Correspondence

G>A transition at 376 position of the glucose-6-phosphate dehydrogenase (G6PD) gene plays a key role in causing G6PD deficiency in the Siddi population of Karnataka

Glucose-6-phosphate dehydrogenase (G6PD) deficiency, a common enzymatic disorder affecting over 400 million people globally, is primarily found in the Sub-Saharan African region, the Middle East, and Asia. In India, the prevalence ranges from 2.3% to 27%, with a higher incidence among tribal populations. Over 400 G6PD variants have been identified, with 217 unique variants solely based on molecular defects. Only 10% of G6PD variants have been structurally and functionally characterized.[1–4]

We investigated the G6PD A– (376A>G and 202G>A) and G6PD A+ (376A>G) variants in the Siddi population of Karnataka, India. There are 50 000 Siddi people in India, with more than a third living in Karnataka. These areas are malaria endemic regions. Previous studies have not investigated both G6PD A– and G6PD A+ variants in Siddi tribes of Karnataka. These mutations are more common in Africans and Siddis have African ancestry.[5–7]

Peripheral blood samples from 120 individuals from the Siddi tribe in North Karnataka, India, where malaria is endemic were obtained. The sample size was calculated using a 95% confidence level and a margin of error of 2%. Samples were collected in an EDTA vacutainer and transferred to the laboratory. Histological analysis was performed on the samples, and reticulocytes were seen under a binocular microscope. Biochemical analysis was performed on the samples, using the G6PD enzymatic activity using the quantitative method. Genetic analysis was carried out on the samples, using the blood and tissue DNA isolation kit. The polymerase chain reaction (PCR) products were treated with restriction enzymes FokI and NIaIII for G6PD 376A>G and G6PD 202G>A variants. The data were analysed using the Statistical Package for Social Sciences 15.0 software, with chi-square tests to determine the distribution of allelic and genotype frequencies. Descriptive statistics were used to calculate the mean and standard deviation for numerical data, and analytical statistics and Student *t*-test were used to assess the statistical significance of the difference between study group means.

Only 41 (68.3%) individuals showed deficit activity in G6PD enzyme activity, suggesting that the remaining 19 (31.7%) individuals may have other deficiency or condition or they may have G6PD deficiency with normal enzyme activity. Deficient G6PD enzyme activity was seen more in men (73.2%) compared to women (26.8%).

The frequency of targeted mutations in G6PD enzymatically defective individuals was 65.9% in our study; 24.4% had the G6PD A+ (376 A>G) variant and 41.5% had the G6PD A– variant (202 A>G and 376 A>G). The biochemical properties of the A– and A+ variant found in Indian Siddis were similar to those in African G6PD A– individuals.

Our findings are similar to other studies with G6PD A+ being low compared to G6PD A–.[8–10] There is a large diversity between Indian states for deleterious G6PD variants, suggesting the need for complete sequencing of the entire G6PD gene in malaria endemic areas for early detection and prevention of G6PD deficiency. Early diagnosis of G6PD deficiency in vulnerable groups will further help the administration of anti-malaria drugs.

TABLE I. Allelic and genotype frequencies for both G6PD A– variant and G6PD A+ variant

G6PD A– 202G>A and 376A>G

Group	Genotype			Allelic frequency		p value
	GG	AG	AA	G	A	
Cases (*n*=41)	24	04	13	0.63	0.37	0.001
Controls (*n*=41)	40	01	00	0.99	0.01	0.99

G6PD A+ (376A>G)

Group	Genotype			Allelic frequency		p value
	AA	AG	GG	A	G	
Cases (*n*=41)	31	02	08	0.78	0.22	0.001
Controls (*n*=41)	39	02	00	0.98	0.02	0.98

GG homozygous wild AG homozygous mutant AA heterozygous

Conflicts of interest. None declared

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