Sickle cell anemia: a significant potential cause of pulmonary hypertension in Brazil

Anemia falciforme: uma importante causa potencial de hipertensão pulmonar no Brasil

Adriana Ignacio de Padua, José Antônio Baddini Martinez

To the Editor:

Sickle cell anemia is the most common monogenic disease in Brazil; although sickle cell anemia primarily affects Black and Mulatto individuals, it can also affect White individuals.[1] The distribution of the *HbS* gene in Brazil is quite heterogeneous and depends on the racial composition of the population in a given region. The prevalence of heterozygotes is higher in the northern and northeastern regions of the country (6-10%) and lower in the southeastern and southern regions (2-3%). Sickle cell anemia is commonly accompanied by infectious, hemolytic, and veno-occlusive events. Pulmonary complications account for 20-30% of all sickle cell anemia-related deaths and primarily include acute chest syndrome and pulmonary hypertension (PH).[1] In addition, bronchospasm seems to be more common in patients with sickle cell anemia than in the general population.[2]

The mortality rates for patients with sickle cell anemia have significantly decreased in recent decades. This is due to the implementation of early diagnosis programs and the consequent establishment of prophylactic measures as early as in the neonatal period. The introduction of treatments with hydroxyurea seems to have equally contributed to reducing the mortality rates among adults. Consequently, mortality from sickle cell anemia is currently higher in later phases of the disease. It is known that the median survival of patients with sickle cell anemia is approximately 42 years for males and 48 years for females.[3] In addition, the probability that sickle cell anemia patients will live to be 40 years of age is approximately 89% for males and 95% for females.

Data from the Brazilian National Ministry of Health presented in a study conducted by Cançado & Jesus in 2007[1] showed that there were 25,000-30,000 patients with sickle cell anemia in Brazil. In addition, approximately 3,500 new cases of the disease are diagnosed in Brazil each year. Recent studies have shown that the prevalence of PH in patients with sickle cell anemia is approximately 27-40%, as determined by echocardiography.[4,5] However, that prevalence has been shown to decrease to 6-10% after right heart catheterization. The prevalence of precapillary PH, as confirmed by hemodynamic assessment, has been reported to range from 2.8% to 3.8%.[4,5] On the basis of those results, we can speculate that sickle cell disease-associated PH can eventually take on alarming proportions in Brazil. If we take into consideration that 3,500 new cases of sickle cell anemia are diagnosed each year; that the probability that patients with the disease will live to be 40 years of age is 0.9; that the true prevalence of precapillary PH is approximately 0.033; and that those rates might remain stable in the coming decades, it is possible that the number of new cases of sickle cell anemia-associated PH per year will soon be 104.

A study conducted in France and investigating PH estimated a prevalence of 15 cases per one million population for all forms of PH and a prevalence of 6 cases per one million population for the idiopathic form.[6] Considering that Brazil currently has a population of approximately 190 million, we can also speculate that the total number of cases of PH in the country is 2,850, of which 1,140 are cases of idiopathic PH. In contrast, the number of potential cases of sickle cell anemia-associated PH is currently 743-891, meaning that sickle cell anemia can eventually account for approximately 30% of all cases of PH in Brazil.

It is obvious that 2006 epidemiological data from France do not automatically apply to Brazil today, a country in which schistosomiasis is also a major cause of PH. In addition, we do not know for sure how many patients with sickle cell anemia will actually live long enough to develop PH. However, this type of mental exercise can alert

us to a potentially serious medical problem. In addition, there is a lack of conclusive evidence regarding the best therapeutic approaches to sickle cell anemia-associated PH. Therefore, we believe that the referral centers for PH in Brazil should conduct, as soon as possible, further studies investigating the incidence and prevalence of sickle cell anemia-associated PH in Brazil, as well as the response of patients to pharmacological treatments.

Adriana Ignacio de Padua
Attending Physician,
Department of Pulmonology,
***Hospital das Clínicas*,**
***Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo* – FMRP-USP,**
University of São Paulo at Ribeirão Preto School of Medicine – Ribeirão Preto, Brazil

José Antônio Baddini Martinez
Associate Professor,
Department of Clinical Medicine,
***Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo* – FMRP-USP,**
University of São Paulo at Ribeirão Preto School of Medicine – Ribeirão Preto, Brazil

References

1. Cançado RD, Jesus JA. A doença falciforme no Brasil. Bras Hematol Hemoter. 2007;29(3):204-6.
2. Vendramini EC, Vianna EO, De Lucena Angulo I, De Castro FB, Martinez JA, Terra-Filho J. Lung function and airway hyperresponsiveness in adult patients with sickle cell disease. Am J Med Sci. 2006;332(2):68-72.
3. Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, et al. Mortality in sickle cell disease. Life expectancy and risk factors for early death. N Engl J Med. 1994;330(23):1639-44.
4. Parent F, Bachir D, Inamo J, Lionnet F, Driss F, Loko G, et al. A hemodynamic study of pulmonary hypertension in sickle cell disease. N Engl J Med. 2011;365(1):44-53.
5. Fonseca GH, Souza R, Salemi VM, Jardim CV, Gualandro SF. Pulmonary hypertension diagnosed by right heart catheterization in sickle cell disease. Eur Respir J. 2011 Sep 8. [Epub ahead of print]
6. Humbert M, Sitbon O, Chaouat A, Bertocchi M, Habib G, Gressin V, et al. Pulmonary arterial hypertension in France: results from a national registry. Am J Respir Crit Care Med. 2006;173(9):1023-30.