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ORIGINAL ARTICLE

Prevalence of sickle cell trait in blood donors in the Midwest region of the State of Minas Gerais

Prevalência de traço falciforme em doadores de sangue da região Centro-Oeste do Estado de Minas Gerais

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ABSTRACT

Introduction: Although sickle cell trait is considered a benign condition, there are studies showing that it presents relevant clinical manifestations, which makes it important to carry out studies to know its prevalence. **Objective:** To estimate the prevalence of sickle cell trait in blood donors in the Midwest region of the state of Minas Gerais (MG). **Methodology:** Information on the presence of HbS in the blood, ethnicity, gender, education, age, hemoglobin levels and origin of blood donors were consulted in the Hemote Plus system of the Hemominas Foundation (FH). **Results:** The mean age of blood donors in the Midwest region of MG was 34.4 ± 11.3 years, 51.4% were male, 52.8% self-declared white, 53.3% had up to high school and the mean hemoglobin levels were 15.1 ± 1.3 g/dL. The prevalence of sickle cell trait was 2.2% in this population. Among the donors with sickle cell trait, there was a higher frequency of self-declared brown, followed by self-declared white (30.7%) and self-declared black (26.5%), aged 21 to 30 years (31.9%) and 31 to 40 years (30.7%) and females (53.9%) were more prevalent and the mean hemoglobin levels were 14.8 ± 1.3 g/dL. **Conclusion:** The prevalence of sickle cell trait found in our study was 2.2%, which is similar to that found in the Brazilian population and is slightly lower than in the state of MG. These findings contribute to other prevalence studies in Brazil.

Palavras-chave: Sickle cell trait; Blood donors; Prevalence.

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RESUMO

Introdução: Apesar do traço falciforme ser considerado uma condição benigna, existem estudos mostrando que apresenta manifestações clínicas relevantes, o que torna importante a realização de estudos para conhecer sua prevalência. **Objetivo:** Estimar a prevalência de traço falciforme em doadores de sangue da região Centro-Oeste do estado de Minas Gerais (MG). **Metodologia:** As informações sobre a presença de HbS no sangue, etnia, gênero, escolaridade, idade, níveis de hemoglobina e procedência dos doadores de sangue foram consultadas no sistema Hemote Plus da Fundação Hemominas (FH). **Resultados:** A média de idade dos doadores de sangue da região Centro-Oeste de MG foi de 34,4±11,3 anos, 51,4% eram do sexo masculino, 52,8% se autodeclararam brancos, 53,3% possuíam até 2º grau completo e a média dos níveis de hemoglobina foi de 15,1±1,3 g/dL. A prevalência de traço falciforme foi de 2,2% nessa população. Entre os doadores portadores do traço falciforme houve maior frequência de autodeclarados pardos, seguidos de autodeclarados brancos (30,7%) e autodeclarados negros (26,5%), as faixas etárias de 21 a 30 anos (31,9%) e de 31 a 40 anos (30,7%) e o sexo feminino (53,9%) foram mais prevalentes e a média dos níveis de hemoglobina foi de 14,8±1,3 g/dL. **Conclusão:** A prevalência de traço falciforme encontrada em nosso estudo foi de 2,2%, o que se assemelha à encontrada na população brasileira e é discretamente menor que a do Estado de MG. Esses achados contribuem com os demais estudos de prevalência no Brasil.

Palavras-chave: Traço Falciforme, Doadores de Sangue, Prevalência.

Introduction

Variant hemoglobinopathies are caused by mutations in structural genes responsible for hemoglobin synthesis, originating hemoglobins with biochemical and physicochemical characteristics different from normal hemoglobins, called variant hemoglobins. These disorders represent a public health problem in many countries due to the high prevalence and severity that their clinical manifestations can present. Hemoglobins S (HbS) and C (HbC) are the most frequent variant hemoglobins in Brazil. The term Sickle Cell Disease (SCD) is used to define hemoglobinopathies in which the predominant phenotype is that of HbS, even when associated with another variant hemoglobin or thalassemia. The most frequent types of SCD are HbSS (sickle cell anemia), HbS-beta thalassemia and the heterozygous pairs HbSC and HbSD. The heterozygous presentation of HbS is called sickle cell trait (HbAS)[1-4].

Individuals with heterozygous HbS tend not to have severe clinical symptoms, except when exposed to exceptional circumstances. Situations that cause low blood oxygen tension (dehydration, intense physical exertion, high and low temperatures, stress) favor sickling of erythrocytes. Sickled erythrocytes increase blood flow viscosity and impair blood perfusion due to vasoocclusion in the microcirculation. This pathological process leads to complications such as ischemia and tissue necrosis, triggering painful crises, hemolytic anemia and several other more serious clinical manifestations [1,2,3]. SCD encompasses a set of different genetic alterations, which can present from mild, asymptomatic forms to severe forms such as the one described above that, even with advances in treatment, still significantly affect the reduction of life expectancy of patients with this disease [4].

Although sickle cell trait is considered a benign condition, numerous studies have shown relevant clinical manifestations related to this condition [5-11]. A case-control study conducted in Atlanta concluded that sickle cell trait is a risk factor for venous thromboembolism[5]. Humphries *et al.* described a case report of a 23-year-old man with recurrent episodes of thrombosis, in which sickle cell trait was the only potential risk factor identified [6]. Naik *et al.* evaluated the association between sickle cell trait and chronic kidney disease (CKD) in African Americans and concluded that heterozygosity for HbS is associated with increased risk of CKD, albuminuria, and decline in estimated glomerular filtration rate (eGFR)[7,8]. A population-based longitudinal study found a significantly higher risk of exertional

rhabdomyolysis among black soldiers with sickle cell trait [9]. Other studies have shown that there is a positive association between the presence of sickle cell trait and stroke 10 and complications in patients with diabetes[11].

As individuals with sickle cell trait are, for the most part, asymptomatic, many discover their condition through blood donation. A donation from an individual heterozygous for HbS may reduce the effectiveness of the transfusion for a recipient who also has sickle cell trait or for a newborn. Thus, with the objective of minimizing these problems and prioritizing the quality of the transfusion, Ordinance No. 158 of February 4, 2016 instituted the mandatory search for HbS in blood donors and those who are positive for HbS research are notified and sent to the Donor Medical Service for clarification on their condition. Blood bags from HbS donors should not be used in patients with hemoglobinopathies, severe acidosis, newborns, intrauterine transfusion patients, surgical procedures with cardiopulmonary bypass and hypothermia[1].

In view of the possible complications that individuals with sickle cell trait can develop, it is of great importance to carry out studies to identify and calculate the prevalence of this population. The prevalence of heterozygosis for HbS is higher in African countries, and in Nigeria it reaches approximately 20%[12]. In Brazil, studies show that this prevalence can range from 0.43% to 9.80%, depending on the region of the country [13,14]. Machado *et al.* [15] identified a prevalence of 0.4% in São Paulo [16] and Soares *et al.* [17] found a value of 3.9% among blood donors in the State of Piauí. Other studies performed analyzing secondary database of neonatal screening records [18,19] and also blood donors[20] described values on the prevalence of sickle cell trait in various regions of the country, however there is no information on the Midwest region of Minas Gerais.

Given the relevance of the topic in question, it is important to estimate the prevalence of sickle cell trait in blood donors in the Midwest region of the State of Minas Gerais, since this region does not have epidemiological studies carried out in this area of interest, thus contributing to other prevalence studies in Brazil.

Methodology

Design

This is a descriptive study based on data from blood donors registered at the Hemonúcleo de Divinópolis/Hemominas Foundation (FH).

Study location and population

The Midwest region of Minas is one of the ten planning regions in the State of Minas Gerais, comprising 56 cities. With a population of almost 2 million inhabitants, its main most populous cities are Arcos, Boa Esperança, Bom Despacho, Campo Belo, Candeias, Cláudio, Divinópolis, Formiga, Iguatama, Itaúna, Itapecerica, Lagoa da Prata, Nova Serrana, Oliveira , Pains, Pardons, Pepper and Piumhi[21,22]. According to the 2010 census of the Brazilian Institute of Geography and Statistics (IBGE), the municipality of Divinópolis/MG has a population of 213,016 inhabitants and the estimated population in 2019 is 238,230 people [23]. The Hemonúcleo de Divinópolis (FH) was created in 1995 by Ordinance No. 1,105 of June 19, 1995 24, based on the partnership between the State Health Department, São João de Deus Hospital (Fundação Geraldo Correa), Hemominas Foundation (FH) and the Municipal Government. The Hemonúcleo de Divinópolis/FH performs hemotherapy and hematology services, serving the entire Midwest region of the State of Minas Gerais through contracts with establishments that provide hemotherapy services in the region, which, during the study period, totaled 42 health services (hospitals, clinics and Emergency Care Units/ UPAs), distributed in 31 cities in the region, including Divinópolis.

Data collection

This study was based on a data source provided by the donor registry sector of the Hemonúcleo of Divinópolis/ FH, from data consultation in the Hemote Plus system, exclusive to the Hemominas Foundation (FH), containing information on the presence or absence of HbS in blood, ethnicity, gender, education, age, hemoglobin levels (g/dL) and origin of blood donors registered at the Hemonúcleo de Divinópolis/FH from January 2018 to December 2019.

The method adopted by the Hemonúcleo de Divinópolis/ Hemominas Foundation (FH) for HbS screening is sodium dithionite and confirmation is made by Hb electrophoresis at alkaline pH[25,26].

Data analysis

The collected data were organized in a Microsoft Excel® spreadsheet. First, donors with more than one donation in the study period were excluded, so as not to be counted twice, as well as those who were classified as eligible in the clinical screening, but did not show up for the donation, either for reasons of withdrawal or inability for screening hematologic. The origins of blood donors were grouped, according to information provided by the Government of the State of Minas Gerais[27], in the Midwest region of the State of Minas Gerais and other regions of the State of Minas Gerais, with only donors from Midwest region. Thus, the prevalence of sickle cell trait was calculated (ratio between the number of positive donors for HbS in the Midwest region and the total number of donors from this same region in the stipulated period). Descriptive analysis of the data obtained as a measure of frequency of the general characteristics of the study participants and those positive for HbS was performed. The chi-square test was performed to compare sex proportions and the Mann-Whitney test to compare age and hemoglobin levels between HbS positive and negative donors.

Ethical Considerations

This project was approved by the Ethics and Research Committees of the Universidade Federal de São João del-Rei - Centro Oeste Dona Lindu Campus and the Hemominas Foundation.

Results

Among the 19,398 blood donors who donated at the Hemonúcleo de Divinópolis/FH from January 2018 to December 2019, 76.9% were from the Midwest region of the State of Minas Gerais, 16.9% from other regions of the State of Minas Gerais, 6.1% from other states in Brazil

Tabela 1. Características gerais dos doadores de sangue da região Centro-Oeste do estado de Minas Gerais (N=14.923).

	N	%
Gender		
Male	7.669	51,4
Female	7.254	48,6
Total	**14.923**	**100**
Age		
16-20 years	1.543	10,3
21-30 years	4.776	32,0
31-40 years	4.365	29,3
41-50 years	2.700	18,1
51-60 years	1.351	9,1
61-70 years	188	1,3
Total	**14.923**	**100**
Ethnic group		
Yellow	141	0,9
White	7.881	52,8
Indigenous	6	0,04
Black	1.434	9,6
Brown	5.428	36,4
No information	33	0,2
Total	**14.890**	**100**
Education		
Illiterate	12	0,1
Up to elementary school	4.212	28,5
Up to complete high school	7.874	53,3
Up to complete high school	2.673	18,1
No information	152	1,0
Total	**14.771**	**100**
Hemoglobin levels (g/dL)	15,1 ± 1,3	

Tabela 2. Características dos doadores de sangue com traço falciforme da região Centro-Oeste do estado de Minas Gerais (N=332).

	N	%	P value*
Gender			
Male	153	46,1	0,055
Female	179	53,9	
Total	**332**	**100**	
Age			0,355
16-20 years	41	12,3	
21-30 years	106	31,9	
31-40 years	102	30,7	
41-50 years	48	14,5	
51-60 years	32	9,6	
61-70 years	3	0,9	
Total	**332**	**100**	
Ethnic group			
Yellow	0	0,0	-
White	102	30,7	
Indigenous	0	0,0	
Black	88	26,5	
Brown	142	42,8	
Total	**332**	**100**	
Education			
Illiterate	0	0,0	-
Up to elementary school	96	29,4	
Up to complete high school	187	57,4	
Up to complete high school	43	13,2	
No information	6	1,8	
Total	**326**	**100**	
Hemoglobin levels (g/dL)	14,8 ± 1,3		<0,001

*Comparison between blood donors in general (Table 1) versus blood donors with sickle cell trait.

and 0.01% from other countries. Among donors from the Midwest region of Minas Gerais (n=14,923), the mean age was 34.4 ± 11.3 years, 51.4% were male, 52.8% self-declared white and 53 .3% had completed high school. The mean hemoglobin levels of these donors was 15.1 ± 1.3 g/dL (Table 1).

Of the 14,923 blood donors in the Midwest region of the State of Minas Gerais, 332 donors were positive for HbS, which means a 2.2% prevalence of sickle cell trait in the population studied.

Regarding blood donors with sickle cell trait, the mean age was 33.8 ± 11.4 years, 53.9% were female, 42.8% self-declared brown and 57.4% had up to high school complete. The mean hemoglobin (Hb) levels of these donors was 14.8 ± 1.3 g/dL (Table 2).

Discussion

The objective of the present study was to estimate the prevalence of sickle cell trait in blood donors in the Midwest region of the State of Minas Gerais, with a value of 2.2%.

The prevalence of sickle cell trait in the Brazilian population is 2.1% .28 A study by Naoum *et al.*[29] showed the prevalence of sickle cell trait for each region of Brazil, resulting in 4.49% in the North region, 4, 05% in the Northeast, 3.11% in the Midwest, 1.87% in the Southeast and 1.87% in the South. In tables 3 and 4 we present studies that described the prevalence of the sickle cell trait for some Brazilian states and municipalities, respectively.

The prevalence of sickle cell trait found in our study was similar to the average of the Brazilian population (2.1%) and slightly below that found in the State of Minas Gerais, which was 3%. It is known that the distribution of the S gene in Brazil is quite heterogeneous, depending on the black or Caucasian composition of the population.[30] The State of Minas Gerais has a higher prevalence of sickle cell trait than Brazil and that of the Southeast region, which was 1,87%. It is expected that the regions that received a larger

Table 3. Studies on the prevalence of sickle cell trait in different Brazilian states.

Regions of Brazil	Location (municipality)	Period	Study population	N	Hb AS	References
North	Rondônia	2003	Neonatal screening	25.446	2,98%	Siqueira *et al.*[47]
	Maranhão	2013-2015	Neonatal screening	283.003	3,8%	Souza *et al.*[48]
	Pernambuco	2007	Neonatal screening	-	4,0%	Cançado *et al.*[30]
	Bahia	2007	Neonatal screening	-	5,3%	Cançado *et al.*[30]
Northeast	Piauí	2014-2015	Neonatal screening	69.180	4,1%	Reis *et al.*[18]
	Sergipe	2011-2012	Neonatal screening	32.906	2,79%	Leite *et al.*[49]
	Sergipe	2004-2005	Blood donors	1.345	4,1%	Vivas *et al.*[43]
	Rio Grande do Norte	2001	Neonatal screening	1.940	1,5%	Araújo *et al.*[50]
Midwest	Distrito Federal	2004-2006	Neonatal screening	116.271	3,23%	Diniz *et al.*[51]
	Mato Grosso do Sul	2000-2005	Neonatal screening	190.809	1,64%	Holsbach *et al.*[52]
	Rio de Janeiro	2000-2001	Neonatal screening	99.260	4,7%	Lobo *et al.*[53]
Southeast	Rio de Janeiro	2007	Neonatal screening	-	4%	Cançado *et al.*[30]
	São Paulo	2007	Neonatal screening	-	2,6%	Cançado *et al.*[30]
	Minas Gerais	2007	Neonatal screening	-	3%	Cançado *et al.*[30]
	Paraná	2001-2004	Neonatal screening	548.810	1,53%	Watanabe *et al.*[54]
South	Rio Grande do Sul	2007	Neonatal screening	-	2,0%	Cançado *et al.*[30]
	Rio Grande do Sul	2003-2004	Neonatal screening	117.320	1,14%	Sommer *et al.*[55]

contingent of slaves will have a higher prevalence of the sickle cell trait, since this condition is closely related to black ethnicity. The Southeast region of the country was a region largely colonized by Europeans and black Africans due to the economic and extractive activities that the region offered at the time of slavery[31,32], especially the State of Minas Gerais, which had a large number of mines, thus demanding great number of slaves to work.

In this study, a higher frequency of self-declared mixed race (42.8%) was found among donors with sickle cell trait, which shows the great influence of miscegenation in this region, followed by self-declared white (30.7%) and self-declared black (26 .5%), a fact justified by the ascendancy of white ethnicity in the Brazilian population and the biases in the categorization of skin color[33]. However, among the self-declared brown, black and white blood donors, 2.6% (142 of 5,428), 6.1% (88 of 1,434) and 1.3% (102 of 7,881) were carriers of the sickle cell trait, respectively. . Thus, for the total population of blood donors evaluated in this study, the sickle cell trait was more prevalent among self-declared blacks, which is expected since it is a common genetic alteration in this ethnic group[4].

It is known that the mutation that gives rise to the sickle cell trait is not linked to sex, so a significant difference in the prevalence of sickle cell trait between men and women is not expected.[34] In this study, of the 332 positive donors for hemoglobin S research , 153 were male and 179 female (46.1% and 53.9% respectively), similarly, the data in table 1, referring to all donors in the Midwest region of the State of Minas Gerais (51.4% and 48.6%, respectively, p = 0.051) showed no significant difference in the proportion between men and women. Soares *et al.*[35] and Bernieri *et al.*[20] found a male predominance among individuals with sickle cell trait, which can be justified by the fact that, in Brazil, according to the National Health Surveillance Agency (ANVISA), the number of male blood donors is higher [36].

Dos 332 doadores com traço falciforme, a maioria está compreendida entre as faixas etárias de 21 a 30 anos (31,9%) e de 31 a 40 anos (30,7%). No estudo de Martins *et al.* observa-se cerca de 53% dos doadores de sangue com traço falciforme em idade fértil [37]. Estes dados nos mostram que estes se encontram em idade reprodutiva, demonstrando a importância de enfatizar a realização do aconselhamento genético com estes indivíduos, a fim de se evitar futuros filhos portadores da forma mais grave da doença.

Flôr *et al.*[38] in a study carried out with blood donors from three major blood donation centers in Brazil, the Pró-Sangue Foundation in São Paulo (São Paulo), Hemominas Foundation (FH) in Belo Horizonte (Minas Gerais) and Fundação Hemope in Recife (Pernambuco), observed that most of the study participants were male (65.4%), under 45 years old (86.6%), with an average age of 32.6 years, reported being brown (42.4%) or white (40.1%) and completed at least 11 years of study (61.4%). These findings are similar to those found in our study and in other studies[39,40], showing that this is a predominant profile among blood donors. The higher level of education among blood donors than the general population of Brazil[41], may be related to the lack of information about the donation process and also to unfounded negative beliefs about blood donation and the consequences that this process could cause among those with low education.[39,40,42]

As expected, the median hemoglobin levels of HbS positive donors are within normal values 14.7 (13.9-15.7), as otherwise they would not be able to donate blood. However, when comparing the median hemoglobin levels between

Table 4. Studies on the prevalence of sickle cell trait in different populations and Brazilian municipalities.

Regions of Brazil	Location (municipality)	Period	Study population	N	Hb AS	References
North	Brejinho de Nazaré/TO	2011	Four quilombola communities	167	4,8%	Souza *et al.*[56]
	Macapá/AP	2016-2017	Blood donors	26.709	1,5%	Pereira *et al.* [57]
	Santarém/PA	2011	Saracura Community	116	1,7%	Cardoso *et al.* [58]
Northeast	Recôncavo Baiano/BA	2006-2009	Neonatal screening	14.773	5,8%	Silva *et al.*[19]
	Fortaleza/CE	2001-2002	Neonatal screening	389	3,85%	Pinheiro *et al.*[34]
Southeast	Uberaba/MG	1996-2000	Blood donors	70.263	0,99%	Martins *et al.*[37]
	Ribeirão Preto/SP	2013	Blood donors	95.527	0,42%	Machado & Oliveira [59]
	Campinas/SP	1992-2000	Neonatal screening	281.884	1,98%	Brandelise *et al.*[60]
	São Carlos/SP	2007-2010	Neonatal screening	10.589	1,85%	Moreira *et al.* [61]
	São José do Rio Preto/SP	1997-1998	Newborns at the Base Hospital of São José do Rio Preto	913	3,72%	Ducatti *et al.*[62]
	Vitória/ES	2006	Marcos Daniel Laboratório's patients	150	1,33%	Moraes & Depianti [63]
South	Caxias do Sul/RS	2001	Blood donors	608	0,99%	Lisot & Silla[32]
	Passo Fundo/RS	2008-2011	Blood donors	32.261	0,4%	Bernieri *et al.*[20]
	Umuarama/PR	2005-2006	Unipar Laboratory Patients	585	2,5%	Seixas *et al.*[64]

donors with and without sickle cell trait, it is noted that the former have slightly lower, but statistically significant, levels when compared to those without sickle cell trait [14,7 (13,9-15,7) vs. 15,1 (14,0-16,1), p <0,001].

Early detection of sickle cell trait has been carried out in Brazil since the 1990s. Thus, donor screening is valuable for those who are of childbearing age and have not been screened by the neonatal screening test, as it allows for guidance of these individuals about their genetic condition and the risks it poses to bear children with sickle cell anemia. In this way, they can opt for an examination to screen their partner for sickle cell trait, if the partner does not know if he/she has this condition, despite the fact that the research on sickle cell anemia by the National Neonatal Screening Program is already consolidated in Minas Gerais since 1998[43] and through the result, together decide for the pregnancy or not. This could thus reduce costs with future complications and treatment for patients with SCD[44, 45].

Conclusion

The data obtained in this study show the importance of calculating the prevalence of sickle cell trait carriers in blood donors in the Midwest region of Minas Gerais, as there are still no published studies on this region and also the benefits of identifying these individuals for know the epidemiological profile and enable the construction of a care network, if necessary. Thus, this study contributed to other prevalence studies in Brazil.

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Conflict of interest

The authors have declared that they have no conflict of interest.

References

1. Ministério da Saúde (BR). Portaria nº. 158, de 04 de fevereiro de 2016 [Internet]. Redefine o regulamento técnico de procedimentos hemoterápicos [Internet]. Brasília (DF): Ministério da Saúde; 2016; [acesso em 2020 Abr 03]. Disponível em: http://bvsms.saude.gov.br/bvs/saudelegis/gm/2016/prt0158_04_02_2016.html

2. Soares LF, Lima EM, Silva JA, Fernandes SS, Silva KMC, Lins SP, et al. Prevalência de hemoglobinas variantes em

comunidades quilombolas no estado do Piauí, Brasil. Ciênc Saúde Colet. 2017 Nov;22(11):3773-80.

3. Manfredini V, Castro S, Wagner S, Benfato MS. A fisiopatologia da anemia falciforme. Infarma Ciências Farmacêuticas. 2007;19(1-2):3-6.
4. Piel FB, Steinberg MH, Ress DC. Sickle cell disease. N Engl J Med. 2017 Abr;376(16):1561-73.
5. Austin H, Key NS, Benson JM, Lally C, Dowling NF, Whitsett C, et al. Sickle cell trait and the risk of venous thromboembolism among blacks. Blood. 2007 Ago;110(3):908-12.
6. Humphries JE, Wheby MS. Case report: sickle cell trait and recurrent deep venous thrombosis. Am J Med Sci. 1992 Fev;303(2):112-4.
7. Naik RP, Derebail VK, Grams ME, Franceschini N, Auer PL, Peloso GM, et al. Association of sickle cell trait with chronic kidney disease and albuminuria in African Americans. JAMA. 2014 Nov;312(20):2115-25.
8. Naik RP, Smith-Whitley K, Hassell KL, Umeh NI, Montalembert M, Sahoa P, et al. Clinical outcomes associated with sickle cell trait. Ann Intern Med. 2018 Out;169(9): 619-36.
9. Nelson DA, Deuster PA, Carter R, Hill OT, Wolcott VL, Kurina LM. Sickle cell trait, rhabdomyolysis, and mortality among U.S. Army Soldiers. N Engl J Med. 2016 Ago;375(5): 435-42.
10. Caughey MC, Loehr LR, Key NS, Darebail VK, Gottesman RF, Kshirsagar AV, et al. Sickle cell trait and incident ischemic stroke in the atherosclerosis risk in communities study. Stroke. 2014 Out;45(10):2863-7.
11. Ajayi AA, Kolawole BA. Sickle cell trait and gender influence type 2 diabetic complications in African patients. Eur J Intern Med. 2004 Ago;15(5):312-5.
12. Burnham-Marusich AE, Ezeanolue CO, Obiefune MC, Yang W, Osuji A, Ogidi AG, et al. Prevalence of sickle cell trait and reliability of self-reported status among expectant parents in Nigeria: implications for targeted newborn screening. Public Health Genomics. 2016;19(5):298-306.
13. Moraes KCM, Galioti JB. A doença falciforme: um estudo genético-populacional a partir de doadores de sangue em São José dos Campos, São Paulo, Brasil. Rev Bras Hematol Hemoter. 2010;32(4):286-90.
14. Adorno EV, Couto FD, Moura Neto JP, Menezes JF, Rego M, Reis MG, et al. Hemoglobinopathies in newborns from Salvador, Bahia, Northeast, Brazil. Cad Saúde Pública. 2005 Fev;21(1):292-8.
15. Machado LAF, Gomes EGC, Oliveira LC, Lima LC, Neto JFN. Prevalência de traço falciforme em doadores de sangue: uma revisão sistemática. Rev Hosp Univ Pedro Ernesto. 2019;18(2):95-102.
16. Alabdulaali MK, Alayed KM, Alshaikh AF, Almashhadani SA. Prevalence of glucose-6-phosphate dehydrogenase deficiency and sickle cell trait among blood donors in Riyadh. Asian J Transfus Sci. 2010;4(1):31-3.
17. Soares LF, Oliveira EH, Lima BI, Silva JM, Mota JT, Bonini-Domingos CR. Hemoglobinas variantes em doadores de sangue do Centro de Hematologia e Hemoterapia do Estado do Piauí (Hemopi): conhecendo o perfil epidemiológico para construir a rede de assistência. Rev Bras Hematol Hemoter. 2009 Jan;31(6):471-2.
18. Reis FMS, Branco RROC, Conceição AM, Trajano LPB, Vieira JFPN, Ferreira PRB, et al. Incidence of variant hemoglobins in newborns attended by a public health laboratory. Einstein (São Paulo). 2018 Jun;16(2):1-7.
19. Silva W, Oliveira R, Ribeiro S, Silva I, Araújo E, Baptista A. Screening for structural hemoglobin variants in Bahia, Brazil. Int J Environ Res Public Health. 2016 Fev;13(2): 225-31.
20. Bernieri T, Fior D, Ardenghi PG. Prevalência de hemoglobina S em doadores de sangue do Hemocentro de Passo Fundo, Rio Grande do Sul, Brasil. Rev Bras Pesqui Saúde. 2018 Mai;19(4):104-8.
21. Governo do Estado de Minas Gerais (BR). Minas Gerais. Regiões de planejamento [Internet]. Belo Horizonte (MG): Governo do Estado de Minas Gerais; 2019; [acesso em 2020 Abr 30]. Disponível em: https://www.mg.gov.br/sites/default/files/paginas/arquivos/2016/ligminas_10_2_02_regplan_listamunicipios.pdf
22. Serviço Nacional de Aprendizagem Comercial (SENAC). Regiões Turísticas: Centro-Oeste [Internet]. Belo Horizonte (MG): SENAC; 2020; [acesso em 2020 Mai 15]. Disponível em: http://www.descubraminas.com.br/Turismo/RegiaoTuristicaDetalhe.aspx?cod_regiaoturistica=6
23. Instituto Brasileiro de Geografia e Estatística (IBGE). Cidades e Estados – Divinópolis [Internet]. Brasília (DF): IBGE; 2019; [acesso em 2020 Jul 10]. Disponível em: https://www.ibge.gov.br/cidades-e-estados/mg/divinopolis.html
24. Fundação Hemominas (FH). Unidades e Contratantes – Hemonúcleo de Divinópolis [Internet]. Divinópolis: Fundação Hemominas; 2016; [acesso em 2020 Jul 10]. Disponível em: http://hemominas.mg.gov.br/unidades-e-contratantes/rede-hemominas/hemonucleo/divinopolis
25. Naoum PC, Naoum FA, Naoum PF. Doença falciforme: diagnóstico laboratorial das doenças das células falciformes [Internet]. São José do Rio Preto: Academia de Ciência e Tecnologia; 2019; [acesso em 2020 Abr 16]. Disponível em: https://www.hemoglobinopatias.com.br/d-falciforme/diagnostico.htm
26. Agência Nacional de Vigilância Sanitária (ANVISA). Manual de diagnóstico e tratamento de doenças falciformes [Internet]. Brasília (DF): ANVISA; 2002; [acesso em 2020 Abr 16]. Disponível em: https://bvsms.saude.gov.br/bvs/publicacoes/anvisa/diagnostico.pdf
27. Governo do Estado de Minas Gerais (BR). Conheça Minas: Geografia [Internet]. Belo Horizonte (MG): Governo do Estado de Minas Gerais; 2019; [acesso em 2020 Abr 19]. Disponível em: https://www.mg.gov.br/conheca-minas/geografia
28. Silva JEP, Giovelli LL. Traço falciforme: uma visão para os centros de hemoterapia. Rev Saúde (Santa Maria). 2011 Fev;36(1):23-9.
29. Naoum PC. Prevalência e controle da hemoglobina S. Rev Bras Hematol Hemoter. 2000;22(Supl 2):142-8.
30. Cançado RD, Jesus JA. A doença falciforme no Brasil. Rev Bras Hematol Hemoter, 2007 Set;29(3):203-6.

31. Lervolino LG, Baldin PEA, Picado SM, Calil KB, Viel AA, Campos LAF. Prevalence of sickle cell disease and sickle cell trait in national neonatal screening studies. Rev Bras Hematol Hemoter. 2011;33(1):49-54.

32. Lisot CLA, Silla LMR. Triagem de hemoglobinopatias em doadores de sangue de Caxias do Sul, Rio Grande do Sul, Brasil: prevalência em área de colonização italiana. Cad Saúde Pública. 2004 Dez;20(6):1595-601.

33. Lembert J. Estrutura étnica e contatos de raças. In: Lembert J, ed. Os dois Brasis. 12ª ed. São Paulo: Companhia Editora Nacional; 1984. p. 85-100.

34. Pinheiro LS, Gonçalves RP, Tomé CAS, Alcântara AEE, Marques ARC, Silva MM. Prevalência de hemoglobina S em recém-nascidos de Fortaleza: importância da investigação neonatal. Rev Bras Ginecol Obstet. 2006 Fev;28(2):1-4.

35. Soares LF, Leal JMA, Vieira JFPN, Oliveira EH. Prevalência das hemoglobinas S e C em heterozigose em duas comunidades de povos de Terreiros na cidade de Teresina, Piauí. Rev Ciênc Farm Básica Apl. 2015 Mar;36(1):91-5.

36. Agência Nacional de Vigilância Sanitária (ANVISA). 6º Boletim de produção hemoterápica [Internet]. Brasília (DF): ANVISA; 2018; [acesso em 2020 Abr 16]. Disponível em: http://portal.anvisa.gov.br/documents/4048533/4993603/6%C2%B0+Boletim+de+Produ%C3%A7%C3%A3o+Hemoter%C3%A1pica+-+Hemoprod+2017/15545fd5-ad1f-4b00-9340-a811aa910bbc

37. Martins PRJ, Pereira GA, Pacheco KD, Oliveira PF, Oliveira AA, Rita CVC, et al. Avaliação da freqüência de hemoglobina A1s nos candidatos à doação de sangue no hemocentro regional de Uberaba, no período de 1996 a 2000: estudo retrospectivo. Rev Méd Minas Gerais. 2004 Jan/Mar;1(15):34-7.

38. Flôr CR. Obesidade, anemia e fatores associados em doadores de sangue [tese]. Divinópolis: Universidade Federal de São João Del-Rei; 2020.

39. Boulware LE, Ratner LE, Ness PM, Cooper LA, Campbell-Lee S, Laveist TA, et al. The contribution of sociodemographic, medical, and attitudinal factors to blood donation among the general public. Transfusion. 2002 Jun;42(6):669-78.

40. Zucoloto ML, Gonçalez T, Custer B, McFarland W, Martinez EZ. Comparison of the demographic and social profile of blood donors and nondonors in Brazil. Health Soc Care Community. 2018 Mar;27(2):330-6.

41. Instituto Brasileiro de Geografia e Estatística (IBGE). Conheça o Brasil - população: educação [Internet]. Brasília (DF): IBGE; 2018; [acesso em 2020 Abr 30]. Disponível em: https://educa.ibge.gov.br/jovens/conheca-o-brasil/populacao/18317-educacao.html

42. Gonçalez TT, Oliveira CL, Carneiro-Proietti ABF, Moreno EC, Miranda C, Larsen N, et al. Motivation and social capital among prospective blood donors in three large blood centers in Brazil. Transfusion. 2012 Set;53(6):1291-301.

43. Rodrigues DOW, Ferreira MCB, Pereira PM, Bustamante MTT, Campos EMS, Oliveira CM. Diagnóstico histórico da triagem neonatal para doença falciforme. Rev APS. 2010 Jan/Mar;13(1):34-45.

44. Centro de Comunicação Social da Faculdade de Medicina da UFMG. Programa de triagem neonatal de Minas Gerais [Internet]. 2020; [acesso em 2020 Abr 06]. Disponível em: https://www.nupad.medicina.ufmg.br/programa-e-acoes/programa-de-triagem-neonatal-de-minas-gerais/

45. Bandeira FMGC, Bezerra MAC, Santos MNN, Gomes YM, Araújo AS, Abath FGC. Importância dos programas de triagem para o gene da hemoglobina S. Rev Bras Hematol Hemoter. 2007 Jun;29(2):179-84.

46. Siqueira BR, Zanotti LC, Nogueira A, Maia ACS. Incidência de anemia falciforme, traço falcêmico e perfil hemoglobínico dos casos diagnosticados na triagem neonatal no estado de Rondônia no ano de 2003. Ver Saber Científ. 2009;2(1):43-53.

47. Souza RC, Miranda Neto PAD, Santos JRF, Monteiro SG, Gonçalves MC, Silva FB, et al. Sickle cell anaemia prevalence among newborns in the Brazilian Amazon-Savanna transition region. Int J Environ Res Public Health. 2018 Mai;16(9):1638-46.

48. Leite DCF, Cipolotti R, Gurgel RQ, Martins Filho PRS, Lopes GD. Spatial distribution of newborns with sickle cell trait in Sergipe, Brazil. Rev Paul Pediatr. 2020;38:1-6.

49. Vivas WLP, Rebouças DS, Fabbro ALD, Cipolotti R. Heterozigose para hemoglobinopatias em doadores de sangue do Centro de Hemoterapia de Sergipe. Rev Bras Hematol Hemoter. 2006 Dez;28(4):284-7.

50. Araújo MCPE, Serafim ESS, Castro Júnior WAP, Medeiros TMD. Prevalência de hemoglobinas anormais em recém-nascidos da cidade de Natal, Rio Grande do Norte, Brasil. Cad Saúde Pública. 2004 Fev;20(1):123-8.

51. Diniz D, Guedes C, Barbosa L, Tauil PL, Magalhães I. Prevalência do traço e da anemia falciforme em recém-nascidos do Distrito Federal, Brasil, 2004 a 2006. Cad Saúde Pública. 2009 Jan;25(1):188-94.

52. Holsbach DR, Ivo ML, Honer MR, Rigo L, Botelho CAO. Ocorrência de hemoglobina S no estado de Mato Grosso do Sul, Brasil. J Bras Patol Med Lab. 2008 Ago;44(4):277-82.

53. Lobo CLC, Bueno LM, Moura P, Ogeda LL, Castilho S, Carvalho SMF. Triagem neonatal para hemoglobinopatias no Rio de Janeiro, Brasil. Rev Panam Salud Pública. 2003;13(2-3):154-9.

54. Watanabe AM, Pianovski MAD, Zanis Neto J, Lichtvan LCL, Chautard-Freire-Maia EA, Domingos MT, et al. Prevalência da hemoglobina S no Estado do Paraná, Brasil, obtida pela triagem neonatal. Cad Saúde Pública. 2008 Mai;24(5):993-1000.

55. Sommer CK, Goldbeck AS, Wagner SC, Castro SM. Triagem neonatal para hemoglobinopatias: experiência de um ano na rede de saúde pública do Rio Grande do Sul, Brasil. Cad Saúde Pública. 2006 Ago;22(8):1709-14.

56. Souza LO, Teles AF, Oliveira RF, Lopes MAO, Souza IB, Inácio VSS, et al. Triagem das hemoglobinas S e C e a influência das condições sociais na sua distribuição: um estudo em quatro comunidades quilombolas do estado do Tocantins. Saúde Soc. 2013 Dez;22(4):1236-46.

57. Pereira YR, Porcy C, Menezes RAO. Prevalência de traço falciforme em doadores de sangue no hemocentro da cidade de Macapá. Rev Eletrônica Acervo Saúde. 2020 Abr;9:2889-96.

58. Cardoso GL, Takanashi SYL, Guerreiro JF. Inherited hemoglobin disorders in an Afro-Amazonian community: Saracura. Genet Mol Biol. 2012;35(3):553-6.

59. Machado LMS, Oliveira MH. Traço Falciforme e sua prevalência em doadores no hemocentro de Ribeirão Preto, núcleos e unidades [dissertação]. Ribeirão Preto (SP): Universidade de São Paulo (USP); 2015.

60. Brandelise S, Pinheiro V, Gabetta CS, Hambleton I, Serjeant B, Sergeant G. Newborn screening for sickle cell disease in Brazil: the Campinas experience. Clin Lab Haematol. 2004 Fev;26(1):15-9.

61. Moreira RMM, Estevão IF, Melo DG. Critical analysis of the neonatal screening program for hemoglobinopathies. Rev Bras Hematol Hemoter. 2011;33(4):318-20.

62. Ducatti RP, Teixeira AEA, Galão HÁ, Bonini-Domingos CR, Fett-Conte AC. Investigação de hemoglobinopatias em sangue de cordão umbilical de recém-nascidos do Hospital de Base de São José do Rio Preto. Rev Bras Hematol Hemoter. 2001 Abr;23(1):23-9.

63. Moraes EA, Depianti JB. Triagem da hemoglobina S em pacientes atendidos pelo Marcos Daniel Laboratório em Vitória, ES. Rev Bras Hematol Hemoter. 2008 Abr;30(2): 162-6.

64. Seixas FAV, Silva CD, Tominaga J, Ferro OC, Nilson LG. Incidence of hemoglobinopathies in Northwest Paraná, Brazil. Rev Bras Hematol Hemoter. 2008 Ago;30(4):287-91.