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ORIGINAL ARTICLE

# Characterization of mortality in children with sickle cell disease diagnosed through the Newborn Screening Program☆,☆☆

Alessandra P. Sabarense[a], Gabriella O. Lima[a], Lívia M.L. Silva[a], Marcos Borato Viana[b,*]

[a] Faculdade de Medicina, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil
[b] Department of Pediatrics, Faculdade de Medicina, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil

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**KEYWORDS**
Sickle cell anemia;
Death rate;
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Acute splenic sequestration;
Neonatal screening

**Abstract**
*Objective:* To characterize the deaths of 193 children with sickle cell disease screened by a neonatal program from 1998 to 2012 and contrast the initial years with the final years.
*Methods:* Deaths were identified by active surveillance of children absent to scheduled appointments in Blood Bank Clinical Centers (Hemominas). Clinical and epidemiological data came from death certificates, neonatal screening database, medical records, and family interviews.
*Results:* Between 1998 and 2012, 3,617,919 children were screened and 2,591 had sickle cell disease (1:1,400). There were 193 deaths (7.4%): 153 with SS/$S\beta^0$-talassemia, 34 SC and 6 $S\beta^+$thalassemia; 76.7% were younger than five years; 78% died in the hospital and 21% at home or in transit. The main causes of death were infection (45%), indeterminate (28%), and acute splenic sequestration (14%). In 46% of death certificates, the term ''sickle cell'' was not recorded. Seven-year death rate for children born between 1998 and 2005 was 5.43% *versus* 5.12% for those born between 2005 and 2012 ($p = 0.72$). Medical care was provided to 75% of children; 24% were unassisted. Medical care was provided within 6 hours of symptom onset in only half of the interviewed cases. In 40.5% of cases, death occurred within the first 24 hours. Low family income was recorded in 90% of cases, and illiteracy in 5%.
*Conclusions:* Although comprehensive and effective, neonatal screening for sickle cell disease was not sufficient to significantly reduce mortality in a newborn screening program. Economic and social development and increase of the knowledge on sickle cell disease among health professionals and family are needed to overcome excessive mortality.


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☆☆ Study conducted at Núcleo de Ações e Pesquisa em Apoio Diagnóstico (Nupad), Faculdade de Medicina, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil.
* Corresponding author.
*E-mail:* vianamb@gmail.com (M.B. Viana).

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**PALAVRAS-CHAVE**
Anemia falciforme;
Mortalidade;
Infecção;
Sequestro esplênico agudo;
Triagem neonatal

**Caracterização do óbito de crianças com doença falciforme diagnosticadas por Programa de Triagem Neonatal**

**Resumo**
*Objetivo:* Caracterizar os 193 óbitos de crianças com doença falciforme diagnosticadas por programa de triagem neonatal entre 1998-2012 e comparar os primeiros com os últimos anos.
*Métodos:* Os óbitos foram identificados pela busca ativa das crianças ausentes nas consultas agendadas nos hemocentros. Dados clínicos e epidemiológicos provieram dos documentos de óbito, banco de dados da triagem neonatal, prontuários médicos e entrevistas com familiares.
*Resultados:* Entre 1998-2012 foram triadas 3.617.919 crianças, 2.591 com doença falciforme (1:1.400). Ocorreram 193 óbitos (7,4%): 153 com SS/S$\beta^0$-talassemia, 34 SC e 6 S$\beta^+$-talassemia; 76,7% em crianças com menos de 5 anos; 78% faleceram em hospitais e 21% em domicílio ou trânsito. Causas principais do óbito: 45% infecção, 28% indeterminada, 14% sequestro esplênico agudo. Em 46% dos documentos de óbito, não houve registro do termo ''falciforme''. A taxa de mortalidade até sete anos das crianças nascidas entre 1998-2005 foi 5,43% *versus* 5,12%, entre 2005-2012 (p=0,72). Receberam assistência médica 75% das crianças; 24% ficaram desassistidas. Pelas entrevistas, atendimento médico teria ocorrido nas primeiras seis horas do início dos sintomas em metade dos casos. O óbito ocorreu em 40,5% dos casos, nas primeiras 24 horas. Baixa renda familiar foi registrada em 90% dos casos e analfabetismo em 5%.
*Conclusões:* A triagem para doença falciforme, mesmo abrangente e eficaz, não foi suficiente para reduzir significativamente a mortalidade no Programa de Triagem Neonatal. Necessita-se de desenvolvimento econômico e social do estado e ampliação, pela educação continuada, do conhecimento sobre a doença falciforme entre os profissionais de saúde e familiares.


## Introduction

Sickle cell disease (SCD) comprises a group of hematologic disorders of genetic origin, whose main feature is the predominance of hemoglobin S (HbS) in red blood cells. SCD has great clinical and epidemiological importance, being considered a public health problem in Brazil.[1–3] HbS in homozygous form (HbSS), called sickle cell anemia (SCA), is the most common genotype and the most severe clinical presentation of the disease. The concept of SCD also includes double heterozygosity for HbS with other hemoglobin variants (HbSC, HbSD-Punjab, and others) and the interaction of HbS with beta thalassemia (HbS/$\beta^0$ and HbS/$\beta$+ thalassemias).[4,5] The main determinants of the clinical manifestations of the disease are the vaso-occlusive phenomena and chronic hemolysis.[4]

Hemoglobinopathies are responsible, worldwide, for 3.4% of deaths in children under 5 years.[6] Patients with SCD have high rates of morbidity and mortality, mainly in developing countries.[7] Even in developed countries, although mortality in children has decreased, SCD is still a significant cause of mortality in adolescents and adults.[8]

A prevalence of 25,000-30,000 individuals with SCD is estimated in Brazil, with an incidence of 3,500 cases per year.[9] In the state of Minas Gerais (MG), the incidence of SCD is 1:1,400 screened newborns, based on data from the Neonatal Screening Program (NSP-MG).[10]

A study conducted in MG[10] characterized the death of 78 children with SCD screened by the NSP-MG in the period of 1998-2005 and concluded that most deaths occurred in children under 2 years and individuals with HbSS, mainly due to infection (septicemia and pneumonia). A predominance of in-hospital deaths was observed; however, the occurrence of at home or in-transit deaths was still significant. An indeterminate cause of death on the death certificate was frequent, which would indicate a lack of knowledge among physicians regarding SCD and acute events that are determinants of death.

This study aimed to characterize the deaths of children with SCD that had been screened by the NSP-MG between 1998 and 2012. Whenever possible, comparative analysis of deaths of children born between March of 1998 and February of 2005 with those born between March of 2005 and December of 2012 was performed to describe possible changes regarding the quality of care provided to these children.

## Methods

The population investigated in this study consisted of 117 children diagnosed with SCD at the NSP-MG, followed-up in the Blood Banks of Fundação Hemominas, and who died in the period from March 1, 2005 to February 29, 2012. In several analyses, 76 deaths that occurred between March of 1998 and February of 2005 were added to the sample (of the 78 deaths reported, two children were excluded, whose birth was prior to March 1,1998),[10] totaling 193 deaths and thus complementing the 14 years of the study.

The NSP-MG performs screening for SCD since March of 1998. All 853 state municipalities are registered. In 2010, 91.44% of the infants born in the state of Minas Gerais were screened at the Center for Diagnostic Support Action and