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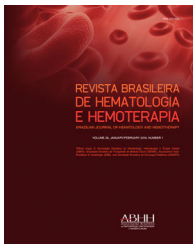

Scientific Comment

Compound heterozygosity for hemoglobin S and D: what do we need to know?☆

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Hemoglobinopathies are among the most common hereditary blood diseases worldwide and are considered a public health problem in some regions. In Brazil, hemoglobin S (Hb S) has a variable frequency between different regions mainly due to the ethnic composition of local populations. Due to the multiethnic characteristics of the Brazilian people, some regions reflect scenarios that allow us to consider the inheritance of the symptomatic forms of Hb S, namely sickle cell disease (SCD) a serious public health problem. These clinically significant forms include the homozygous inheritance of Hb S – sickle cell anemia (Hb SS), inheritance with thalassemia, especially beta thalassemia (Hb S/beta thalassemia) and compound heterozygotes in which Hb S is inherited in combination with another hemoglobin variant; the most common in Brazil are Hb SC and Hb SD.

The application of accurate laboratory methodologies associated to routine techniques such as electrophoresis and high pressure liquid chromatography (HPLC) along with hematologic information and family data are essential for the correct identification of SCD and, consequently, adequate clinical and family guidance that can guarantee a promising prognosis. However, the differentiation between Hb SS and the Hb SD profile is not possible by simple tests such as electrophoresis in alkaline pH as, in these conditions, the migrations of the variants overlap. Additional methods are needed to elucidate this double heterozygosity. Automated systems such as capillary electrophoresis, HPLC cation exchange, isoelectric focusing (IEF) and simplified combinations of electrophoretic systems with variations in the pH are available.[1,2]

There is certain lack of information about the phenotypic manifestations of Hb SD and its variations in publications. In the literature there are some reports of cases of Hb SD with microcytic and hypochromic anemia, pain crises and clinical complications.[3–5] The presence of associated genetic factors may modulate the clinical expression and the presence of elevated Hb F levels and the co-inheritance of alpha thalassemia, for example, should be investigated.[6] The correct identification of individuals and at least the suggestion of potential genetic modulators may assist in estimating the response to treatment using hydroxyurea (HU).[7]

In our laboratory, 1537 patients with SCD from the southeastern region of Brazil were evaluated and 26 (1.69%) had the Hb SD profile confirmed by molecular analysis (polymerase chain reaction-restriction fragment length polymorphism). Of these, ten (38.46%) individuals were on blood transfusions and presented microcytosis, hypochromia and hemolytic indexes that suggested clinically severe disease. Regarding clinical manifestations, all 26 patients had 2–5 pain crises within one year that not necessarily required hospitalization but had to be seen in a follow-up service. Moreover, the patients suffered from strokes (2), retinopathies (3), cardiac insufficiency (3), acute chest syndrome (6), pulmonary hypertension (2), cholelithiasis (3), renal failure (3) and ulcers (2).

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☆ See paper by Rezende et al. on pages 240–6.

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The authors of the article "Clinical, hematological and genetic data in a cohort of children with hemoglobin SD" in this issue of the Revista Brasileira de Hematologia e Hemoterapia (RBHH) show the clinical and hematologic diversity of a group of children with this double heterozygosity and highlight the importance of the differential diagnosis.[8]

Conflicts of interest

The author declares no conflicts of interest.

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