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GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY AMONG THE BHOKSA MALES: A STUDY FROM DEHRADUN, UTTARAKHAND, INDIA

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ABSTRACT

Glucose-6-phosphate dehydrogenase is one of the most common enzymopathies in humans caused by inherited mutations of the X-linked gene G6PD, affecting around 400 million people worldwide. In India its prevalence varies between 0-28% in different caste, tribe and ethnic groups. Though the affected individuals remain clinically silent, exposure to oxidative stress causing factors can trigger life threatening complications. Therefore, early detection and awareness can help in prevention and better management of the condition.

The present study aims to estimate prevalence of G6PD deficiency among the Bhoksa tribe of Dehradun, Uttarakhand. Blood samples from 104 unrelated Bhoksa males were collected through finger prick method and screened for G6PD deficiency by using Fluorescent spot test. Of a total sample of 104 males tested, 2 (i.e., 1.923%) were found to be G6PD deficient. They both belonged to the younger age group (<=30 years). Neonatal and adult screening for G6PD deficiency is extremely important for better management of the disease especially among the tribal populations inhabiting remote rural areas with restricted access to healthcare services.

Keywords: Glucose-6-phosphate dehydrogenase, Bhoksa tribe, Buksa tribe, G6PD deficiency

INTRODUCTION

Glucose-6-Phosphate Dehydrogenase deficiency is one of the most common enzymopathies in humans caused by inherited mutations of the X-linked gene G6PD, affecting around 400 million people worldwide (Luzzatto *et al*.,1985, 2020). Glucose-6-phosphate dehydrogenase is one of the key enzymes of hexose monophosphate shunt/ pentose phosphate pathway. It catalyses the first reaction in the pentose phosphate pathway, providing reducing power to all cells in the form of NADPH (reduced form of nicotinamide adenine dinucleotide phosphate). NADPH enables cells to counterbalance oxidative stress that can be triggered

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by several oxidative stress causing agents. Since red blood cells do not contain mitochondria, the pentose phosphate pathway is their only source of NADPH; therefore, defence against oxidative damage is dependent on G6PD (Luzzatto *et al.*, 2001; Cappellini and Fiorelli, 2008). People with this disorder, however, never experience any signs or symptoms and are unaware that they have the condition unless faced by adverse oxidative stress causing factors. The most common clinical manifestations are neonatal jaundice and acute haemolytic anaemia, which in most patients is triggered by exogenous agents like infection, anti-malarial and other oxidative stress inducing drugs (Luzzatto et al.,1985; Cappellini and Fiorelli, 2008). It can also be triggered after eating fava beans or inhaling pollen from fava plants (Crosby,1956). Studies have sustained that G6PD deficiency is protective against malaria infection (Ruwende *et al.,*1995: 246-249; Luzzatto *et al.,*1980: 257-263; Cappadoro *et al*.,1998). Selective advantage of mutated G6PD deficient alleles is believed to be the reason behind higher frequencies of such mutants especially in malaria endemic regions. Anthropologists have always been interested in G6PD as a biological marker to study human populations as it is a good tool to study human evolution and genetic variation, which is one of the core themes of biological anthropology.

In India, research on G6PD deficiency gained traction after it was first reported by Baxi *et al.* (1961). Since then numerous studies have been conducted across India on different population sets which indicate that its prevalence varies between 0-28% in different caste, tribe and ethnic groups (Tripathy and Reddy, 2007). In the case of the tribal population of India prevalence varies from 2.3 to 27.0 per cent with an overall prevalence of 7.7 per cent in different tribal groups (Mukherjee *et al.,* 2015). According to the World Health Organisation the prevalence of G6PD deficiency in India ranges between 0-10%.

The present study tries to find the prevalence of G6PD deficiency among the Bhoksa tribe of Dehradun, Uttarakhand. Bhoksa is one of the five major tribes of Uttarakhand mostly concentrated in Dehradun and Nainital Districts in the foothills of outer Himalayas. Not much genetic or allied study has been carried out in this population group so far; hence this study aims to fill the literature caveat in this field through G6pd deficiency study.

MATERIALS AND METHODS

For the present study, data was collected in three villages, viz., Sabhawala, Tiparpur and Sherpur, in Dehradun District of Uttarakhand, India. Blood samples were collected through finger prick method from 104 Bhoksa males, ranging in age from 5-74 years, after obtaining informed and written consent from each participant and in case of minors from the guardian of the minor participant. Ethical clearance was obtained from the Ethics Committee, Department of Anthropology, University of Delhi, prior to commencement of the study.

Blood samples were drawn in eppendorf containing 10 micro lit. EDTA,

following the finger prick method. Blood relatives up to first cousins were avoided in the present study. Screening for G6pd deficiency was performed by employing Fluorescent Spot Test (Beutler and Mitchell, 1968).

RESULTS AND DISCUSSION

The present study aimed to investigate the prevalence of G6PD deficiency among the Bhoksa tribe of Uttarakhand. For this blood samples were collected from 104 unrelated male individuals of the Bhoksa tribe, as G-6-PD deficiency is an X linked recessive trait and the hemizygous males can show full expression of the condition. The study found that out of a total sample of 104 males, 2 (i.e.,1.923%) were found to be G6PD deficient. These two individuals had ages of 16 and 23 years, respectively, at the time of field investigation (Jan. 2020).

Table: 1. Distribution of G6PD deficiency among Bhoksa males of Dehradun, Uttarakhand

		Normal		Deficient		Allele frequency
Sex	No. Tested	No.	Percentile	No.	Percentile	Gd* def
Male	104	102	0.981	02	0.019	0.019

Various studies on G6PD deficiency and its prevalence have been carried out among different tribal groups, states and caste groups in India. Tribal population-based studies on different regions indicate that frequencies of the Gd- gene in different states of India show a heterogeneous picture (Tripathy and Reddy, 2007). In comparison, a higher frequency (>10%) of the Gd- gene is observed among the tribal groups of Nagaland, Chhattisgarh, West Bengal, Dadra & Nagar Haveli and Gujarat. On the other hand, uniformly low frequencies (<5%) of Gd- gene have been reported in Tripura followed by Himachal Pradesh, Uttarakhand, Andhra Pradesh and Madhya Pradesh (Tripathy and Reddy, 2007). Data from North India is uniformly low and the prevalence varies from 1.2 to 4.4 per cent (Tripathy and Reddy, 2007; Bhatia and Rao, 1986).

Data on G6PD among the neighbouring tribes of Bhoksa is limited. Kapoor and Vaid (1982) reported G6PD deficient percentage of 1.28 % among Marcha Bhotias and 3.19 % among Tolcha Bhotias of Chamoli district, Uttarakhand.

Age Wise distribution of G6PD deficiency in the present study population indicates higher prevalence among the younger age group (<30 years) and absent among the higher age group (> 30 years). This finding presents a contrasting picture to a study conducted among Muslims of Lucknow by Kant *et al.* (2019), which found a comparatively higher prevalence of G6PD deficiency among the higher age group than younger age group. Authors of the study reasoned that with advancement in pharmacology, the younger generations are exposed to an array of drugs since birth. Since G6PD deficient individuals are usually asymptomatic, unknown to the deficiency the younger age groups are exposed to various drugs which might be life threatening for them.

This explanation may hold ground for that particular population as Muslims of Lucknow are a plain dwelling urban community with easy and affordable access to healthcare services and thus exposure to drugs and medication since childhood. But it may not fit in the case of the target population of present study, the Bhoksa tribe.

The contrasting age-wise distribution of G6PD deficiency among the Bhoksa can be explained through their distinct bio-social, socio-economic, cultural, and geographical attributes. They are a tribal population residing in rural, remote hilly terrain with restricted access to healthcare services and thus less exposure to administration of a variety of drugs and medication. This can explain higher prevalence of G6PD deficiency among the younger population as they are not much exposed to trigger stresses of drugs. Also, with increasing age the cardiovascular and other non-communicable complications rise up and the older individuals with G6PD deficiency are at disadvantage on the face of onslaught caused by these comorbidities as they canot cope with the resulting oxidative stress and the restricted access to healthcare services makes the situation worse. Thus, these individuals have a higher chance of getting eliminated from the population resulting in decreased reporting of the allele's prevalence in the higher age group (> 30 years). Their socio-cultural milieu and low economic status also hinder penetration of awareness and healthcare facilities among the community. Implementation of government schemes and public health initiatives can help improve the condition in future.

This study was conducted in January 2020, that is before the covid outbreak in India. But covid outbreak created a new set of challenges for G6PD research. There is potential in each drug designed for one disease to be used in other new conditions in future and one latest example was use of Hydroxychloroquine in the first line treatment method for covid patients while outbreak of the novel coronavirus disease. This strategy backfired in case of G6PD deficient covid patients who were so far asymptomatic and unaware of this genetic deficiency. COVID-19 infection itself can trigger haemolysis in a patient with G6PD deficiency and haemolysis can be possibly worsened by hydroxychloroquine administration (Beauverd *et al.,* 2020). Covid Patients with G6PD deficiency were at high risk of drug induced acute hemolytic anaemia. Such unfortunate incidents and healthcare mismanagement could have been avoided had the patients been screened earlier and had it in their medical records.

Among the scheduled tribes which constitute 2.9 % of total population of the state of Uttarakhand, there are a total 5 notified scheduled tribes here, viz., Bhotia, Buksa/ Bhoksa, Jaunsari, Rajii and Tharu. According to census 2011, Bhoksa constitute 18.5% of the tribal population of the state and live predominantly in rural areas. In the present study, the G6PD deficient % is 1.92 which falls within the range as found out in different studies conducted in the region. The estimated percentage may appear low but further screening for the deficiency cannot be ruled out as with bigger sample size and resources a

clearer picture can be obtained of the G6PD status of the Bhoksa tribe. Some data is available on Bhotias of Uttarakhand and their G6PD deficient prevalence is in the same range as the prevalence found among Bokshas in the present study. But this may not be sufficient for effective comparison as there is dearth of substantial data on the neighboring tribes.

CONCLUSIONS

Regular screening of G6PD deficiency in population groups is important as it helps in safe administration of antimalarial drugs and other oxidative stress causing drugs that can trigger manifestations of G6PD deficiency in otherwise asymptomatic G6PD deficient individuals.

Neonatal screening for G6PD deficiency is highly recommended now more than ever as with advancement in pharmacology people are exposed to an array of drugs from childhood to old age.

Maintaining G6PD status maps through neonatal and adult screening for G6PD deficiency and maintenance of medical records for tribal populations is very important to formulate healthcare policy, mitigation measures and treatment courses. Tribals inhabit mostly remote and rural areas with scarce resources and restricted access to healthcare services which makes it even more important to have data on this important biogenetic marker, as G6PD status is closely interlinked to healthcare management.

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