

Epidemiology of sickle cell disease hospital admissions in Brazil

Monique Morgado Loureiro and Suely Rozenfeld

Escola Nacional de Saúde Pública. Fundação Oswaldo Cruz. Rio de Janeiro, RJ, Brasil

Keywords

Sickle cell anemia, epidemiology.
Sickle cell anemia, diagnosis. Hospital information system.

Abstract

Objective

Sickle cell disease is a hereditary disease, which affects mainly the black population. The aim of the present study was to analyze hospital admissions due to acute events resulting from sickle cell disease, at the epidemiological and clinical levels.

Methods

The study population included 9,349 patients with sickle cell disease admitted to hospitals in Bahia, Rio de Janeiro, and São Paulo, between 2000 and 2002. The national hospital database of the Brazilian Healthcare System was used. Response variables were death and mean duration of hospital admission. Covariables included sex, age, type of admission, and hospital legal status. Proportions were compared using Chi-square or Fischer tests; for continuous variables, the Mann-Whitney or Kruskal-Wallis tests were used.

Results

Median age ranged between 11.0 and 12.0 years, and 70% of admissions were of patients below age 20 years. Length of stay varied with age and type of admission. Emergency rooms were the most frequent form of admission (65.6 to 90.8%). Mortality was higher among adults. Median age of death was low (26.5 to 31.5 years).

Conclusions

Our results confirm the high morbidity among youngsters and show a predominance of death among young adults.

INTRODUCTION

Sickle cell disease is the most prevalent hereditary hematological disease worldwide.¹⁵ It affects hemoglobin (Hb), generating an altered form of this protein known as hemoglobin S (HbS). In certain situations, the polymerization of HbS may occur, leading to the deformation of red blood cells (which assume a sickle-like conformation), vascular obstruction phenomena, episodes of pain, and organ lesions.⁶ It is estimated that approximately 7% of the world population is affected by hemoglobin disorders, represented mostly by thalassemias and sickle cell dis-

ease. Late diagnosis of such diseases may lead to death during the first years of life.¹⁶

The highest prevalence of HbS is found in tropical Africa and among the black population of countries formerly involved in slave trade.¹⁵ In Brazil, between 0.1 and 0.3% of the black population is affected by this disease,^{7,12} and there is an estimated prevalence of at least two million heterozygous HbS carriers in the population. In the Southeast Region, the estimated prevalence of heterozygous carriers is 2% in the general population and between 6 and 10% in the black population.⁶ A population-based study⁸ conducted

Correspondence:

Monique Morgado Loureiro
Rua Barão de Lucena, 140 Apto 901 Botafogo
22260-020 Rio de Janeiro, RJ, Brasil
E-mail: mmorgado@uol.com.br

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in the state of Minas Gerais, Southeastern Brazil, found an incidence of one new homozygous case of sickle cell disease for every 2,800 births. In the state of Rio de Janeiro, also in Southeastern Brazil, Lobo et al⁵ found an incidence of one new case in every 1,196 births. The clinical manifestations of the disease begin in the first year of life and last for the entire lifetime, showing great clinical variability.⁶ The most frequent clinical presentation is vasocclusive pain crisis.⁹ Other clinically relevant interurrences include acute chest syndrome¹⁴ and bacterial infections,³ which, together with vasocclusive pain, can lead to hospital admission, morbidity, and death.¹⁰ In Brazil, Alves¹ found that 78.6% of deaths due to sickle cell disease occurred before age 29 years, and that 37.5% were concentrated among children under nine years old. The high lethality, mainly among youngsters, reflects the severity of the disease.

The Brazilian literature provides little information on the different aspects of sickle cell disease. The hospital admission authorization (HAA) is necessary for hospital admission and for authorizing clinical or surgical procedures in all hospitals run by the Brazilian Unified Healthcare System (*Sistema Único de Saúde* – SUS). HAA data are made available in a CD-ROM version, published monthly by the SUS Hospital Information System (SIH/SUS).^{*} The demographic and clinical data present in the HAA may provide important complementary epidemiological information on sickle cell disease.

The aim of the present study was to analyze hospital admissions due to complications of sickle cell disease, focusing on epidemiological and clinical aspects. We describe the characteristics of the sickle cell hospital admissions reported by SUS, characterizing patients, admissions, and hospitals.

METHODS

The study population was composed of patients with diagnosis of sickle cell disease admitted to hospitals in the states of Bahia (BA), Rio de Janeiro (RJ), and Sao Paulo (SP) in 2000, 2001, and 2002. These three states were chosen for being those with the largest black populations according to the Brazilian Institute of Geography and Statistics (2000). The state of Bahia has the highest proportion of blacks among all Brazilian states.

Data were obtained in from the annual SIH/SUS database in a reduced form. Cases were selected according to type of morbidity, following the classifica-

tion adopted by the 10th International Classification of Diseases (ICD-10). For case selection, the presence of the following ICD codes in the “primary diagnosis” or “secondary diagnosis” fields were selected: D57.0 (sickle cell disease with crisis), D57.1 (sickle cell disease without crisis), D57.2 (double heterozygous sickle cell disorders), or D57.8 (other sickle cell disorders). Cases with ICD codes different from those above were excluded. Outcome variables were death and mean duration of hospital admission. Covariables included sex, age, type of admission, and legal status of the hospital.

Cases aged 0-19 years were classified as children/adolescents, and cases aged 20 years or older were classified as adults. Such classification has already been reported in the literature and was used to allow for comparisons with the results of other studies.^{3,4,10}

Statistical analysis was performed using SPSS 10.0 software. Proportions were compared using Chi-square or Fischer tests; for continuous variables, the Mann-Whitney or Kruskal-Wallis tests were used.

RESULTS

We selected 9,349 hospital admissions, of which 610 were in BA, 2,799 in RJ, and 5,940 in SP. Sickle cell diseases represented 0.03%, 0.12%, and 0.10% of all SUS admissions in BA, RJ, and SP, respectively (obstetric admissions not included).

The proportion of male cases was similar in the three states, corresponding to roughly half the cases (BA=50.5%; RJ=50.3%; SP=49.8%). In all three states, the majority of admissions lasted for eight days or less. Median duration of admission was 5.0 days in BA and RJ and 4.0 days in SP.

Table 1 shows the distribution of admissions by state and year and sickle cell admission rates per 100,000 resident population, both total and black, for the 2000-2001 period. When the denominator was total population, the highest rates were seen in RJ; when it was black population, higher rates were seen in SP. Despite having the largest black population in absolute terms, rates in BA were the lowest among the three states. The difference between states increased slightly during the study period, the ratio between SP and BA, considering the black population only, being of 9.8 in 2002.

Table 2 shows the comparison between mean duration of admission (MDA) among children and ado-

^{*}Departamento de Informática do SUS (Datasis). Movimento de autorização de internação hospitalar: arquivos mensais, período janeiro de 2000 a dezembro de 2002 [CD-ROM]. Brasília (DF): Ministério da Saúde; 2000.

Table 1 - Number of hospital admissions due to sickle cell disease and morbidity rates according to resident population, total and black. Bahia, Rio de Janeiro, and Sao Paulo, Brazil, 2000-2002.

Population	Admissions								
	2000			2001			2002		
	BA (N=183)	RJ (N=859)	SP (N=1.510)	BA (N=183)	RJ (N=890)	SP (N=2.129)	BA (N=244)	RJ (N=1.050)	SP (N=2.301)
	Rates (100.000 population)								
Total	1.4	6.0	4.1	1.4	6.1	5.6	1.8	7.0	6.0
Negra	11.0	56.0	91.0	11.0	58.0	128.0	14.0	67.0	137.0

Sources: Sistema de Internações Hospitalares do Sistema Único de Saúde, 2000-2002 and Instituto Brasileiro de Geografia e Estatística

BA: Bahia; RJ: Rio de Janeiro; SP: Sao Paulo

lescents (=19 years) and adults (=20 years). MDAs were similar except for RJ, where the MDA was significantly higher among adults ($p < 0.001$).

The most frequent type of admission in all three states was via the emergency room. This type of admission accounted for 90.8% of all admissions in BA, 83.5% in RJ, and 65.6% in SP. We found significantly shorter MDA among cases admitted via emergency room when compared to those entering by other routes in BA ($p < 0.001$) and RJ ($p < 0.001$).

Mean age among fatal cases was 26.5 years in BA, 31.5 years in RJ, and 30.0 years in SP. Hospital mortality rates were 2.0 % in BA, 2.1% in RJ, and 1.0 % in SP. Mortality rates among adults were about five times higher than those found among children and adolescents (Table 3), a statistically significant difference in BA ($p = 0.006$), RJ ($p < 0.001$), and SP ($p < 0.001$).

Table 4 shows the distribution of cases according to age and the proportion of deaths by sickle cell disease for each age group. Admissions are concentrated in younger age groups, with about 70% corresponding to the =19 years age group. Median ages were 11.0 years in BA and RJ and 12.0 years in SP ($p = 0.70$). Median age was higher among female cases (BA: $p = 0.003$; RJ: $p < 0.001$; SP: $p < 0.001$). In BA, 50% of deaths were among patients aged 20-29 years. In SP there was a concentration of deaths among children aged up to four years, followed by a decline, with a subsequent rise beginning at age 15 years.

In 2000, hospital lethality varied depending on the system used as a source – SIH/SUS or SIM (Mortality Information System).^{1,*} Lethality according to SIM was greater than that reported by SIH/SUS. The ratio of deaths reported by the two systems was 5.7 in BA, 1.6 in RJ, and 2.1 in SP.

Regardless of the hospital's legal status, mortality was generally higher among adults when compared to children and adolescents. Highest lethality was seen in BA among adults admitted to university hos-

pitals. In RJ, lethality among adults in state hospitals was 2.5 times higher than among adults in university hospitals. In SP, lethality among adults was similar in state, philanthropic, and university hospitals; among children and adolescents, lethality in philanthropic hospitals was four times higher than in university hospitals and twice that of state hospitals.

In all three states, the procedures more frequently reported were “adult congenital or acquired hemolytic anemia” and “child congenital or acquired hemolytic anemia” (BA=73%; RJ=63,6%; SP=60,6%). Most secondary diagnosis fields were left blank.

DISCUSSION

According to Naoum et al,⁷ the prevalence of sickle cell disease in Brazil in 1987 was 0.04% among the general population and 0.22% among the black population. According to these authors, BA showed the greatest frequency of cases of the disease. Even though these data were obtained almost 20 years ago, and the structure of the population in terms of disease prevalence may have changed, we do not expect great variations

Table 2 - Distribution of mean duration of admission (MDA) due to sickle cell disease, according to age group. Bahia, Rio de Janeiro, and Sao Paulo, Brazil, 2000-2002.

Age group	MDA (days)		
	Bahia	Rio de Janeiro	Sao Paulo
<19 years	5.0	4.0	4.0
≥20 years	5.0	8.0	4.0
p value*	0.53	<0.001	0.13

Source: Sistema de Internações Hospitalares do Sistema Único de Saúde, 2000 a 2002

*Mann-Whitney

Tabela 3 - Taxa de óbito hospitalar por doença falciforme, segundo faixa etária. Bahia, Rio de Janeiro e São Paulo, 2000 a 2002.

Age group	Mortality rate* (x100)		
	Bahia	Rio de Janeiro	Sao Paulo
<19 years	0.9	0.8	0.4
≥20 years	4.6	4.8	2.3
Deaths ratio	5.1	5.6	5.1

Source: Sistema de Internações Hospitalares do Sistema Único de Saúde, 2000-2002

*Number of deaths/ number of admissions

Table 4 - Distribution of admissions and proportion of deaths due to sickle cell disease, according to age group. Bahia, Rio de Janeiro, and Sao Paulo, Brazil, 2000-2002.

Age group (years)	Bahia		State (%) Rio de Janeiro		Sao Paulo	
	Admissions	Deaths	Admissions	Deaths	Admissions	Deaths
0-4	19.3	8.3	21.0	5.0	20.7	15.3
5-9	25.4	0	23.1	6.7	20.6	5.1
10-14	13.8	8.3	14.1	5.0	13.5	1.7
15-19	13.1	16.7	9.1	10.0	15.9	10.2
20-29	16.6	50.0	17.5	21.7	16.6	16.9
30-39	6.7	8.3	7.8	13.3	6.2	16.9
≥40	5.1	8.3	7.4	38.3	6.5	33.9

Source: Sistema de Internações Hospitalares do Sistema Único de Saúde, 2000 a 2002

to have happened during this period. Furthermore, the available measures of prevalence are for the country as a whole. Notwithstanding, we believe that there was no loss due to the use of these prevalences for the states included in the present analysis. Thus, using the prevalence of 0.22% of the black population, the expected number of cases would be 11,339 in BA, 10,191 in RJ, and 10,918 in SP, that is, the ratio between expected cases would be 1:1:1 for the three states. However, the relationship observed between admission rates was 1:4.6:9.7 (BA:RJ:SP). There are no studies in the literature providing evidence of the expected frequency of complications requiring hospital admission among these patients; however, we did not expect such large difference between admission frequencies. The possibility that BA residents require hospital admission less frequently than residents of other states is unlikely. It is possible that, in BA, the low frequency of admissions and low admission rates be due to underregistration of cases requiring hospital admission. This may be due either to the patient remaining in the emergency ward throughout his or her stay in the hospital, a scenario that does not lead to the emission of an HAA and to registration by SIH/SUS; or to the incorrect use of ICD among admitted cases. A third possibility would be the a severe shortcoming in the hospital care for patients with sickle cell anemia in this state. These observations may suggest that admission rates due to sickle cell disease may be markers of the poor quality medical care provided to these patients, and may reflect the great inter-regional social inequalities seen in Brazil.

Admissions were concentrated among younger age groups, which is in agreement with reports found in the literature,¹ revealing the great social impact of the disease and warning as to the importance of optimizing the care provided to sickle cell patients.

The MDA found in the present study was not high, which is in agreement with the clinical characteristics of the disease. Vasocclusive crisis, the most frequent cause for admission, is resolved in five days in average.¹⁵ In RJ, age was significantly associated with MDA, duration of admission being longer among

adults. The shorter MDA found in BA and RJ among cases entering via the emergency room was probably due to the fact that the majority of patients admitted through this route presented with vasocclusive crisis. The lack of clinical data did not allow for a more in-depth analysis of factors influencing MDA.

The type of admission in most cases was via emergency room. This information is in agreement with the clinical history of sickle cell disease, characterized by acute complications among both children/adolescents and adults.¹⁵ Secondary preventive measures may decrease the number of admissions, but will not be able to render admission 'elective.' Vasocclusive crisis, the most common reason for admission, has no specific preventive measure, with the exception of cases in which hydroxyurea may decrease the frequency of crises.²

We observed a discrepancy between the number of deaths reported by SIH/SUS and SIM, with an underestimation of the number of deaths by the former. This discrepancy suggests difficulties in the adequate completion of HAA forms. The reasons for such discrepancy are not known, but this finding should serve as a warning as to the quality of the information present in the country's healthcare systems. The literature on sickle cell disease recognizes the importance of the relationship between age and mortality. According to the international literature, there is a peak of mortality in the 1-3 years age group,^{4,13} bacterial infections being the major underlying cause.³ A comparison between the survival curves of black patients with sickle cell disease and the general black population shows that life expectancy among the former is reduced by 25-30 years.¹⁰

Clinical circumstances at the time of death and the direct causes of death could not be determined. A hypothesis for the low frequency of deaths observed during the first years of life in BA and RJ when compared to the frequency reported in the literature is the underregistration of deaths attributed to the disease. The lack of knowledge regarding the diagnosis of this disease in the first years of life and the difficulties

inherent to this diagnosis may contribute to underregistration. Sickle cell disease may remain unnoticed in case the disease is asymptomatic or oligosymptomatic, or if the child is not evaluated for the presence of anemia during the first years of life. The first clinical manifestation of this disease may already lead to death. Fortunately, a neonatal hemoglobin trial program was introduced in Brazil in 2001,¹¹ and will probably allow for early diagnosis of children with sickle cell disease, follow-up of affected children, and countrywide monitoring of the disease.

In a cohort study conducted by Platt et al,¹⁰ mean age at death in patients with SS hemoglobinopathy was 42 years among men and 48 years among women. In patients with SC hemoglobinopathy, mean age increased to 60 years among men and 68 years among women. In another cohort, conducted in Jamaica, Wierenga et al¹⁷ reported median survival of 53 years in men and 58.5 years in women with SS hemoglobinopathy. In the present study, median age of death was 26.5 years in BA, 31.5 years in RJ, and 30,0 years in SP, indicating low age at the time of death and a difference in median age at death according to geographical area. A direct comparison between the present results and those reported in the above mentioned cohorts cannot be made, since measures were obtained using different methodologies. However, the early lethality found in this country reflects the social inequalities that exist between Brazil and other countries, as well as between the different Brazilian Regions.

SIH/SUS contains information relative to most of the admissions taken place within the Brazilian territory. It is believed that the majority of deaths due to complications of sickle cell disease occurs in patients admitted to hospitals. Thus, it is possible that SIH/SUS is a source of identification for a large share of sickle cell deaths. Therefore, a potential bias is the loss of cases of the disease not acknowledged as such and with fatal outcomes. Considering the concentration of the disease in childhood, when the lack of diagnosis is more prevalent, such bias would lead to an increase in median age of death. Thus, if deaths occurred in children with undiagnosed sickle cell disease were computed, median age at time of death would be even lower. On the other hand, since the

majority of secondary ICD-10 fields were left blank, deaths of sickle cell patients admitted for causes not directly related to the disease (e.g. external causes) could not be identified. We were unable to predict if there was an influence of the loss of these cases in median age at death.

The lack of early diagnosis, family orientation at the first signs of complications, access to preventive measures against infections, governmental programs providing regular outpatient medication, and efficacious medical care during clinical interurrences surely contribute to the low age at death found in the present study.

A potential limitation of the present study is its internal validity. In RJ, sickle cell admissions in one of the university hospitals (a reference center in care for patients with sickle cell disease) are not systematically registered in SIH/SUS. This leads to the underestimation of the frequency of admissions. Also, the lack of completion of the secondary ICD-10 field hindered the study of comorbidity.

The procedures employed in the SIH/SUS did not provide further information on the cause of admission. Procedures "adult congenital or acquired hemolytic anemia" and "child congenital or acquired hemolytic anemia," which account for the majority of the procedures performed, are redundant with the ICD-10 and are thus of little value in the recognition of other associated diagnoses.

The accountancy and financial logistics on which HAA and SIH/SUS are based is a limiting factor to the information present in the system (a general characteristic of administrative databases). On the other hand, the nationwide coverage of hospital admission information and the easy access to this database encourage its use as a source of information in the field of healthcare. The critical and continued use of this system by healthcare professionals with diverse interests will surely lead to its improvement.

Considering the above mentioned limitations, the present study should contribute to the knowledge of sickle cell disease in Brazil and to improvements in the care for patients affected by this disease.

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