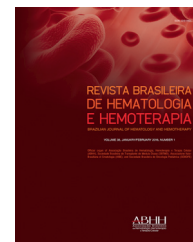




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Original article

Physical activity level and performance in the  
six-minute walk test of children and adolescents  
with sickle cell anemia

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ABSTRACT

**Background:** To establish determinants of maximum walking distance in the 6-minute walk test of children and adolescents with sickle cell anemia, and to compare the performance in this test with physical activity level between patients and healthy controls.

**Methods:** A cross-sectional study was performed in which the participants answered the Physical Activity Questionnaire for Older Children and Adolescents, and completed the 6-minute walk test.

**Main results:** Fifty-seven patients and 58 controls were studied. By univariate analysis of the patients, age ( $p < 0.0001$ ) and indirect bilirubin ( $p = 0.008$ ) were associated with maximum walking distance in the 6-minute walk test. In multivariate analysis, age was positively associated ( $p < 0.0001$ ; beta: 0.75), while body mass index was inversely associated with distance walked ( $p = 0.047$ ; beta:  $-0.32$ ). This yields the following equation: maximum distance walked =  $487.7 (\text{age} \times 18.3) - (12 \times \text{body mass index})$  meters. Patients reported lower physical activity level however there was no difference in the distance walked in six minutes between patients ( $500.6 \pm 88.7$  m) and controls ( $536.3 \pm 94$  m).

**Conclusion:** The determinants for the 6-minute walk test in children and adolescents with sickle cell anemia were age and body mass index. There was no difference in the 6-minute walk test but patients with sickle cell anemia had a lower physical activity level compared to healthy controls.

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## Introduction

Sickle cell anemia (SCA) is the most common monogenic hereditary disease in Brazil. The main characteristic is the inheritance of the beta-globin gene S (gene  $\beta$ s), which is responsible for a mutant hemoglobin (Hb), Hb S. It is estimated that 2–8% of the Brazilian population is heterozygous for Hb S.<sup>1</sup>

Several clinical manifestations are commonly observed in patients with SCA, such as occlusive crisis, acute chest syndrome, stroke, chronic hemolysis and chronic organ dysfunction.<sup>2</sup> These clinical manifestations also appear to be associated with changes in physical capacity, higher basal metabolic rate,<sup>3</sup> lower levels of Hb, pulmonary and vascular diseases, and myopathy.<sup>4</sup>

Different methods are available in the clinical practice to assess physical capacity, such as the six-minute walk test (6MWT), whose main response variable is the maximum walking distance (6MWD), and cardiopulmonary stress test. The 6MWT is a simple and inexpensive test that is widely used in chronic diseases such as chronic obstructive pulmonary disease and heart failure.<sup>5</sup>

Recently, results of the 6MWT in the evaluation of patients with SCA were published<sup>6,7</sup> in an attempt to assess the adequacy of the instrument in this study population. A previous study showed that the determinants of the 6MWD in SCA patients were low Hb level, low concentration of fetal Hb and reduced deformability of red blood cells.<sup>8</sup> However, there are no studies in the Brazilian population, which, being multiracial, does not allow the direct extrapolation of results obtained in more genetically homogeneous populations.<sup>9</sup>

In this sense, recurring complications and hospitalizations appear to be associated with low physical activity levels (PAL) in patients with SCA.<sup>3</sup>

The 6MWT and specific questionnaires, with the main advantages of safety and low cost, are widely used to evaluate the physical capacity and PAL.<sup>10-12</sup> Assessment of the PAL in patients with SCA, whether by questionnaires or by direct testing,<sup>13,14</sup> shows a tendency of a sedentary lifestyle.<sup>15</sup>

The adapted Borg scale<sup>16</sup> is intended to classify the subjective and individual perception of effort in performing the 6MWT in a scale from 0 to 10. This may be analyzed in association with exercise-induced desaturation, that is, the reduction in transcutaneous saturation oxygen by three or more percentage points after testing compared to baseline, both measured using a portable digital oximeter.<sup>17</sup>

The aim of this study was to establish the determinants of the 6MWD in children and adolescents with SCA, as well as to compare PAL and performance in the 6MWT between SCA patients to healthy controls.

## Methods

This is a cross-sectional study conducted in an Outpatients' Clinic of a tertiary teaching hospital in northeastern Brazil. This hospital is the regional referral center for the treatment of patients with SCA.

The project was approved by the Ethics Committee of the Universidade Federal de Sergipe (UFS – protocol: 30661314.0.0000.5546). The legal guardians of both patients and controls signed a written informed consent form.

### Patient group

Patients were enrolled from October 2014 to May 2015. Of the patients with SCA (Hb SS) confirmed by Hb electrophoresis, those who were from 6 to 18 years old, in steady-state, with no blood transfusions in the previous three months and with no acute symptoms for at least one month prior to study entry were considered eligible for this study. Results of molecular tests and a family study were not available. Patients with neurological or orthopedic impairment were excluded.

### Clinical and laboratory data

Hematological data (Hb, hematocrit, the red blood cell, platelet, leukocyte and reticulocyte counts, indirect bilirubin, mean corpuscular volume and lactate dehydrogenase), Hb electrophoresis (fetal Hb and Hb S) and spirometry data were obtained from an electronic database created especially for this research. All the exams were carried out within four weeks before the test and under stable clinical conditions. All the tests were performed at the central laboratory of the hospital, using standard techniques and equipment.

### Current medication intake

All patients were taking folic acid supplement (2 mg/day). Those who were taking hydroxyurea received an initial dose of 15 mg/kg/day and were receiving the standard dose of 20–35 mg/kg/day for at least 12 months.<sup>18</sup>

### Data collection

Data on variables considered potentially associated with the 6MWD were collected. These included age, gender, hydroxyurea therapy, body mass index (BMI), resting heart rate, heart rate at the end of the test, and transcutaneous oxygen saturation at rest and at the end of testing. Furthermore, blood tests were performed including Hb, hematocrit, red blood cell, platelet, leukocyte, neutrophil and reticulocyte count, indirect bilirubin, mean corpuscular volume, lactate dehydrogenase, and Hb fetal and Hb S concentrations. Moreover, the scores obtained with the application of the Physical Activity Questionnaire for Older Children and Adolescents (PAQ-C) and the adapted Borg Scale<sup>16</sup> were included as variables.

### Physical activity questionnaire for older children and adolescents

Immediately before the 6MWT, all the patients answered the Brazilian version of the PAQ-C,<sup>10,19</sup> composed of nine questions about sports, games and other physical activities at school and for recreation. This questionnaire aims to provide a complete picture of the type of activities that the participant had been performing during the previous seven days. Each question was scored on a scale of 1 to 5: very sedentary (1),

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