

The role of the G6PD A-376G/968C allele in glucose-6-phosphate dehydrogenase deficiency in the seerer population of Senegal

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is common in tropical Sub-Saharan countries. The allele most frequently associated with G6PD deficiency in this a region is G6PD 376G/202A. Here, we show that, the prevalence of G6PD deficiency is 12% in the Sereer ethnic group from Senegal ant that the 376G/968C genotype is predominant; the frequency of the 376G/202A genotype is very low in this ethnic group.

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In Sub-Saharan Africa, the predominant cause of glucose-6-phosphate dehydrogenase (G6PD) deficiency is G6PD A- (376G/202A). 376 G is a polymorphic mutation (allele A) and 202A is responsible for the enzyme deficiency.¹ However, the 376G mutation may also be associated with other deleterious mutations: 376G/680T, 376G/968C (G6PD A) and 376G/542T (G6PD Santamaria). The aim of this study was to establish the prevalence of G6PD deficiency in the Sereer group from Senegal. This was done by molecular analysis because enzymatic activity was difficult to measure locally.

The study took place in the Niakhar area located 150 km southeast of Dakar, where the large majority of people belong to the Sereer ethnic group. We investigated 430 unrelated children (220 girls and 210 boys). DNA analysis was performed by polymerase chain reaction (PCR). For amplification of exons of the *G6PD* gene, we used specific 5'-biotinylated primers in order to screen for the mutations 202A, 376G, 542T, 680T, 968C by reverse dot blot hybridization.

The Sereer group is the second most important ethnic group in Senegal (17%). Using a molecular technique we established the prevalence of G6PD genotypes in this population living in a tropical region of Africa. The frequencies of the G6PD B (376A), A+ (376G), A- (376G/202A; 376G/680T; 376G/968C) and Santamaria (376G/542T) alleles were 0.68, 0.20, 0.11 and 0.01 respectively. Several genotypes were observed in the females. Three girls (1.4%) were enzyme-deficient (A-/A-) and 40 girls (18.2%) were carriers of a deleterious mutation. The frequency of the wild type B allele was relatively high in this group and similar to that reported by Pinto *et al.*² in Equatorial Guinea (0.72). The frequency of the B allele is lower in other tropical Sub-Saharan countries: 0.51 in Gabon³ and in the Ivory Coast.⁴ The prevalence of G6PD deficiency in the Sereer group was relatively low (12% among males) compared to that in other tropical Sub-Saharan countries: around 21% in several African populations;¹ 22% in the Ivory Coast and 24% in Nigeria.⁵ The distribution of the deleterious mutations screened for is shown in Table 1. In males, the prevalence of the A- alleles (376G/202A; 376G/680T and 376G/968C) was 1%, 0% and 10%, respectively, while the prevalence of G6PD Santamaria was 1%. The 376G/968C allele represented 84% of the

Table 1. Prevalence of the four deleterious mutations causing G6PD deficiency in children carrying the G6PD 376G genotype. These children belonged to the Sereer ethnic group from Senegal.

G6PD genotypes	Number of children	Prevalence %	Alleles frequency
Males	210	—	—
376G/202A hemizygous	2	1	0.01
376G/542T hemizygous	2	1	0.01
376G/680T hemizygous	0	0	0
376G/968C hemizygous	21	10	0.10
Females	220	—	—
376G/202A heterozygous	4	1.82	—
376G/542T heterozygous	3	1.36	—
376G/680T heterozygous	0	0	—
376G/968C heterozygous	33	15	—
376G/968C homozygous	3	1.36	—
Alleles			
376G/202A	—	—	0.01
376G/542T	—	—	0.01
376G/680T	—	—	0
376G/968C	—	—	0.09

deficient variants among boys. In females, the prevalence of the 376G/202A heterozygous, 376G/542T heterozygous, 376G/968C homozygous and 376G/968C heterozygous genotypes was 1.82%, 1.36%, 1.36% and 15%, respectively. The most striking feature in this Sereer population was the predominance of the 376G/968C genotype in association with a low frequency of 376G/202A. This is in contrast to other reports from tropical Sub-Saharan countries, in which 376G/202A was the only deficient variant identified. A predominance of the 376G/968C allele in an African Sub-Saharan population has not been described elsewhere. Rare cases of 376G/968C and 376G/542T have been described in Spain,⁶ Costa Rica⁷ and the Canary Islands.^{2,8} Haplotype analysis has indicated that the common G6PD A- allele (376G/202A) has arisen on only one occasion.^{1,9} Screening for G6PD mutations in different ethnic groups, Xu *et al.*⁸ demonstrated an identical haplotype for 376G/968C and 376G/542T alleles in samples from Canary Islands. From the haplotype analysis of G6PD A- (376G/968C) genes, Pinto *et al.*² deduced an African Sub-Saharan influence on the population of the Canary Islands. The rare cases found elsewhere probably derive from migrations through trans-Saharan and trans-Atlantic routes. The prevalence of 376G/968C was particularly high in the Seerer group, suggesting that this variant arose in this part of Africa.

Our study also highlights several issues relevant to population screening for G6PD deficiency. Since the PCR reaction has become so ubiquitous there has been a tendency to rely more on genotype analysis than on phenotypic screening, although it clearly remains preferable to employ both methods. Here, phenotypic screening was not possible and the survey relied on screening for mutations known to be prevalent in this part of the world. The

unexpectedly high frequency of the 376G/968C allele that we observed suggests that other studies in Africa that have been based on the genotypic detection of the 376G/202A allele alone may have underestimated the proportion of G6PD deficient individuals.

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