Is sickle cell disease the same everywhere?

Jane Hankins

St. Jude Children's Research Hospital
Memphis, TN, USA

Sickle Cell Disease (SCD) is the most common genetic disease in Brazil where 4% of the general population carries the sickle cell gene and it is estimated that one out of 1000 live births have the disease[1,2]. Although most complications of SCD in children are well-known and understood, they were mostly studied in North American, European, and Caribbean Children, and there is still paucity of clinical data among other populations, such as those from Africa, the Middle East, India, and especially South America. In this cohort study, Dr. Silva Filho and colleagues studied a cohort of very young children (all under six years of age) with different sickle genotypes[3]. The population sampling strategy and rationale for duration of follow-up was not well defined or justified which could leave room for possible sampling bias. Nonetheless, this study offers good descriptive information of clinical and laboratory characteristics of young children with SCD in Brazil, specifically in the State of Rio de Janeiro, where the incidence of the disease is one of the highest in the country.

Febrile illness and splenic sequestration were the most common complications in this group, followed by dactylitis and classic painful events. These findings are in agreement with the description of symptoms in other pediatric groups with SCD such as those from North America[4], and underline the importance of acute and prophylactic treatment of infections. Measures, such as the appropriate management of presumed sepsis during febrile events (preemptive use of antibiotics and blood culture), the use of prophylactic penicillin in under five-year olds, and immunization against encapsulated organisms (*pneumococcus* and *meningococcus*), are all important and should take place in early childhood. Additionally, aggressive parental education regarding signs and symptoms of splenic sequestration, as well as early assessment and treatment of this complication are essential due to its high prevalence and mortality risk.

The incidence of acute chest syndrome (ACS) events was not as high as that described in other pediatric reports; however, the present study used much stricter criteria to define ACS episodes. This Brazilian cohort study classified ACS as new pulmonary infiltrate associated with severe respiratory symptoms, hypoxemia, and need for a blood transfusion. These criteria selected a group of children with ACS events toward the high end of the severity spectrum and did not capture milder ones, which is typically reported in the literature[5].

Laboratory findings, including the most common haplotypes, found in this study confirmed prior reports that the most common haplotypes of SCD patients in Brazil are Bantu and Benin. Fetal hemoglobin (Hb F) values were comparable with those from other populations with similar haplotypes, but as expected, lower than those with the Arab-Indian type[6,7]. Brazilian children with SCD had similar Hb F values compared to American and African descent groups, as well as the expected decline of Hb F values with increased age.

The presence of alpha thalassemia is known to decrease risk of elevated transcranial Doppler velocities (TCD) and stroke, among other complications in patients with SCD[8]. In the present cohort study, the presence of one (silent carrier) or two (trait) alpha gene deletions was associated with a lower incidence of febrile illness (infections), which is an intriguing finding. There is no apparent reason to think that increased hemoglobin concentration and decreased MCV would lead to less bacterial infections. Other effects of alpha thalassemia that might be associated with protection against infection, beyond those known in malaria protection, may be unknown at present and perhaps should be investigated.

The mortality in this study was low compared to what has been reported in literature for Brazilian children with SCD[1]. However, because this cohort was not followed from birth, and not followed for a long period, it is possible that deaths were missed prior to, or after the end of the observation period.

One important aspect of this study is the fact that no information of hydroxyurea or transfusion therapy was provided for this cohort. If a sizeable number of these children were treated with hydroxyurea or chronic transfusions, the outcome of clinical complications would have been modified by these interventions. Future studies involving

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Corresponding author:
Jane Hankins
St. Jude Children's Research Hospital
262 Danny Thomas Place - Mail Stop 800
38105 Memphis, TN, USA
Phone: 901 595 4153
jane.hankins@stjude.org

www.rbhh.org or www.scielo.br/rbhh

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the incidence of complications from SCD should include a description of treatment interventions, so we will be able to understand the impact of therapies in the overall health of individuals living with SCD.

In summary, Brazilian children with SCD are very similar to other pediatric populations of SCD around the world, especially those living in North America, Africa and Europe. It is important to understand clinical and laboratory features of the Brazilian population, so global measures of prevention can be applied and the same desirable outcomes could be expected. Similarities of the SCD population in Brazil to other populations allow for direct comparisons of clinical and laboratory outcomes of interventions provided to other groups, so response to treatment and prevalence of complications from new treatments can be compared to those of other populations worldwide.

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