# Genetic burden of red cell enzyme glucose-6-phosphate dehydrogenase deficiency in two major Scheduled Tribes of Sundargarh district, Northwestern Orissa, India

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**The inherited deficiency of erythrocytic glucose-6-phosphate dehydrogenase (G-6-PD) enzyme is an important metabolic, genetic and public health problem in malaria-endemic areas of India. It is a predisposing factor in the causation of drug-induced haemolytic anaemia and congenital non-spherocytic haemolytic disease resulting in oxidative damage to red blood cell membrane and haemolysis. Although a number of genetic studies have been carried out among the tribes, data on prevalence of G-6-PD deficiency in indigenous tribal people of Orissa are limited. This study was carried out with the aim of field evaluation of the incidence/prevalence of G-6-PD deficiency in two tribal populations, Bhuyan and Kharia of Orissa. It was found that the overall deficiency of enzyme was high in both Kharia (24.9%) and Bhuyan (16.9%) Scheduled Tribes and the difference between them was also statistically highly significant ($P < 0.001$). Both males and females were equally vulnerable. The frequency of G-6-PD deficiency was recorded to be 22.5, 16.8 and 13.7% in Paraja, Paik and Paudi Bhuyans, respectively in Sundargarh District, Orissa. The deficiency was higher in Dhelki Kharia (30.4%) in comparison to Dudh Kharia (20.4%), suggesting their genetic divergence from each other in due course of time ($P < 0.001$). The deficiency of 30.4% in Dhelki Kharia tribal community reported from Orissa is the highest in India. The genetic burden of G-6-PD deficiency is very high in these tribal populations of Orissa, which may result in a high degree of morbidity, mortality and neonatal wastage. From clinical point of view, antimalarials should be administered with caution in malaria-endemic tribal populations.**

**Keywords:** Bhuyan tribe, G-6-PD deficiency, haemolytic genetic disorder, Kharia tribe, tribal health.

LIKE in other South Asian countries, the tribal population of India offers great opportunities to study genetic variability. Perhaps nowhere in the world is such an amalgamation of a large number of caste, ethnic, religious and linguistic groups available as in India and South East Asian countries. All these groups of people living side-by-side for hundreds or even thousands of years independently, try to retain their separate and unique identities by practising endogamy[1]. Such human isolates are of significant importance and owe a tremendous wealth to the students of biological anthropology, human biology, human population genetics, genomics and molecular medicine.

Glucose-6-phosphate dehydrogenase (G-6-PD) deficiency is inherited as an X-linked trait with intermediate dominance and the gene for G-6-PD is located on chromosome Xq28 in juxtaposition with the gene for colour blindness and haemophilia A. Full expression of the deficiency occurs in hemizygous males and homozygous females. More than 300 G-6-PD variants have so far been detected in the world. It has been estimated that more than 200–400 million people are suffering from this defect throughout the world[2]. G-6-PD deficiency is mainly found in populations originating from tropical and sub-tropical areas of the world. The geographic distribution is similar to that of falciparum malaria. The deficiency of G-6-PD is found in the belt extending from the Mediterranean area through South-west Asia, India to South East Asia[3].

The inherited deficiency of erythrocytic G-6-PD enzyme is an important metabolic, genetic and public health problem in malaria-endemic areas of India. It is a predisposing factor in the causation of drug-induced haemolytic anaemia and congenital non-spherocytic haemolytic disease. G-6-PD deficiency is the most common defect in hexose monophosphate (HMP) shunt pathway resulting in oxidative damage to red blood cell (RBC) membrane and resultant haemolysis. The combined effect of HMP shunt is to metabolize glutathione (GSH) responsible for protecting intracellular proteins from oxidative stress. The process of haemolysis can be triggered by a variety of insults, including exposure to drugs, fava beans, toxins or viral/bacterial infections. The interaction of oxygen with heme in the presence of these offending agents, results in production of oxidants. These oxidants are not effectively neutralized due to deficiency of G-6-PD enzyme resulting in cellular damage and death of RBC corpuscles.

Orissa occupies a unique position in the tribal map of India, having the largest number of Scheduled Tribes (STs 62), including 13 primitive tribes, unevenly distributed in

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forest and hilly areas, with a tribal population of over 8.15 million constituting 22.3% of the population of the State according to the 2001 census. Genetic studies so far undertaken on them are scanty, patchy and incomplete[4]. Hereditary haemolytic disorders, especially G-6-PD deficiency, occur in high frequency among tribal populations, which result in a high degree of morbidity, mortality and neonatal wastage due to haemolysis and are important genetic and public-health problems. Although a number of genetic studies have been carried out elsewhere among the STs, data on prevalence of G-6-PD deficiency in indigenous tribal people of Orissa are limited. This study was aimed at a field evaluation of the incidence/prevalence of G-6-PD deficiency in two tribal populations of Orissa.

## Materials and methods

### *Geographical location*

The study was carried out in Sundargarh District, Orissa. This district in Northwestern Orissa is surrounded by Jharkhand in the north, Chhattisgarh in the west, Keonjhar District in the east, and Jharsuguda, Sambalpur, and Deogarh districts in the southern part of the district (Figure 1).

### *Background of tribes*

This study was part of our larger project for screening of major ST communities for haemoglobinopathies in Sundargarh District. Two tribes, namely Bhuyan and Kharia and their subgroups were studied. Traditionally, the Bhuyan and Kharia tribes are hunting and food-gathering communities, practising shifting cultivation, and follow tribal endogamy. The Kharia tribe has two distinct subgroups, Dudh (Pure) Kharia and Dhelki (Late Comer) Kharia, based on religious and socio-cultural practices, although originally they belonged to one ethnic stock. Dudh Kharias are now converted Christians, whereas Dhelki Kharias are Hinduised tribe. Marriages between these two sects are now unheard of. The Bhuyan tribe also has three subgroups, i.e. Paik or Khandayat (Warrior), Paraja (Public), and Pahari or Paudi (Hill), distinguished from each other on the basis of three grades of primitive culture in Orissa. The Hill Bhuyans, the primitive and backward section, represent the hunting and food-gathering stage of economic life along with the practice of rudimentary shifting cultivation and primitive culture. The Paraja Bhuyans represent the more advanced culture practising plough-cultivation and food production. The Khandayat or Paik Bhuyans have the most advanced culture, which equates them with other nontribal populations of the region. Inter-group marriges do not take place at all. Reproductively and genetically, they are completely isolated from each other.

### *Sampling procedure*

According to the 1991 census, the total population of Sundargarh District was 1,573,617, which constituted 50.7% of the tribal population in the district. Out of the total 40 STs,

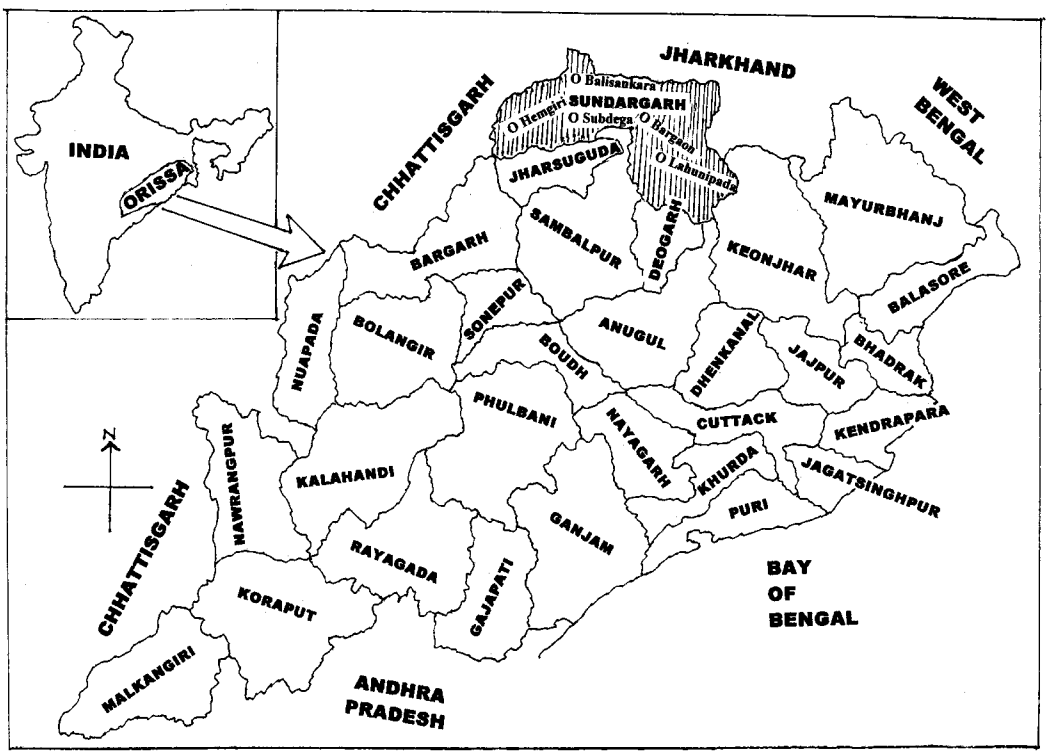


**Figure 1.** Area of Orissa showing thirty districts and the study area (shaded).

there are five major tribes in the district, namely Bhuyan, Kharia, Kissan, Munda and Oraon, each having more than one lakh population according to the 2001 census. The scatter and distribution of these STs in a particular locality are shown in the *Adivasi Atlas of Orissa*[5].

Following the probability proportionate to size cluster sampling procedure for villages, the present study was carried out randomly selecting exclusive villages of each subgroup of tribes in five blocks, namely Balisankara (Dhelki Kharia), Bargaon and Subdega (Dudh Kharia) for Kharia tribe, Hemgiri (Paik and Paraja Bhuyan) and Lahunipada (Paudi Bhuyan) for Bhuyan tribe (Figure 1). Randomized sampling procedure was adopted for each subgroup irrespective of age, sex and individual morbidity (susceptibility) pattern. A total of 767 persons of the Kharia tribe were studied. There were overall 422 persons (196 males and 226 females) who belonged to Dudh Kharia tribe and 345 persons (181 males and 164 females) were of the Dhelki Kharia tribe. Similarly, out of a total 836 Bhuyans, there were 213 (106 males and 107 females) Parajas, 244 (117 males and 127 females) Khandayat or Paik, and 379 (184 males and 195 females) Pahari or Paudi Bhuyans. On the whole, a total of 1603 Bhuyan and Kharia tribes were studied.

### *Blood collection*

About 2–3 ml intravenous blood samples was collected using ethylene diamine tetraacetic acid as anticoagulant using disposable syringes and needles from each individual, after obtaining informed/written consent in the presence of a doctor and community leaders. Any other ailment present was treated/referred to local health facilities. Blood samples so collected were transported to the laboratory at Bhubaneswar under ice-cold conditions within 24 h of collection. Laboratory investigations were carried out following standard procedures after cross-checking for quality control from time to time.

### *Laboratory analysis*

G-6-PD enzyme deficiency was detected using dichlorophenol indophenol dye as described by Bernstein[6] and subsequently confirmed by WHO procedures[7] and those of Beutler and coworkers[8].

Females heterozygous for G-6-PD deficiency have two populations of cells, one with normal G-6-PD activity and the other deficient. This is the result of inactivation (Lyon's hypothesis) of one of the two X-chromosomes in individual cells early in the development of the embryo. All progeny (somatic) cells in females will have the characteristics of only the active X-chromosome. Total G-6-PD activity of blood in females will depend on the proportion of normal to deficient cells. In most cases, the activity will be between 20 and 80% of the normal. However, a few heterozygotes (about 1%) may have almost only normal or only G-6-PD-deficient cells. The present study did not encounter any such ambiguity; 60–80% of the cells were either normal or deficient in all cases.

### *Statistical analysis*

Results obtained were statistically tested to find the differences, if any, between the distribution of G-6-PD deficiency in the two tribes and their subtribes. The chi-square test was used for statistical significance.

## Results

The sex-wise distribution of G-6-PD deficiency in Bhuyan and Kharia tribes and subtribes of Sundargarh District is presented in Table 1. It is apparent that overall deficiency of this enzyme is high in both Kharia (24.9%) as well as Bhuyan (16.9%) tribes and the difference between the tribes is statistically highly significant ($P < 0.001$). Both males and females are equally vulnerable. The frequency of G-6-PD deficiency was quite high in Paraja Bhuyan tribe (22.5%), being predominant in males (15.0%) compared to females (7.5%). The deficiency detected was also high in Paik Bhuyan tribe (16.8%), with males (10.2%) prepondering over females (6.6%). The frequency of G-6-PD deficiency was recorded to be 22.5, 16.8 and 13.7% in Paraja, Paik and Paudi Bhuyans, respectively in Sundargarh district. However, the only difference between Paraja Bhuyan and Paudi Bhuyan subtribes was statistically significant ($P < 0.01$). Both homozygote and heterozygote females were encountered indicating a major genetic and public health problem related to malaria in these tribal communities.

G-6-PD enzyme deficiency was higher in Dhelki Kharia (30.4%) in comparison to Dudh Kharia (20.4%) subtribes, suggesting their genetic diversion from each other ($P < 0.001$) in due course of time. Both sexes in both the subtribes of Kharia showed high incidence of deficiency (Table 1). Therefore, from a clinical point of view as Sundargarh District is highly endemic for malaria, antimalarial drugs should be administered with caution in these tribal populations.

## Discussion

It is now well established that the genetic burden of G-6-PD deficiency in Bhuyan (range 13.7–22.5%; average 16.9%) and Kharia (range 20.4–30.4%; average 24.9%) tribes and their subtribes is heavy owing to hyper endemicity of malaria, especially of *Plasmodium falciparum* leading to considerable morbidity and mortality in Sundargarh District (Table 1). The frequency of G-6-PD deficiency in Dhelki Kharia subtribe (30.4%) is the highest so far reported from India. Earlier, high incidence was reported in Vataliya Prajapati

**Table 1.** Distribution of glucose-6-phosphate dehydrogenase deficiency in Bhuyan and Kharia tribes of Sundargarh District, Orissa

| | | Glucose-6-phosphate dehydrogenase deficiency | | | | | |
|---|---|---|---|---|---|---|---|
| | | Male | | Female | | Total | |
| Tribe/subtribe | *N* | Number | Percentage | Number | Percentage | Number | Percentage |
| Dudh Kharia | 422 | 41 | 9.7 | 45 | 10.7 | 86 | 20.4 |
| Dhelki Kharia | 345 | 54 | 15.6 | 51 | 14.8 | 105 | 30.4 |
| All Kharias | 767 | 95 | 12.4 | 96 | 12.5 | 191 | 24.9 |
| Paraja Bhuyan | 213 | 32 | 15.0 | 16 | 7.5 | 48 | 22.5 |
| Paik Bhuyan | 244 | 26 | 10.6 | 15 | 6.1 | 41 | 16.8 |
| Paudi Bhuyan | 379 | 30 | 7.9 | 22 | 5.8 | 52 | 13.7 |
| All Bhuyans | 836 | 88 | 10.5 | 53 | 6.3 | 141 | 16.9 |

Difference between Bhuyan and Kharia tribes statistically highly significant ($P < 0.001$).
Difference between Dhelki Kharia and Dudh Kharia subtribes statistically highly significant ($P < 0.001$).
Difference between Paraja Bhuyan and Paudi Bhuyan subtribes statistically significant ($P < 0.01$).

caste (27.9%), Surat, Gujarat[9], followed by Angamy Nagas (27.1%) of Nagaland[10], and Gonds (24.4%), Warli (19.5%), Parsis (15.7%) of Maharashtra (see Balgir[11]).

The inherited deficiency of erythrocytic enzyme G-6-PD is a predisposing factor in the causation of drug-induced haemolytic anaemia and congenital non-spherocytic haemolytic disease. The older red cells with enzyme deficiency are more susceptible to oxidative damage, whereas the younger cells with higher enzyme activity are more resistant to haemolysis. Patients with G-6-PD deficiency present haemolytic anaemia of varying degrees of severity. There is no specific cure and treatment, and the management varies from the type of enzyme deficiency and nature of drug dosage. Haemolysis is usually self-limiting and corrected after discontinuation of the drug. Darkening of urine, jaundice and neonatal hyperbilirubinaemia are the common clinical features reported from various parts of India[2,11].

Most of the studies on G-6-PD deficiency published prior to the WHO report[7] were based on investigations carried out on patients in hospitals, manifesting clinical conditions such as haemoglobinuria, neonatal jaundice, drug-induced haemolytic anaemia, etc. Therefore, studies on well-defined populations are too scanty to draw valid conclusions regarding regional variations in enzyme deficiency[1].

The enzyme deficiency was quite high, varying from 5.1 to 15.9% among 15 major STs studied from Orissa[12,13]. The frequency of G-6-PD deficiency was high in males (range 4.3–17.4%) than in females (range 0.0–13.6%). Both deficient female heterozygotes and homozygotes were encountered. High incidence of G-6-PD deficiency was observed among Munda (15.9%), Paraja (15.9%), Kolha (9.8%), Bathudi (9.5%), Bhumiz (9.5%), Santal (9.0%) and Oraon (8.2%) tribes[12,13]. The highest allele ($Gd^-$) frequency of G-6-PD deficiency was observed in Paraja (13.4%) and the lowest in Kissan (2.9%) tribe of Orissa[12].

Table 2 represents the geographical distribution, linguistic affiliation of tribes, and tribal diversity for G-6-PD deficiency in Orissa. It is interesting to note that the deficiency was equally high among the Austro-Asiatic as well as Indo-Aryan speakers (Table 2). The most likely explanation for this situation is that the Austro-Asiatic speakers whose ancestors probably came to Central India or southern Orissa during prehistoric or historical times, had brought this deficient allele with them and later, through the process of admixture, spread it into the populations of Dravidian and Indo-Aryan speakers. Thus the allele frequency of G-6-PD deficiency is low (2.9–5.4%) among the Dravidian tribes of Orissa, viz. Gond, Kondh, Kissan and Oraon (Table 2).

Prevalence of G-6-PD deficiency varies from 1 to 27% in different communities and regions of India, as reviewed earlier[11]. The review shows varying frequencies in different regions and ethnic groups depending upon the hyperendemicity of malaria. In eastern India, the frequency is highest in Angamy Nagas (27.1%), followed by Adi (19.4%), Apatani (16.7%), Nishi (16%), Rabha (15.8%), Mikir (15.6%), Santal (14.1%), etc.[11]. In western India, higher frequency is found in the Vataliya Prajapati (caste) community (27.9%) of Surat, Gujarat[9], Gonds (24.4%), Warli (19.5%), Parsis (15.7%), Madia (14.4%), Cutchi Bhanushalis (13%), etc. In the North, high frequency has been shown in Meghwal-Chamars (15.1%) and Punjabi Khatris (14%) for this defective enzyme. In South India, high incidence of G-6-PD deficiency is found in tribals (13%) of Andhra Pradesh and Kurumba tribe (11.9%) of Kerala[11]. The present study presents the highest frequency of 30.4% in Dhelki Kharia tribal community from Sundargarh district.

There are polymorphic variants of G-6-PD deficiency that have achieved high frequency in some populations and represent balanced polymorphism. On the basis of specific biochemical properties, several rare variants of G-6-PD deficiency have been identified in India, which need mention: G-6-$PD^{Cutch14}$, G-6-$PD^{Jammu15}$, G-6-$PD^{Kalyan16}$, G-6-$PD^{Kerala17}$, G-6-$PD^{Porbandar14,18}$, G-6-$PD^{West\ Bengal17}$ and G-6-$PD^{Orissa19}$. The well-known polymorphic variants are G-6-$PD^{Mediterranean}$ (slow moving G-6-$PD^{B-}$ or 563C → T),

**Table 2.** Distribution of G-6-PD deficiency ($Gd^-$) in different tribes of Orissa

| Tribe | Number tested | $Gd^+$ (%) | $Gd^-$ (%) | Allele frequency $Gd^-$ | Reference |
|---|---|---|---|---|---|
| Austro-Asiatic (Mundari) speakers | | | | | |
| Northern Orissa | | | | | |
| Bhumiz | 116 | 90.5 | 9.5 | 0.076 | 12 |
| Juang | 879 | 86.9 | 13.1 | 0.131 | 26 |
| Juang (males) | 53 | 86.8 | 13.2 | 0.132 | 27 |
| Dudh Kharia | 422 | 79.6 | 20.4 | 0.204 | Present study |
| Dhelki Kharia | 345 | 69.6 | 30.4 | 0.304 | Present study |
| Kharia | 54 | 85.8 | 14.2 | 0.080 | 12 |
| Kolha | 102 | 90.2 | 9.8 | 0.125 | 12 |
| Munda | 96 | 84.1 | 15.9 | 0.114 | 12 |
| Munda (males) | 52 | 88.5 | 11.5 | 0.115 | 27 |
| Munda (males) | 104 | 86.6 | 13.4 | 0.134 | 19 |
| Santal | 100 | 91.0 | 9.0 | 0.074 | 12 |
| Santal (males) | 53 | 88.7 | 11.3 | 0.113 | 19 |
| Southern Orissa | | | | | |
| Bondo | 839 | 99.6 | 0.4 | 0.004 | 26 |
| Didayi | 1014 | 98.3 | 1.7 | 0.017 | 26 |
| Saora | 177 | 92.1 | 7.9 | 0.071 | 12 |
| Dravidian (Gondi or Kuvi) speakers | | | | | |
| Gond | 219 | 94.1 | 5.9 | 0.044 | 12 |
| Kissan | 130 | 94.9 | 5.1 | 0.029 | 12 |
| Koda (males) | 56 | 91.1 | 8.9 | 0.089 | 19 |
| Kondh | 645 | 92.1 | 7.9 | 0.079 | 26 |
| Kondh | 254 | 93.3 | 6.7 | 0.054 | 12 |
| Kutia Kondh | 65 | 93.9 | 6.1 | 0.061 | 28 |
| Oraon | 104 | 91.8 | 8.2 | 0.040 | 12 |
| Paraja | 176 | 84.1 | 15.9 | 0.134 | 12 |
| Indo-Aryan or Indo-Europeans | | | | | |
| Bathudi (males) | 106 | 88.7 | 11.3 | 0.113 | 19 |
| Bathudi | 95 | 90.5 | 9.5 | 0.071 | 12 |
| Bhatra | 166 | 93.4 | 6.6 | 0.057 | 12 |
| Bhatra | 105 | 97.2 | 2.8 | 0.028 | 29 |
| Bhuyan | 92 | 87.1 | 12.9 | 0.045 | 12 |
| Bhuyan (males) | 102 | 85.3 | 14.7 | 0.147 | 27 |
| Bhuyan (males) | 204 | 85.3 | 14.7 | 0.147 | 19 |
| Paraja Bhuyan | 213 | 77.5 | 22.5 | 0.225 | Present study |
| Paik Bhuyan | 244 | 83.2 | 16.8 | 0.168 | Present study |
| Paudi Bhuyan | 379 | 86.3 | 13.7 | 0.137 | Present study |
| Lodha | 78 | 94.9 | 5.1 | 0.051 | 12 |
| Saunti (males) | 52 | 92.3 | 7.7 | 0.077 | 19 |

G-6-PDAfrican (fast-moving G-6-$PD^{A-}$) and G-6-$PD^{Oriental}$. There are biochemically characterized about 13–14 variants reported from the Indian population. However, not all of these variants have been characterized at the molecular level. It was also found that variants that were thought to be biochemically distinct shared the same mutation. The variants, G-6-$PD^{Kerala}$ and G-6-$PD^{Kalyan}$ reported as two distinct biochemical variants were later shown to have the same (969G → A) mutation[20]. Similarly, two distinct biochemical variants, G-6-$PD^{Rohini}$ and G-6-$PD^{Jamnagar}$ were also found to have the same (949G → A) mutation.

G-6-PD enzyme deficiency among STs (including the tribes of the present study) of India has molecularly been characterized and identified as G-6-$PD^{Mediterranean}$ and a new variant called G-6-$PD^{Orissa}$ (131C → G), which has only 10–20% of the normal enzyme activity and normal electrophoretic mobility, but has fivefold higher Michael's constant for substrates, which actually translates roughly into five-fold lower activity at limiting substrate concentrations and shows increased thermostability than normal enzyme[19]. This means that anti-malarial drugs like primaquine and many other compounds such as phenacetin, furadantin, certain sulphonamides and acetyl salicylic acid (aspirin), etc. should be administered with caution among the tribal populations of India, including those in Orissa, which may cause haemolytic crisis and sometimes may even be fatal[13].

Tribal studies in Orissa[13] have shown an evolutionary trend for inverse relationship between the sickle cell allele and G-6-PD deficiency, and sickle cell and $\beta$-thalassaemia allele in a cross-section of malaria (*P. falciparum*) endemic tribal communities. When the frequency of sickle cell

**Table 3.** Age distribution of G-6-PD deficiency cases belonging to tribes and subtribes of Bhuyan and Kharia in Sundargarh District

| Age groups (years) | Dudh $N = 422$ | | Dhelki $N = 345$ | | Total Kharia $N = 767$ | | Paraja $N = 213$ | | Paik $N = 244$ | | Paudi $N = 379$ | | Total Bhuyan $N = 836$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Number | Percentage | Number | Percentage | Number | Percentage | Number | Percentage | Number | Percentage | Number | Percentage | Number | Percentage |
| 00–10 | 20 | 23.3 | 29 | 27.6 | 49 | 25.7 | 6 | 12.5 | 7 | 17.1 | 12 | 23.1 | 25 | 17.7 |
| 11–20 | 18 | 20.9 | 16 | 15.3 | 34 | 17.8 | 13 | 27.0 | 6 | 14.6 | 14 | 26.9 | 33 | 23.4 |
| 21–30 | 17 | 19.8 | 17 | 16.2 | 34 | 17.8 | 7 | 14.6 | 8 | 19.5 | 11 | 21.2 | 26 | 18.5 |
| 31–40 | 16 | 18.6 | 17 | 16.2 | 33 | 17.3 | 12 | 25.0 | 4 | 9.8 | 9 | 17.3 | 25 | 17.7 |
| 41–50 | 6 | 7.0 | 10 | 9.5 | 16 | 8.4 | 6 | 12.5 | 6 | 14.6 | 1 | 1.9 | 13 | 9.2 |
| 51-60 | 7 | 8.1 | 8 | 7.6 | 15 | 7.8 | 2 | 4.2 | 7 | 17.1 | 2 | 3.8 | 11 | 7.8 |
| 61+ | 2 | 2.3 | 8 | 7.6 | 10 | 5.2 | 2 | 4.2 | 3 | 7.3 | 3 | 5.8 | 8 | 5.7 |
| Total | 86 | 100.0 | 105 | 100.0 | 191 | 100.0 | 48 | 100.0 | 41 | 100.0 | 52 | 100.0 | 141 | 100.0 |

allele decreases in a cross-section of malaria-endemic tribal population, the frequency of G-6-PD enzyme deficiency and $\beta$-thalassaemia allele increases and vice versa. The detrimental variant of sickle cell allele is being replaced by G-6-PD deficiency allele because of mild clinical manifestations of enzyme deficiency in comparison to crippling manifestations of sickle cell allele in Orissa. Natural selection has played a major role in favour of sickle cell, $\beta$-thalassaemia and G-6-PD mutation alleles, so that they have probably evolved as a protective mechanism against the lethal effects of malaria in this part of the country[13].

The infant mortality rate was comparatively found to be higher in couples with sickle cell trait (75.9), $\beta$-thalassaemia (184.2), and sickle cell/$\beta$-thalassaemia (70.2) compared to normal couples (26.3) in Orissa[21]. Reproductive wastage (abortions, stillbirths and neonatal deaths) and the number of offspring dead below one year of age (infant mortality) and below 10 years of age (childhood mortality) among affected couples in such families were also statistically significantly higher compared to normal parents[21]. Due to prenatal selection and foetal developmental disturbances, the incidence of spontaneous abortions during the first trimester was reported to be higher (21.7%) in women of heterozygous carriers of G-6-PD deficiency compared to control (9.3%) group[22]. Such studies need to be replicated in India.

Table 3 shows the distribution of G-6-PD deficiency cases of Bhuyan and Kharia tribes in different age-group categories. It is interesting to note that there emerges a consistent pattern of declination as we move from lower age to higher age categories, i.e. the number of cases of G-6-PD deficiency decreases consistently in both Bhuyan and Kharia communities under natural environmental conditions. This probably suggests that those with G-6-PD deficiency are unable to cope with the stressful conditions in life and succumb to various types of haemolytic crises and adverse circumstances, and die early or at a prime age. These findings get further support from our earlier studies carried out on haemoglobinopathies in Orissa[23,24].

Early detection and prevention is the key strategy to successful management and control[25]. Genetic counselling, prenatal diagnosis, and health education and public awareness can provide benefits by way of preventive genetics to the affected individuals and their families[25]. It is emphasized that there is further need to evaluate the clinical and prognostic aspects of the G-6-PD enzyme deficiency among the tribal populations of Orissa, which will yield some definite insights into this genetic health problem in Orissa.


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