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Hemoglobin S identification in blood donors: A cross section of prevalence

Fernanda Lima Kroger [a], *Ianka Cristina Ernesto* [b], *Marina Schuffner Silva* [b], *Olivia Franco dos Santos* [c], *Renato Lourenço de Medeiros* [d], *Daniela de Oliveira Werneck Rodrigues* [e,*]

[a] *Prefeitura Municipal de Barueri, Barueri, SP, Brazil*
[b] *Faculdade de Medicina da Universidade Presidente Antônio Carlos (UNIPAC), Juiz de Fora, MG, Brazil*
[c] *Universidade Federal de Juiz de Fora(UFJF), Juiz de Fora, Brazil*
[d] *Faculdade de Ciências Médicas e da Saúde de Juiz de Fora (SUPREMA), Juiz de Fora, MG, Brazil*
[e] *Fundação Hemominas, Juiz de Fora, MG, Brazil*

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ABSTRACT

Introduction: In Brazil, the sickle cell trait (SCT) has an average prevalence of 4% in the general population and 6–10% among Afro-descendants. Although SCT is highly prevalent, a large segment of the population ignores their status. The Therapeutic Guidelines prohibit the transfusion of SCT red blood cells into patients with hemoglobin disorders or severe acidosis and newborns.

Methods: This was a cross-sectional study with data from 37,310 blood donation candidates. The study included only eligible first-time donors qualified to be tested for the presence of hemoglobin S (HbS) at the Fundação Hemominas Juiz de Fora, Brazil. The variables studied were gender, skin color, age, type of donation, place of birth, blood type, result of the solubility test for hemoglobin S (HbST) and hemoglobin electrophoresis (HbEF). Statistical analysis was performed using the Q square test and the Kappa index of agreement for comparing biochemical methods. This project was approved by the National Research Ethics Committee.

Results: The analysis of first-time donor data showed that 7166 were considered eligible. A total of 127 of the 7166 donors were carriers of SCT (1.77%). Among the blood donors, 73.23% were from the local area. The HbST and HbEF were found to be 100% in concordance. Sensitivity was not tested in the present study.

Conclusions: The HbST is highly specific for identifying the HbS, but sensitivity was not tested in this study. The screening of blood donors for abnormal hemoglobins is useful, helping to detect and counsel heterozygous people. The study seeks to identify the prevalence of SCT in a region of Brazil.

* *Corresponding author at*: Fundação Hemominas, Rua Barão de Cataguases s/n-Centro, Juiz de Fora, Minas Gerais, Brazil.
E-mail address: daniela.werneck@hemominas.mg.gov.br (D.O. Rodrigues).

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Introduction

In Brazil, the sickle cell trait (SCT) has a prevalence of 4% in the general population and is observed in 200,000 annual births.[1] In this context, the Brazilian Ministry of Health has implemented two types of screens to identify the presence of hemoglobin S (HbS) in the population, the first of which occurs shortly after birth in the National Neonatal Screening Program (NNSP), mandatory since 2001, essential for the orientation and early diagnosis and the other, upon donation to find abnormal hemoglobins in the donated blood, instituted in 2004.[2–4] In the state of Minas Gerais, located in the southeastern region of Brazil, according to the NNSP, the incidence of SCT is 1:30.[5]

The Minas Gerais State Center of Blood Transfusion and Hematology, Fundação Hemominas (FH), belongs to the public System of Health. It collects transfusions in the State for public and private hospital usage.[5]

Over 35 years of activity, the FH has been offering hematology and hemotherapy services to the population through its units, which are part of a network comprising 22 decentralized units in the state's macroregions. This network has the superior hemotherapy coverage of 95% across the state[5]. The Fundação Hemominas of Juiz de Fora (FHJFO), is one of the units of this network, located in the region of Zona da Mata and is responsible for the collection of about 2872 units of blood per month that are processed and distributed to 57 hospitals located in 27 cities in the rural and metropolitan areas of the Juiz de Fora. This region covers more than 70 municipalities.[6] According to the 2018 IBGE (Brazilian Institute of Geography and Statistics) estimates[7] of the current population of Juiz de Fora, it has approximately 564,310 inhabitants.

At the FH, the protocol for screening donated blood for identification of the HbS was established in 2001, along with a solubility test for hemoglobin S (HbST), followed by its confirmation using hemoglobin electrophoresis (Hb EF).[8]

The aim of this study was to identify the prevalence of SCT in blood donors at the FHJFO and discuss the use of these units of red blood bags, considering that the presence of HbS could be harmful to some patients.[9]

Materials and methods

This is a retrospective cross-sectional study using data from 37,310 donor candidates at FHJFO from January to December 2008. The FH defines the donor status at first, sporadic and repeat times as for the donation type in voluntary and replacement donations.[5] The inclusion criteria for this study contemplated first-time donors eligible for clinical and hematological screening and excluded from this analysis repeat donors, donor candidates who gave up during the process ("dropouts") and those who were not eligible to donate blood based on the standards of the National Health Surveillance Agency (ANVISA - RDC 158, 2016)[4] by the Ministry of Health and FH standards in clinical screening, which determined the Technical Regulations for Hemotherapeutic Procedures.

The first-time donors underwent the HbST by the sodium metabisulphite method and, if it were positive, the samples were sent for the performance of hemoglobin electrophoresis (Hb EF) by the cellulose acetate method at an alkaline pH, according to the FH standard operating procedure.[5]

Table 1 – Donor candidates: repeat donors, sporadic donors and first-time donors at the FHJFO in 2008.

	n	%
Type of donor		
1st-time	9.975	26,74
Repeat/Sporadic donors	27.335	73,26
Total candidates	37.310	100

Source: Consolidated Statistical Bulletin/ANVISA sheet 1.2, 2008.

Table 2 – Apt and inapt blood donor candidates and dropouts in clinical screening at the FHJFO in 2008.

	n	%
Donor candidates		
Apt	30,431	81.56
Inapt	6719	18.01
Dropouts	160	0.43
Total candidates	37,310	100

Source: Consolidated Statistical Bulletin/ANVISA sheet 1.1, 2008.

The variables analyzed in first-time donors were gender, skin color, age, type of donation, birthplace, blood type and HbST and Hb EF results. All this information was collected based on the standard donation form and data collection forms elaborated by the researchers.

All the data collected were stored in a computerized database. Statistical analysis was performed using the Statistical Package for Social Sciences®, version 14.0. Frequency measures were calculated with confidence intervals of 95%. We used the Kappa index of concordance for analysis of biochemical methods. The rejection level of the null hypothesis with a two-tailed test was an α of 0.05% and a β of 0.10%.

This project was approved by the FH Ethics Research Committee, Protocol No. 247/2009, and registered at the National Ethics Research Committee.

Results

The FHJFO received 37,310 donor candidates, of which 73.26% were repeat (17,082) and sporadic (10,154) donors and 26.74% were first-time donors (Brazil National Volunteer Donor Program, 2009) (Table 1). Of these, 30,431 were considered eligible (81.56%), 6719 were deferred (18.01 %) and 160 (0.43%) were dropouts, either before or after screening (Table 2).

The analysis of first-time donor data showed that 7166 were considered eligible and 2748 were deferred in the clinical screening based on the standards utilized by the Ministry of Health and FH. The HbST and HbEF were positive in 127 donors (1.77%) of the 7166 first-time donors in 2008.

There was no significant gender difference among the SCT carriers (50.39% females versus 49.61% males) ($p > 0.05\%$). Skin color data was collected through a self-assessed statement from the donor and had three options: white, black and other. Based on this, 44.10% of the donors reported being white, 15.74%, black and 40.16%, other (56 white, 20 black and 51 other = 127). Most of the SCT carriers were between 18 and 29

Table 3 – Epidemiologic profile of Hb AS blood donors at the FHJFO in 2008.

	n	%		n	%
Gender			Age (years old)		
Male	63	49.61	18–29	83	65.35
Female	64	50.39	>29	44	34.64
Total	127	100	Total	127	100
Color			ABO/Rh		
White	56	44.09	A	50	39.37
Black	20	15.74	B	12	9.44
Other	51	40.15	O	61	48.03
Total	127	100	AB	4	3.14
			Total	127	100

Source: standard donation form and data collection tools elaborated by the researchers.

Table 4 – Hb AS blood donor birthplaces at the FHJFO in 2008, according to the Minas Gerais State zones.

	n	%
Region		
Central	8	6.3
Central-West	1	0.79
North	1	0.79
South	3	2.36
Zona da Mata	93	73.23
Out of federative geographical limit	21	16.53
Total	127	100

Source: Standard donation form and data collection tools elaborated by the researchers.

years of age (65.35%) and those over the age of 29 represented 34.64% of the group. Blood type O was the most prevalent (48.03%), followed by group A (39.37%) and B (9.44%), as shown in Table 3. Regarding the type of donation, 76.38% were voluntary, 22.05% were repeat donors and 1.57% of the donations were autologous or directed (Table 3).

The majority of donors (73.23%) were from the southeastern Minas Gerais State ("Zona da Mata Mineira") and 16.53% were from cities located outside the state of Minas Gerais, mostly from Rio de Janeiro State, which represented 8.66% of the cities (Table 4).

Regarding the blood samples of the 7166 first-time donors who performed the solubility test, 127 samples with the presence of HbS were identified through this test. According to the Brazil Ministry of Health Guidance and recommended in good hemotherapy practices, hemoglobin electrophoresis was performed to confirm the presence of HbS. The samples had 100% agreement in the two laboratory tests performed (kappa = 1). A limitation of our study was the failure to perform hemoglobin electrophoresis in donors with a negative solubility test.

All red blood bags containing HbS have been properly identified in the system and on the label and have not been used in patients with hemoglobin disorders or severe acidosis, nor in newborns and other special cases.

Discussion

The SCT was found in 1.77% of the tested individuals. This value was close to the one found in a study with 83,213 blood donors from the Parana Institute of Hemotherapy and Hematology (Brazil), conducted from January 2008 to December 2009, in which SCT was detected in 0.9% of the participants.[10] In a study that analyzed 32,261 records of blood donors from Passo Fundo (Rio Grande do Sul - Brazil), the SCT was found in 0.4% of the individuals.[11] In a retrospective analysis using donor screening tests at a blood bank in Maringá (Paraná, Brazil), 1.36% of the 78,303 donors tested positive for hemoglobinopathy.[12] In Bragança Paulista (São Paulo, Brazil) a prevalence of 1.68% of hemoglobinopathies and 1.13% of the SCT was found among 1846 blood donors.[13]

In a study of 101,000 blood samples from 65 cities in all Brazilian regions, a general prevalence of SCT of 2.1% was shown. The prevalence of SCT was higher in the northern region (4.49%) and gradually decreased towards the south: northeast (4.05 %), midwest (3.11%), southeast (1.87%) and south (1.87%).[14] In a study of 23,981 blood donors from the region of Uberlândia (Minas Gerais), 820 (3.42%) had hemoglobinopathies, of which 2.48% were from SCT[15]. A much higher percentage of the SCT (11.3%) was found among the 150 blood donors in a study in Ghana.[16] In another cross-sectional study conducted at a hospital in Ghana with 200 blood donors, a prevalence of 12.5% of the SCT was shown.[17] This difference probably occurred because there is a higher prevalence of people with SCT in Ghana than in Brazil.

In the donors of this study, 8.66% that were positive for HbS were from the State of Rio de Janeiro, Brazil, showing that the area covered by the blood center is more extensive than that determined by the legal borders of Minas Gerais State.

Considering gender, 49.61% of the bags with HbS were from men and 50.39% from women. A significant difference in the prevalence of hemoglobins between genders was not expected, as the gene encoding the synthesis of the hemoglobin beta chain is not linked to sex. However, the result found differs from other studies.[10,16]

In regard to age, the majority of donors were single and were between 18 and 29 years old, hence they would benefit from premarital genetic counselling and to be able to decide about their reproductive life, especially those who do not yet have any offspring. The age group with the most donors was close to that found in the study by Antwi-Baffour et al.,[16] which ranged from 20 to 24 years.

When the skin color is analyzed, the majority of donors were either non-white (40.15%) or black (15.74), which was expected.[1] In the study by Lidane et al.,[10] most donors were Euro-Brazilians (90.9%), followed by Afro-Brazilians (9%) and Asians (0.05%). In the study by Naoum,[14] the prevalence was 1.18% among white people and 4.87%, among Afro-descendants.

The blood type O was the most prevalent in the population of this study (48.03%) and the data published by Ramalho et al. and Novaretti et al. also identified that group O was more prevalent in African blood donors.[18,19]

The effectiveness of the HbST was confirmed by cross-comparison with the hemoglobin electrophoresis test and the solubility test is an exam of easy execution and low cost, with a high rate of reproducibility. The results of HbST were confirmed by HbEF, the gold standard for diagnosis of hemoglobinopathies, which showed the high negative pre-

dictive value and high rate of concordance (kappa = 1.0), as reported previously by Prudencio et al.[20]

It is important to realize that negative HbST tests were not reassessed by hemoglobin electrophoresis (Hb EF cellulose acetate method at alkaline pH). Thus, false negatives may have occurred, underestimating the percentage value of the sickle cell trait in the study. This is surely a limitation of our study. In the literature, Clark (1972)[21] identified 1.1% false negatives and Surve et al.,[22] 6.2% false negatives for the gel centrifugation technique in donor screening for HbS. However, Naoum,[14] Huntsman et al.,[23] Balasubramaniam et al.,[24] Oshiro et al.,[25] Ballard et al.,[26] Matusik et al.,[27] Del Guidice et al.[28] and Tubman and Field[29] reported sensitivity results from 97.3% to 99% in addition to considering the cost and benefit of population screening, therefore, complementary studies with statistical methodology are needed to better investigate false negatives. Our results regarding the methodology were similar to those of Prudêncio et al.,[20] that also did not study the sensitivity of the HbST.

The Brazilian Ministry of Health assessed the proportion of live births with heterozygosity or HbS diagnosed by the NNSP, which was published in 2008 in the Handbook of Health Education and found that the State of Minas Gerais had a high rate of SCT carriers, i.e., one carrier of the trait for every 23 live births, besides confirming that such traits are most prevalent among Afro-descendants and the poor population.[15] It is worthwhile to highlight that the entry and spread of the HbS gene in the southeastern part of the country was mostly through the states of Bahia and Rio de Janeiro (bordering on Minas Gerais State), where approximately 3.6 million Africans settled during the colonial period.[30] Currently, in Minas Gerais State, according to the NNSP, the incidence of sickle cell disease is 1:1,400 newborns and the incidence of the SCT is 1:30.[5]

Gallo et al.[31] analyzed the personal feelings, opinions and attitudes about reproductive decisions of a group of SCT patients. They relied on their personal and/or religious experiences to answer the questionnaire and reported some difficulty in convincing the partner to perform the test that identifies the presence of HbS. A sense of guilt among those who had children with the disease or trait was reported. Many of them expressed interest in having children, although they knew the risks involved, and due to that, the vast majority agreed that the solution would be to choose a partner who carries neither the SCT, nor the disease. Populational studies regarding both adults and neonatal screening, along with genetic counselling, will enable a change in pre-natal advice and should be seen as a public health concern.

Carriers of the sickle cell trait are clinically and hematologically healthy and therefore, able to donate blood, but the administration of units with the sickle trait can be harmful to some patients.[9] In Brazil, the Clinical Protocol and Therapeutic Guidelines (2010) prohibit the transfusion of SCT Red Blood Cells (RBCs) into patients with hemoglobin disorders or severe acidosis and newborns, exchange transfusions, patients whose blood oxygenation might be compromised and intrauterine transfusion.[32] According to the Guidelines on Red Cell Transfusion in Sickle Cell Disease of the British Society for Haematology, the blood provided for SCD patients should be HbS negative.[33] The 2018 Patient Blood Management (PBM) International Consensus defined the current status of the PBM evidence base for clinical practice and research purposes.[34]

There is no global standard practice to screen all blood donors or to use SCT RBCs for transfusion. In the United States, there are no national recommendations for routine screening for the sickle cell trait. Therefore, donors are not notified of their testing during the informed consent process.[35] However, problems associated with filtration of SCT blood donors have been increasingly noted since the implementation of universal leucodepletion in several countries. At the Oklahoma Blood Institute, all non-Caucasians are tested for SCT[9] and in the white book of the European Network of Transfusion Medicine Societies (Euro Net-TMS) there is yet no recommendations whether to screen or to use blood from SCT donors.[36] Research suggest that RBCs from blood donors with SCT can be difficult to filter and may not be leucoreduced satisfactorily. When abnormal filtration occurs, the donated blood cannot be used for transfusion. Increased oxygenation has been shown to improve the filterability of SCT donor blood units, suggesting the association of the sickle cell trait with a poor filterability index.[37]

Conclusions

The HbST and HbEF were found to be 100% in concordance. Sensitivity was not tested in the present study. The HbST is highly specific for identifying HbS, but sensitivity was not tested in the present study. Administration of units with SCT RBCs may be disadvantageous for certain populations and screening blood donors for abnormal hemoglobins is useful to detect and counsel heterozygous people. At the FH, all blood donors with SCT are informed and guided by the multidisciplinary team.

Conflicts of interest

The authors declare no conflicts of interest.

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