# Beta-S globin haplotypes in patients with sickle cell anemia: one approach to understand the diversity in Brazil

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Sickle cell anemia (SCA) is defined as a monogenic disease that characterizes the homozygous state of hemoglobin S (Hb S). Hemoglobin S polymerizes under adverse conditions such as deoxygenation, acidosis or dehydration. Its polymers deform erythrocytes and lead to a diverse and complex pathophysiology[1,2]. Beta-S globin haplotypes ($\beta^S$ haplotypes) are important in the comprehension of the clinical diversity of SCA patients. Five haplotypes have been associated with different ethnic groups. They are identified at specific restriction sites and named according to their region of origin and prevalence: Bantu, Benin, Senegal, Arabic-Indian (Saudi) and Cameroon[3]. This study aimed to assess the frequencies of $\beta^S$ haplotypes in patients with SCA from Rio de Janeiro State, Brazil. We analyzed DNA samples from 790 patients with sickle cell disease (SCD) and classified them according to their haplotypes through an analysis of six polymorphic sites reported by Sutton et al.[4]. According to these authors, haplotypes that do not exhibit known digestion patterns should be classified as atypical. The polymorphic sites were evaluated by polymerase chain reaction (PCR) followed by restriction fragment length polymorphism (RFLP)[4,5]. Of the 790 patients, 527 had SCA with the following frequencies of genotyped $\beta^S$ haplotypes: 295 (56.0%) Bantu/Bantu; 128 (24.3%) Bantu/Benin; 44 (8.3%) Bantu/Atypical; 36 (6.84%) Benin/Benin; 10 (1.9%) Benin/Atypical; three (0.57%) Bantu/Cameroon; three (0.57%) Benin/Cameroon; three (0.57%) Atypical/Atypical; two (0.38%) Bantu/Saudi; two (0.38%) Bantu/Senegal and one (0.19%) Benin/Saudi. From the total number of 1054 chromosomes analyzed, 769 (72.96%) were identified with the Bantu allele according to the allelic frequency evaluation; 214 (20.3%) Benin; 60 (5.7%) Atypical; six (0.57%) Cameroon; three (0.28%) Saudi and two (0.19%) Senegal. Data from genotype and allele frequencies are shown in Table 1. The high frequencies of Bantu and Benin haplotypes demonstrate the influence of Western and South-Central African on the evolution of the Brazilian population[6]. We identified atypical haplotypes which may have originated due to genetic mechanisms such as gene conversions and the intense miscegenation between ethnic groups that inhabit Rio de Janeiro State and Brazil. We emphasize the need of identifying and characterizing these genetic variations in order to better understand the clinical aspects and phenotypic diversity found in Brazilian SCD patients.

Table 1 - Allelic and genotypic frequency of beta-S globin haplotypes

| Haplotype $\beta^S/\beta^S$ | Genotypic frequency n (%) | Haplotype globin $\beta^S$ | Allelic frequency n (%) |
|---|---|---|---|
| Bantu/Bantu | 295 (56) | Bantu | 769 (72.96) |
| Bantu/Benin | 128 (24.3) | Benin | 214 (20.3) |
| Bantu/Atypical | 44 (8.3) | Atypical | 60 (5.7) |
| Benin/Benin | 36 (6.84) | Cameroon | 6 (0.57) |
| Benin/Atypical | 10 (1.9) | Saudi | 3 (0.28) |
| Bantu/Cameroon | 3 (0.57) | Senegal | 2 (0.19) |
| Benin/Cameroon | 3 (0.57) | | |
| Atypical/Atypical | 3 (0.57) | | |
| Bantu/Saudi | 2 (0.38) | | |
| Bantu/Senegal | 2 (0.38) | | |
| Benin/Saudi | 1 (0.19) | | |
| **Total** | **527 (100)** | | **1054 (100)** |

$\beta^S$: beta-S globin
Genotype Frequency: number of individuals with respective haplotype
Allele Frequency: number of chromosomes with respective haplotype

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