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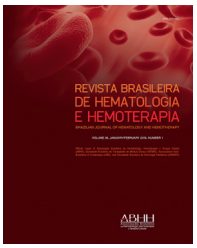

Original article

Mortality in children, adolescents and adults with sickle cell anemia in Rio de Janeiro, Brazil

Clarisse Lopes de Castro Lobo[a], *Emilia Matos do Nascimento*[a,b], *Leonardo José Carvalho de Jesus*[a], *Thiago Gotelip de Freitas*[a], *Jocemir Ronaldo Lugon*[c], *Samir K. Ballas*[a,d,*]

[a] *Instituto de Hematologia Arthur de Siqueira Cavalcanti (HEMORIO), Rio de Janeiro, RJ, Brazil*
[b] *Centro Universitário Estadual da Zona Oeste (UEZO), Rio de Janeiro, RJ, Brazil*
[c] *Universidade Federal Fluminense (UFF), Niteroi, RJ, Brazil*
[d] *Cardeza Foundation, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, United States*

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ABSTRACT

Objective: To determine the mortality rate of children, adolescents and adults with sickle cell anemia in Rio de Janeiro, Brazil.
Methods: The number of deaths, the mortality rate and the causes of deaths in patients with sickle cell anemia who were treated and followed up at our institution for 15 years were determined and compared to data available for the Brazilian population.
Results: The overall number of deaths was 281 patients with a mortality rate of 16.77%. Survival probability was significantly higher in females. The number of deaths and the mortality rate were age-specific with a significant increase in the 19- to 29-year-old age group. The remaining life expectancy of the patients with sickle cell anemia was less than that of Brazilians at large. The gap between the two was about 20 years for ages between one and five years with this gap decreasing to ten years after the age of 65 years. The most common causes of death were infection, acute chest syndrome, overt stroke, organ damage and sudden death during painful crises.
Conclusion: To the best of our knowledge, this is the first Brazilian study in a single institution in Rio de Janeiro; the mortality rate was 18.87% among adult patients with sickle cell anemia. The mortality rates in children and adults are higher than those reported in developed countries of the northern hemisphere.

* *Corresponding author at*: Cardeza Foundation, Department of Medicine, Sidney Kimmel Medical College, Thomas Jefferson University, 1020 Locust Street, Philadelphia, PA 19107, United States.
E-mail address: samir.ballas@jefferson.edu (S.K. Ballas).
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Introduction

The mortality rate among infants, children and young adults with sickle cell disease (SCD) in general and sickle cell anemia (SCA) in particular is high. The overall death rates in under 20-year-old children reported by the Cooperative Study of Sickle Cell Disease (CSSCD) about 30 years ago were 2.6% for patients with all types of SCD and 3.3% for patients with SCA.[1] Sickle cell disease-related mortality decreased significantly from 1999 to 2009 in the USA in all pediatric age groups up to age 19 years.[2] This decline in mortality was the highest for children younger than one year where the decrease was 61% less than the mortality rate during 1979–1998.[2] The mortality in young adults (ages 20–24 years), however, increased sharply compared to the mortality in children ages 15–19 years from 0.6/100,000 to 1.4/100,000.[2] This increase is attributed to problems associated with the transition from pediatric to adult care.

Unlike the USA, the mortality rate in developing countries continues to be high especially in Africa.[3,4] In the state of Minas Gerais, Brazil the mortality rate among children with SCD born during 2009–2011 was not significantly different from that for children born during 1999–2001 (6.2% vs. 5.8%).[5] This suggests that newborn screening alone is not enough to reduce the mortality rate of children with SCA. Regular follow-ups, compliance to treatment, family support and the style of life are important factors to maintain the decreases in both morbidity and mortality rates. The purpose of this study was to determine the mortality rates and the cause of death in children, adolescents and adults with SCA followed-up at a single institution in Rio de Janeiro and compare these rates to Brazilian children and adults at large.

Methods

Patients

Data of patients with SCA including patients with sickle/β^0-thalassemia (S/β^0thal), who were seen and followed at HEMORIO for 15 years from January 1, 1998 through December 31, 2012 were retrospectively collected and analyzed. Children (<18 years old) and adults (≥18 years) were included in the study. Age and sex related mortality were also determined and compared to available data of the Brazilian population at large.

The diagnosis of SCA including S/β^0thal was confirmed by high performance liquid chromatography (HPLC) as previously described.[6] The date and cause of deaths were confirmed on patients' charts if death occurred at HEMORIO. Death outside HEMORIO, suspected when patients failed to show up for a follow-up, was confirmed by interviews with the patient's families and from death certificates. Accordingly, the death of 69 patients occurred outside HEMORIO. The family brought the death certificates of 62 patients. Of these 13 deaths were due to accidents unrelated to SCA and in 49 patients, death was due to stroke, acute chest syndrome (ACS) or infection. The cause of death in the remaining seven patients was not clear or could not be confirmed and hence, their cause of death was included in the unknown category.

The study was approved by the Institutional Review Board of HEMORIO.

Statistical analysis

Statistical analysis was performed using the R software[7] and the Kaplan–Meier estimator to assess the overall survival of patients with SCA. Comparison of survival curves was made using the Tarone-Ware test.[8] Exclusions from statistical analyses included patients whose deaths were unrelated to SCD and those whose cause of death was unknown. Comparisons of frequencies between nominal variables were made using the chi-squared test without continuity correction or the Fisher exact test. Determination of the average remaining life expectancy was determined by the empirical likelihood (Emplik) ratio test package[9] of the R software. Statistical significance was based on a p-value <0.05.

Results

The total number of patients enrolled in this study was 1676. Age (both at enrollment and at death) and sex are summarized in Table 1. A total of 281 patients died during the study period (Table 1). The mortality rate is summarized in Table 2.

A Kaplan Meier analysis[8] of the survival probability of all enrolled patients showed that survival of females was significantly higher than males (p-value = 0.007). The median age of survival was 53.3 years for males and 56.5 years for females (Figure 1). The median age at death was 28.98 years for men and 34.02 years for women (Table 1).

Table 1 – Characteristics of patients with sickle cell anemia.

	Female	Male	Total
Patients – n (%)	889 (53)	787 (47)	1676 (100)
Deaths – n (%)	139 (49)	142 (51)	281 (100)
Age at enrollment (years) – mean ± SD	12.52 ± 11.06	10.99 ± 10.46	11.80 ± 10.81
Median (range)	8.89 (0.02–66.99)	7.30 (0.14–62.66)	8.12 (0.02–66.99)
Age at death (years) – mean ± SD	33.85 ± 14.80	32.71 ± 14.25	33.27 ± 14.51
Median (range)	34.02 (2.74–74.79)	28.98 (0.56–68.03)	31.98 (0.56–74.79)

SD: standard deviation.

Table 2 – Mortality rate of the enrolled patients.

	Patients n	Deaths n	Mortality rate %
Children (<18 years old)	420	44	10.48
Adults (>18 years old)	1256	237	18.87
All patients	1676	281	16.77

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