Phosphate Dehydrogenase Deficiency in Indian Population

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Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest enzymopathy in human estimated to affect 400 million individuals worldwide. G6PD is a housekeeping enzyme which catalyzes the first step in the pentose phosphate pathway (PPP). Through a series of reactions PPP converts glucose-6-phosphate (G6P) to ribose-5-phospate, a precursor of many important molecules like RNA, DNA, ATP, CoA, NAD, FAD. The PPP also produces NADPH molecules which function as an electron donor and thus provides the reducing energy of the cell by maintaining the reduced glutathione in the cell. Reduced glutathione functions as an antioxidant and protects the cells against oxidative damage.G6PD deficient individuals are usually asymptomatic but acute haemolysis may occur with oxidative stress induced by ingestion of drugs, certain type of food, exposure to certain chemical substances or when there is accompanying infection or hypoxia. Rarely, it may cause chronic non-spherocytic haemolytic anemia. The prevalence of G6PD deficiency detected by using the biochemical screening methods in different populations is found to be in the range of 0-65% in males (Livingstone,1985 & Oppenheim, 1993). Since the morbidity related to G6PD deficiency is manifested only in case of certain stress, it has been suggested that in the absence of stress G6PD deficiency does not lead to morbidity. A number of studies reviewed by Beutler(1991), have shown that even in the absence of any stress the G6PD-deficient individuals show clinical abnormalities One of the most important complications of G6PD deficiency is severe neonatal hyperbilirubinemia and the risk of developing kernicterus, a problem especially seen in G6PD-deficient individuals in the Mediterranean and Asia (Beutler, 1991; Brown and Boon, 1968; Tan1981; Fok and Lau, 1986).
In India, G6PD deficiency was first reported by Baxi et al (1963). The prevalence rate varied from 0 to 27% in different caste & ethnic groups. The frequency is higher among the tribals than the caste populations. Studies in the last few years also support the trend. Warli and Dhodia, tribal populations in Dadra and Nagar, Haveli have a frequency of 10.1% and 13.5% respectively, while Rajput, caste group from the same geographical region, and have low frequency of 2.1% (Rai & Kumar, 2012).

Sukumar et al, (2002) reported that most of drug-induced hemolytic anemia in G6PD-deficient individuals in India is due to administration of anti-malarial drugs. Information about the prevalence of specific variants is lacking in many populations. Such information is necessary for the implementation of anti-malaria program, especially in malarial endemic areas. Therefore, comprehensive studies of G6PD gene are recommended among the populations in the malarial endemic areas. The G6PD gene also provides an opportunity to study how selection has affected the genetic variability in the Indian populations.

Key words: G-6-PD, distribution of G-6-PD, Indian Population.

Materials and Methods

The objective of the present work is to study the frequency of G-6-PD deficiency in different endogamous groups of India in relation to malaria, altitude, caste and tribal status.

The data on G-6-PD of different groups were collected from coastal population of Maharashtra (Maratha, Kubi, Bhandari and Kharavi) and Goa (Kharavi & Bhandari) and Odisha (Nolia). Comparative data has been taken from published papers (Bala & Seth, 1978; Singh et al., 1974; Shanbhang & Bhatia, 1973; Jolly et al., 1972; Khanduja et al., Aggarwal et al., 1974; Baxi et al., 1969; Mehta et al., 1969; Hakin et al., 1973; Mutalik et al. 1974; Dacosta et al. 1967; Kate et al., 1974; Shanbhang and Bhatia, 1974; Flatg et al., 1972; Chatterjee, 1966; Papiha and Chhaparwal, 1973; Meera khan, 1964; Kapoor,1981; Kapoor and Vaid, 1982; Kapoor and Tiwari, 1983).

Results and Discussions:

The frequency of the G-6-PD deficiency, attitude and mode of the residence in different cis-himalayan populations are presented in Table-1. G-6-PD deficiency was found to be absent in Jumli Thakurs living at an altitude of 12,000 feet whereas it is highest 4.50% in Rajput of India living at both Nepal and India living at an altitude of 2000 to 3,500 feet. Brahmans and Rajputs of Nepal and India, Shilpkars, Johari and Tolcha Bhotia show almost similar frequencies of G-6-PD. These seem to be variations among different Himalayan populations because they inhabit different niches as well. One of the reasons for the decreased increase of G-6-PD deficiency at high altitude could be attributed to absence of malaria. It is therefore possible that the heterogeneity observed in the incidence of G-6-PD deficiency in high and low

altitude populations in the cis- Himalayan region is determined by some sort of selective pressure associated with malaria.

From, the distribution of G-6-PD deficiency in the different population groups in India (Table-2), it has been observed that the frequency of G-6-PD gene is highly variable. It varies from 0.76% among Koya Dora of Andhra Pradesh (Meera khan, 1964) to 27.6% among Angami Nagas of Nagaland (Seth & Seth, 1971). However, many of the populations so far studied from India do not show the presence of this trait.

In western India, the highest frequency of G-6-PD deficiency is shown by the Parsis (17-19%). This high value may be because Parsi is an endogamous group with a high incidence of consanguinity. No deficiency was found among Hindus and Christians of Bombay. Gujrati speaking population of this zone show low frequency of G-6-PD gene except for the Cutchi-Bhamushali group in which the frequency is as high as 13.8%.

North India presents a heterogeneous picture of enzyme deficiency (2% to 11.1%). Mittal et al (1967) reported 6% of G-6-PD deficiency from Agra, U.P. and Ahmad et al (1972) reported 11.1% from Allahabad. The frequency of the enzyme deficiency in central Himalayas Rajput (Delhi Univ., 1976) of Baskat, U.P. The frequency is not very high in western Himalayas.

Among the population group of east India, a high Frequency of G-6-PD deficiency has been reported among reported among Angami Nagas of Nagaland (27.06%); 15.66 % (Das et al., 1982); santhal tribe 14.3%(kate et al,1975); Rajhanski 11.65% (Das et al., 1982). These observations show that the tribal populations show a higher incidence of G-6-PD deficiency than the non-tribal population.From available reports it is seen that the frequency among Muslims of Madhya Pradesh is 3.9% while the Hindus show a higher frequency of 7.5% (Papiha and Chaparvel,1973). In south India,the highest frequency (12.5%) is found among Kurumbas of Nilgiri hills. Insome populations of Madras and Hindus of Hyderabad, the frequency range is 9-12.5%.

Table –3 shows that among the coastal population, distribution of G-6-PD and sickle cell trait has been found nil. Most of the genetic variation in the genome is thought to evolve under the conditions of neutrality and variations can be explained due to random genetic drift. Selection may have been an important force in shaping human genetic variation. Absence of G-6-PD in coastal population, may be due to coastal environmental factors , including the type of fish they take and endogamous nature of each population which has different historical perspective affecting the inbreeding phenomenon. More studies are needed on coastal populations to throw the light in this direction.

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Table : 1

Glucose-6 Phosphate dehydrogenase deficiency, altitude and mode of residence in cis-Himalayan Populations.

Populations	Number Studies	Altitude (Ft.)	Percentage of deficiency	Mode of Residence	Investigation
Johari Bhotias	168	2000-6500	2.98	Settled	Kapoor, 1981
Rang Bhotias	180	3000-8000	4.44	Migratory	Kapoor, 1981
Maschha Bhotias	235	3000-9500	1.28	Migratory	Kapoor & Vaid, 1982
Tolcha Bhotias	219	3000-9500	3.20	Migratory	Kapoor & Vaid, 1982
Jaad Bhotias	51	3000-8500	1.96	Migratory	Kapoor & Vaid, 1982
Brahmans (Nepal)	109	2500-3500	2.75	Settled	Kapoor & Vaid, 1983
Rajputs (Nepal)	109	2500-3500	1.R1	Settled	- do-
Jumli Thakurs (Nepal)	31	12000	0.00	Migratory	- do-
Brahmans (India)	117	2000-3500	2.56	Settled	- do-
Rajputs (India)	111	2000-3500	4.50	Settled	- do-
Shilpkars (India)	67	2000-3500	2.98	Settled	- do-

Table : 2
Distribution of G-6-PD Deficiency among various Populations of India

Area	Population	No. Tested	G-6 PD No.	Deficient %	Bala & Seth (1978)
I. North India					
Western Himalayas					
Jammu and Kashmir	Pandits	61	3	4.91	Bala & Seth (1978)
Srinagar	Muslims	63	4	6.35	Bala & Seth (1978)
Punjab	Punjabi Brahmin	72	2	2.77	Singh et. Al. (1974)
	Punjabi Khatri	78	3	3.84	Singh et. Al. (1974)
	Punjabi Arora	51	2	3.92	Singh et. Al. (1974)
	Punjabi Jat	121	4	3.3	Singh et. Al. (1974)
	Punjabi Total	322	11	3.42	Singh et. Al. (1974)
	Khatri	98		14.0	Shanbhag & Bhatia (1973)
	Punjabis	1650		7.1	Jolly et.al (1972)
Sind	Lohana	90		3.13	Shanbhag & Bhatia (1973)
Delhi	Children	362	10	2.76	Khanduja et. Al (1966)
Lucknow	Pandits	239	4	1.67	Aggarwal, Sharma & Farooqui, (1974)
Allahabad		1324	176	13.29	Ahmed et. al. (1972)
II. West India					
Gujarat	Visa Oswal Jain	107	3	2.8	Baxi et. al. (1969)
	Lad Vania	128	1	0.78	Baxi et. al. (1969)
	Brahmin	141	5	3.55	Baxi et. al. (1969)
	Cutchi	208		13.8	Mehta et.al. (1972)
	Bhanushali Lohana	95		3.2	Shanbhag & Bhatia (1973)
	Khoja	222		2.0	Hakim et.al. (1973)
	Bohra	130	0	0.0	Hakim et.al. (1973)
Maharashtra Bombay	Parsis	100	19	19.0	Mutalik et.al (1974)
	Mahars	200	1	0.5	Parikh et.al (1969)
	Maharashtrians	381	9	1.08	Dacosta et.al. (1967)
Poona District	Parsi	310	37	11.93	Kate et.al. (1974)
	Christians	44	1	2.27	Kate et.al. (1974)
	Nava Budha	271	7	2.58	Kate et.al. (1974)
	Jain Marvedi	144	4	2.77	Kate et.al. (1974)
	Dhangar (Nomadic)	211	5	2.4	Kate et.al. (1974)
Aurangabad	Mahar	100	10	10.0	Deshmukh & Sharma (1968)
Chitarpur	Saraswat Brahmins	101		0.99	Bhanbhag & Bhatia (1974)
Mangalore	Saraswat Brahmins	109	0	0.0	Shanbhag & Bhatia (1973)

Goa	Goan Saraswat	52	0	0.0	Ektaee (1973)
	Goan Saraswat	179		1.1	Shanbhag & Bhatia (1973)
	Goan Catholic	64		0.0	Shanbhag Bhatia (1973)
Nagpur	Mahars	205		9.2	Kher et. al. (1967)
	Gond	104	89.0	11.0	Kher et. al. (1967)
III. East India					
Assam	Assamese	185	8	4.3	Flatz et.al. (1972)
	Khasi	100	7	7.0	Flatz et.al. (1972)
	Ahom	130	7	5.4	Flatz et.al. (1972)
Kohima	Angami Nagas	85	23	27.08	Seth & Seth (1971)
Calcutta	Bengalis	56	2	3.6	Chatterjee (1966)
Bengal	Santhals	169	23	14.03	Kate et.al. (1978)
	Bengali	103	4	3.9	Chatterjee (1966)
IV. Central India					
Madhya Pradesh	Hindu	109		7.5	Papiha & Chhaparwal (1973)
	Muslim	102		3.9	Papiha & chhaparwal (1973)
Jhabua Dist.	J Bhals	120	8	6.7	Papiha et.al. (1978)
V. South India					
A. Andhra Pradesh					
Hyderabad	Hindu	1200		9.5	Padma (1974)
Polavaram	Non-tribal	238	0	0.0	Meera Khan (1964)
Thallavaram	Koya Dora	113	1	0.76	Meera Khan (1964)
Vishakhapatnam	General	68	3	4.41	Veerarja et.al. (1978)
B. Tamil Nadu					
Nilgiri Hills	Trulas	89	8	9.0	Saha et.al (1976)
	Kurumbas	16	2	12.5	Saha et.al. (1976)
	Todas	48	0	0.0	Saha et.al. (1976)
Madras					
Kerala	Dravidians	1372	18	1.3	Saha et.al. (1976)
	Kadar	107	0	0.0	Saha et.al. (1976)
	Moplahs	186	0	0.0	Hakim et.al. (1973)
	Syrian Christians	70		1.0	Baxi. (1973)

TABLE -3 : G-6-PD & SICKLE CELL TRAIT

COASTAL POPULATION	NUMBER	G-6-PD	SICKLE CELL TRAIT
MAHARASHTRA			
MARATHA	143	NIL	NIL
KUMBI	127	NIL	NIL
BHANDARI	109	NIL	NIL
KHARAVI	131	NIL	NIL
GOA			
KHARAVI	137	NIL	NIL
BHANDARI	137	NIL	NIL
ODISHA			
NOLIA	126	NIL	NIL