

## **Higher prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency in tribal population against urban population: a signal to natural selection.**

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### **Abstract**

**Background:** Human genetic variation is interlinked to genetic drift and gene flow. Interplay amongst these leads to evolution in natural populations. Studies suggest that Glucose-6- Phosphate Dehydrogenase (G6PD)-deficient alleles show some signatures of selection. Deficiency in G6PD is the most common enzyme deficiency of human erythrocyte which affects over 400 million people worldwide. There is no comprehensive information available about the prevalence of this disease across the entire map of Gujarat, India.

**Methods:** Cross-section retrospective study was conducted to determine prevalence of G6PD deficiency in population of Gujarat. 3467 samples from different hospitals throughout the state of Gujarat from September 2014 to September 2015 were analyzed. The G6PD activity was measured quantitatively by spectroscopic absorbance at 340 nm in kinetic mode.

**Results:** The drastic variation in the prevalence amongst the tribal and urban population was observed. Frequency varied from 11.18% in tribal populations to as low as 1.2% in the urban population. Urban areas such as Kutch, Bhuj, Lunawada and Kapadwanj showing relatively high prevalence have been known to be inhabited by tribal population.

**Conclusions:** Heterozygosity levels, linkage disequilibrium patterns and frequencies of alleles segregating in a population play a vital role in the prevalence of any genetic deficiency. However how this polymorphism is being maintained is not deciphered yet. Our study signals the need for rigorous research to understand the pattern of natural selection and establishment of selection coefficients for different genotypes.

**Keywords:** Glucose-6-phosphate dehydrogenase, Epidemiology, Natural selection.

*Accepted on June 07, 2016*

### **Introduction**

Glucose-6- Phosphate dehydrogenase (G6PD) deficiency is the most common enzyme deficiency of human erythrocyte which affects more than 400 million people worldwide [1]. Glucose-6-phosphate dehydrogenase enzyme catalyzes the first step in the hexose monophosphate pathway, converting glucose-6-phosphate to 6-phosphogluconolactone and reducing the cofactor nicotinamide-adenine dinucleotide phosphate (NADP) to NADPH. In the red blood cell this pathway is the only source of NADPH, which is necessary to protect the cell and its hemoglobin from oxidation [1]. G6PD deficiency make erythrocytes prone to H<sub>2</sub>O<sub>2</sub> and other Reactive Oxygen Species (ROS) that can lead to non-immune hemolytic anemia, favism, Chronic Nonspherocytic Hemolysis (CNSH), spontaneous abortions and neonatal hyperbilirubinemia resulting in neonatal kernicterus[2,3]. In more serious cases, hemolytic anemia can also leads to death. Various chemicals in food and medicines, various infections and stress can trigger various signs and symptoms of Glucose-6-phosphate dehydrogenase deficiency

and therefore early recognition of G6PD deficiency can help prevent serious complications. In India, study of G6PD deficiency started after its first reporting by Baxi et al. in 1963 [4]. The various studies have reported prevalence of G6PD deficiency ranging from 0% to 27% among various caste, ethnic and linguistic groups in India [5]. In Gujarat, the prevalence of G6PD deficiency has been studied in very few castes but there is no information available about G6PD deficiency in overall population of Gujarat. The objective of the present work is to study the frequency of G-6-PD deficiency in the population of Gujarat.

### **Materials and Method**

Cross section retrospective study was conducted to determine the prevalence of G6PD deficiency in population of Gujarat, India. Prior to the commencement of the study, the approval of Ethical Research Committee was taken (Reference No.ECR/144/ Indt/GJ/2014). Survey of 3367 samples suspected to be G6PD deficient frequenting the hospitals and leading

laboratories across Gujarat were analyzed for confirmation of the G6PD deficiency.

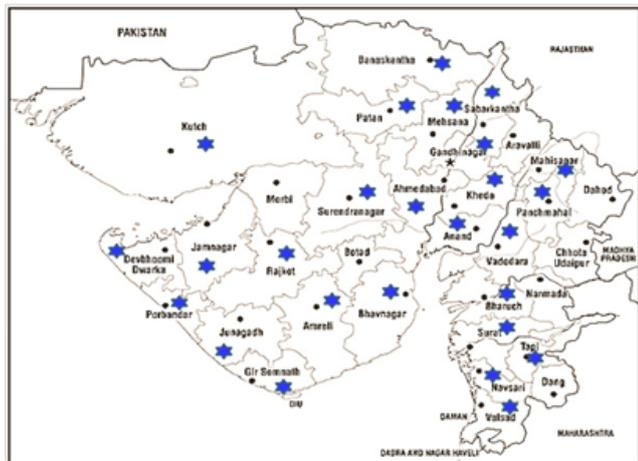


Figure 1. The locations of survey.

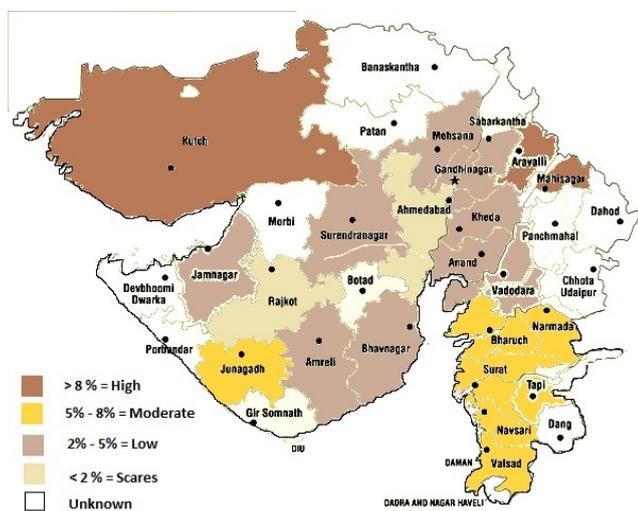


Figure 2. Prevalence in various areas of Gujarat.

Samples of patients from urban population were tested directly in the lab where the blood was collected. Data was collected from 26 different locations across Gujarat (Figure 1). G6PD activity was analysed by production of NADPH measured at 340 A in kinetic mode. Samples identified as deficient with cutoff  $\leq 4.6$  U/gHb. (Normal range 4.6-13.5 U/gHb). Tribal population were initially screened by color reduction test involving reduction of a blue dye, dichlorophenol indophenol, to a colourless state, produced by Sigma Diagnostics, which was confirmed by spectrophotometric analysis for NADPH production at 340 A in kinetic modes (Figure 2).

**Results**

In our study, the level of the prevalence of G6PD deficiency was classified under four categories: High, Moderate, Low and Scars. The frequency of G6PD deficiency was found to be ranging from 1.27% to 11.18%. The G6PD deficiency was

found high as 11.18% in kapadwanj followed by 9.52% in Kutch and Bhuj and 8.33% in Lunawada. Here, Kutch and Bhuj as well as Lunawada and Kapadwanj represent only some part / population of northern and eastern Gujarat respectively. Prevalence of G6PD deficiency was found to be moderate ranging between 4.55 to 7.81% in Southern Gujarat which includes regions like Surat, Valsad, Vapi, Vyara, Navsari, Bharuch and Karjan. Also Junagadh from western Gujarat falls under moderate category. While in other regions of Gujarat such as Gandhinagar, Anand, Nadiad, Surendranagar, Amreli, Jamnagar and Bhavnagar low prevalence of G6PD deficiency was found. Areas like Ahmedabad and Rajkot falls under scares category with 1.76% and 1.27% respectively (Table 1).

Table 1. Classification of areas of Gujarat based on prevalence of G6PD deficiency.

Prevalence level	Area	Prevalence	Range of Prevalence
High (>8%)	Kutch and Bhuj	9.52	
	Lunawada	8.33	8.33-11.88
	Kapadwanj	11.88	
Moderate (5%-8%)	Karjan	4.55	
	Bharuch	7.14	
	Valsad	7.81	
	Vapi	6.67	4.55 - 7.81
	Vyara	5.56	
	Navsari	5.56	
	Surat	4.55	
	Junagadh	5.00	
	Amreli	3.78	
	Jamnagar	4.00	
Low (2%-5%)	Bhavnagar	4.00	
	Anand	4.00	3.64 - 4.44
	Gandhinagar	3.90	
	Surendranagar	4.00	
	Nadiad	4.44	
Scars (<2%)	Vadodara	3.64	
	Ahmedabad	1.76	1.76 - 1.27
	Rajkot	1.27	

**Discussion**

In India, G6PD deficiency was first reported in 1963 [4], however the prevalence varied from 0 to 27% amongst the different caste, ethnic, and linguistic groups. The frequency has been found higher among the tribal/scheduled caste populations [5] and recent studies in Uttar Pradesh also support the trend [6]. Also it is notable that the occurrence of the G6PD

deficiency reported is higher in South India than North and West India while very few studies from eastern parts of India have been reported [7]. Several reports regarding G6PD deficiency have been published in several castes or tribes such as Rajputs [8], Brahmins [8], Danguria Tharus [9], Muslims [10], Jats [11], Koyadoras [12], Nayakpods [12], Rellies [13], Kolams [14], Nilgiris [15], Badagas [16], Kannikars [17], Kissans [17], Ao Nagas [18], Mizos [19], Kabuis [20], Bhuyans [21], Kharias [21], Rajbangshis [22], Sindhis [23], Murias [24], Halbas [24], Bhatras [24], Jarwas [25], Warlis [26], Dhodias [27], Parsees [5] and many more from all over India.

Although a lot of studies regarding prevalence of G6PD deficiency have been carried out in India, very limited reports on the prevalence of G6PD deficiency in populations of Gujarat have been found. In Gujarat frequency of G6PD deficiency was found upto 27.5% in Vataliya Prajapati community in Western and Southern regions [28,29]. Apart from that, in 1969 Baxi et al. found frequency of G6PD deficiency 2.8%, 0.78% and 3.55% in three Gujarati communities Visa Oswal Jains, Lad Vanias and Brahmins respectively. However the subjects were residing at Bombay [30]. In another studies the prevalence of G6PD deficiency was reported upto 13.7% in members of Cutchhi Bhanushali community residing at Bombay [31] [32].

Even though some previous reports show high prevalence of G6PD deficiency in certain communities, our results are definitely indicative of low prevalence of G6PD deficiency in overall population of Gujarat. Our study is also suggestive of distinct variation in the prevalence of G6PD deficiency across the population of the Gujarat as Kutch and Bhuj from Northern Gujarat as well as Lunawada and Kapadwanj from Eastern Gujarat show high prevalence of G6PD deficiency as 9.52%, 8.33% and 11.88% respectively. Subsequently the prevalence was found moderate in southern Gujarat (4.55-7.81), while other regions of Gujarat show low prevalence of G6PD deficiency (3.64-4.44%). Areas like Ahmedabad and Rajkot falls under scares category having 1.76% and 1.27% prevalence respectively. The reason behind high prevalence of G6PD deficiency in regions like Kutch, Bhuj, Lunawada and Kapadwanj might be the large number of tribes as inhabitants. During the course of the study it was found notable that the frequency of testing for G6PD deficiency is quite low in Kutch, Bhuj, Lunawada and Kapadwanj considering the high prevalence of G6PD deficiency in these areas. Various aspects such as lack of awareness, illiteracy, socio economic status, various social and personnel believes etc. might be responsible for less frequency of testing for G6PD deficiency. Early detection and prevention is the key strategy to successful management and control of G6PD deficiency. Genetic counselling, prenatal diagnosis, health education, and public awareness can provide benefits to the affected individuals and their families. Heterozygosity levels, linkage disequilibrium patterns and frequencies of alleles segregating in a population play a vital role in the prevalence of any genetic deficiency. However how this polymorphism is being maintained is yet to be deciphered. Our study signals the need for rigorous research

to understand the pattern of natural selection and establishment of selection coefficients for the different genotypes. We emphasize that there is a need for much intensive investigation to evaluate the clinical aspects of the G6PD enzyme deficiency among the urban as well as tribal populations of Gujarat.

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