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Prevalence of variant hemoglobins and thalassemias in a maroon community in Sergipe, Brazil

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ABSTRACT. Current analysis investigates the sickle-cell syndrome among members of a maroon community (*comunidade quilombola*) in the state of Sergipe, Brazil. The entire population, comprising five hundred and ninety-three people, was screened. Blood samples were collected from 318 people, aged between six months and fifty years, who underwent a solubility test to assess the presence of HbS, followed by Sickle-Cell Test to confirm its presence. Results revealed that 2.2% of the three hundred and eighteen people tested have hemoglobin HbS in their blood; 57% have type HbAS and 43% have a combination between thalassemia and heterozygous with a variable percentage of HbS ranging between 24.9 and 37.9%. Blood sampling revealed that only five out of the 318 people belonged to different families. Results are highly relevant for public health policies on the sickle-cell syndrome and its management.

Keywords: sickle cell syndrome, maroon community, diagnosis.

Prevalência de hemoglobinas variantes e talassemia em uma comunidade quilombola em Sergipe, Brasil

RESUMO. Este trabalho investiga a síndrome da anemia falciforme entre os membros de uma comunidade quilombola no Estado de Sergipe, Brasil. Foi rastreada toda a população, que compreende 593 pessoas. Amostras de sangue foram coletadas de 318 pessoas, com idades entre seis meses e 50 anos, que foram submetidas a um teste de solubilidade para avaliar a presença de HbS, seguido pelo teste de falcização para confirmar a sua presença. Os resultados revelaram que 2,2% das 318 pessoas testadas apresentaram hemoglobina variante HbS em seu sangue; 57% possuíam a variante HbAS e 43% apresentaram uma combinação entre talassemia e heterozigotos com percentagens variáveis de HbS entre 24,9 e 37,9%. A coleta de sangue revelou que apenas cinco das 318 pessoas pertenciam a famílias distintas. Os resultados são altamente relevantes para o planejamento e gestão de políticas públicas de saúde sobre a síndrome falciforme.

Palavras-chave: anemia falciforme, quilombolas, diagnóstico.

Introduction

Sickle-cell syndromes are composed of a group of genetic diseases characterized by the synthesis of structurally abnormal polypeptide chains (hemoglobin structural variants) or decreased synthesis of one or more globin chains (thalassemia). It has been estimated that approximately 7% of world population have different hereditary disorders of hemoglobin, as one of the most common monogenic diseases (WEATHERALL, 2001).

The sickle-cell disease is a generic term used to determine a group of genetic disorders characterized by the predominance of hemoglobin S (HbS). These changes include sickle cell anemia (HbSS), double heterozygosis, namely, associations with other Hb variant hemoglobins such as HBD, HbC, and interactions with thalassemia (HbS/β0 thalassemia, HbS / β + thalassemia, HbS / α thalassemia). Sickle-cell syndromes also include sickle-cell trait (HbAS) and sickle-cell anemia, associated with the hereditary persistence of fetal hemoglobin (HbS / HPFH) (BRASIL, 2001a).

Gene dispersion for hemoglobin variants and thalassemia in Brazil are closely related to the ethnicity of Brazilian populations, involving the colonization process characterized by the migration of various peoples. Since the Brazilian population has several different racial backgrounds, with varied and progressive miscegenation, this fact certainly influenced the prevalence of thalassemia and hemoglobin variants in different regions of the country (REIS et al., 2005).

Diseases caused by hemoglobin variants affect about 3.4% of children's deaths before the age of five (4-6). The distribution of the S gene in Brazil is very heterogeneous. It is related to the Negroid and Caucasoid composition; heterozygotes for HbS are more prevalent in the North and Northeast regions (between 6 and 10%), whereas prevalence is lower in the South and Southeast regions (between 2 and 3%). In the specific case of miscegenation in Afro-descendants, molecular studies have identified five HbS haplotypes, featuring the Senegal, Benin and Bantu haplotypes as the most widespread in the Americas due to the slave trade (BRASIL, 2001b).

Hemoglobin S is a hematological abnormality caused by mutations in the beta gene globin, specifically due to the exchange of a nitrogenous base codon GAG to GTG, resulting in the substitution of valine at position 6 for glutamic acid. Erythrocytes with variant hemoglobin S (HbS) undergo sickle-cell process, physiologically caused by low oxygen tension, acidosis and dehydration. Consequently, sickle-cells start taking the shape of a sickle or of a crescent moon, with variable clinical consequences to the carriers, depending on their concentration (NAOUM, 1999). Patients present organ damage since childhood, resulting from repeated vein-occlusive episodes (NAOUM, 2000; BANDEIRA et al., 2004).

The carrier (heterozygous sickle-cell trait or S) affects 500 individuals per 100,000 births, even though children do not show signs of the disease until they are six months old. When symptoms occur, they are similar to sickle-cell anemia and related to severe pulmonary infections, albeit with a markedly lower intensity. Generally, the affected individual remains asymptomatic throughout life and the disease may only be diagnosed by laboratory tests (EDELSTEIN, 1986; NAOUM, 1999; LEONELIL et al., 2000). The high prevalence of hemoglobin S, with sharp regional differences marked by miscegenation processes of the Brazilian population, has been the object of several studies not merely in patients with sickle-cell anemia (homozygous for hemoglobin S - HbSS), but also in individuals with the variant hemoglobin as heterozygous (HbAS). Genetic and environmental factors influence the clinical complications of these patients (LEONELIL et al., 2000).

Thalassemias are due to the imbalance in the concentrations of alpha and beta globins, affected during their synthesis, which diminish or suppress the production of alpha or beta globin chains that make up the hemoglobin tetramer molecule (NAOUM; BONINI-DOMINGUES, 2007). The reduction in the production of one or more polypeptide chains generally results in the development and hypochromic microcytic anemia. Since the reduction of the synthesis may be total or partial, thalassemias are classified according to the affected globin chain, alpha, beta, delta, delta-beta, and gamma-delta-beta. The β-thalassemia is the most important clinical manifestation due to its morbidity and mortality and because of its hemolytic anemia (WEATHERALL, 2001; SAKAMOTO et al., 2008).

The Brazilian state of Sergipe has 23 acknowledged maroon communities (Portuguese *quilombolas*), distributed homogeneously on its territory (SANTOS, 2006). Owing to the specific health demands of these population groups, a population-based study is required to identify the hemoglobin variants HbS and thalassemia, for which inferences are made to strengthen and implement public health policies. Current analysis studies the sickle-cell syndrome in the maroon community called Patioba, in Sergipe, Brazil, and identifies its socio-environmental characteristics.

Material and Methods

Current investigation is a cross-sectional study with a quantitative approach, conducted between January and December 2009, and approved by the Committee for Ethics in Research (Protocol # 361208).

The study area was the Patioba maroon community in the municipality of Japaratuba, Sergipe State, Brazil. In 2009, the community comprised 593 inhabitants, representing 186 families enrolled in the Primary Care Information System (Sistema de Informação da Atenção Básica, SIAB). The socio-environmental survey was conducted with the entire population under analysis, whose members participated in the interviews without ado. The serological survey included individuals aged between 6 months and 50 years, of both genders, totaling 318 participants. Blood samples were collected in an appropriate premise for such procedure by which 10 mL of blood were harvested with a vacuum system; 5 mL tubes contained EDTA anticoagulant for HbS research and 5 mL for Blood Cell Counts (BCC). The blood samples were stored at 4°C during transport, sent to the Central Laboratory of Biomedicine of Tiradentes University (UNIT) and then screened for sickle syndromes by solubility and sickle tests. The positive samples underwent Hb S hemoglobin electrophoresis by high performance liquid chromatography (HPLC), coupled to a complete blood count performed by the flow cytometry method.

The prevalence rate of HbS and hemoglobin variants was calculated, with a 95% confidence interval. Laboratory changings for the diagnosis of sickle-cell syndrome, based on reference rates, was analyzed. The degree of kinship between individuals was also investigated by genogram.

Results and discussion

The Patioba community consists of 593 inhabitants distributed in 186 families, with an age range from zero to 100 years. Most respondents (69%) had no labor records and only 31% of workers had any formal labor contract. Most waged workers received only one minimum wage. Further, 25.1% of the population are illiterate.

The prevalence of sickle-cell syndrome among individuals between six months old to fifty years old in the maroon community Patioba, Sergipe State, Brazil, reached 2.2%. No case of sickle-cell anemia was found in current study. However, the dispersion of a single variant hemoglobin (Hb S gene) was reported, coupled to associated alpha and beta thalassemias in the maroon population under analysis (Table 1).

In the Sergipe maroon community under analysis, three cases of individuals with sickle-cell trait were reported (Table 1). HbAS gene flow is concentrated in two households, or rather, two cases with parental and filial relationship; two cases of consanguineous brothers, and another case of great-aunt and great-nephews (Figure 1).

The solubility screening test confirmed all positive blood samples (100%) for depranocytes during the sickle-cell test (Table 2).

In the first serological survey for positive screening for hemoglobin S cases, the solubility test revealed 7 cases in the Sergipe maroon community (2.2%): the highest number comprised people within the 21-30 years age bracket (3 cases); followed by the 10-20 years age bracket (2 cases); 6 months to 9 years (1 case); and 41-50 years (1 case).

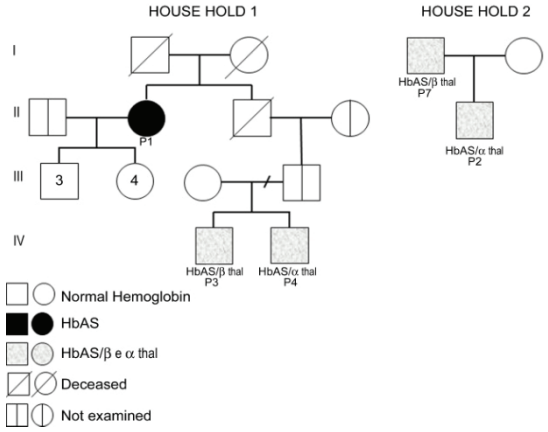

Figure 1. Genograms of households with HbAS occurrences for thalassemia in the maroon community, Sergipe, 2009.

Table 2. Age distribution of the frequency of HbS positivity in solubility and sickle-cell tests in Patioba maroon community, Sergipe, Brazil, 2009.

Age group	HbS		N	%
	Positive	Negative		
6 months - 9 years old	1	85	86	27.0
10-20 years old	2	101	103	32.4
21-30 years old	3	48	51	16.0
31-40 years old	0	45	45	14.2
41-50 years old	1	32	33	10.4
Total	7	311	318	100.0

These people had varying degrees of anemia and suggestive processes ranging from mild iron deficiency anemia in patient P1, moderate iron deficiency anemia in patient P2, to iron deficiency anemia - iron deficiency in patient P3.

Gene flow of Hemoglobin AS circulates in the community of the Patioba maroon community primarily in two households, especially in male individuals (Figure 1), with a frequency of approximately 2.15% of the households.

Table 1. Prevalence of hemoglobin variants and thalassemia in the Patioba maroon community, related to laboratory abnormalities. Sergipe, Brazil, 2009.

Person	Age	Solubility test	Sickle-cell test	Genotypes					MCV	Morphology	Sickle-cell syndrome
				A1	A2	F	S	C			
P1 (♀)	49	Positive	Positive	59.1%	3.2%	0.3%	37.4%	-	84.6	Normal	HbAS
P2 (♂)	02	Positive	Positive	64.3%	3.4%	1.7%	30.6%	-	70.7	Low Hypochromy Low Microcytosis HCM lowered	HbAS/ α thal
P3 (♂)	17	Positive	Positive	70.8%	3.7%	0.6%	24.9%	-	57.2	Hypochromy moderate/severe Microcytosis hightened HCM diminished	HbAS/ β thal
P4 (♂)	11	Positive	Positive	64.8%	3.4%	0.8%	31.0%	-	72.8	Low Hypochromy Low Microcytosis HCM lowered	HbAS/α thal
P5 (♀)	21	Positive	Positive	59.3%	3.4%	0.4%	36.9%	-	85.0	Normal	HbAS
P6 (♀)	24	Positive	Positive	58.8%	3.0%	0.3%	37.9%	-	91.1	Normal	HbAS
P7 (♂)	21	Positive	Positive	62.3%	3.9%	0.6%	33.2%	-	79.6	Normal	HbAS/ β thal

References: Solubility: Reference value: negative, positive sickle cells: presence of drepanocytes; Electrophoresis: Values: Hemoglobin A1 (96-98%); Hemoglobin A2 (2.5 to 3.4%); Fetal Hemoglobin (up to 2%), Hemoglobin S and C (0%); MCV - (Medium Corpuscular Volume-Males (81-99 fL); Females (80 98 fL). ♂ - male; ♀ - female.

In household 1, the gene flow of HbAS was identified in one female patient (P1), generation II, 49 years old, and who had seven children born in two different marriages. Among the seven, two minor children underwent serological screening and were identified as negative for sickle cell-sickle cell trait. The older children, however, failed to attend to the biological material collection for serologic evaluation. It is presumed that the sickle cell trait occurs in every generation outlined. Although in generation I, the couple of parents were former residents of the maroon community, the man was deceased and the woman was absent from the community when the study began. In Generation III, the sickle-cell trait gene was probably transmitted by the male individual, father of P3 and P4, who is not a permanent resident in the maroon community under study anymore, having divorced the spouse (Figure 1) and began a new marital relationship. The above aspect denotes the new family relationships in contemporary society, as well as the output of HbAS gene flow out of the maroon community. Family 2 has a gene flow of the latest hemoglobin AS circulating among individuals with first-degree consanguinity, with male bearers, father (P7) and son (P2).

Discussion

Recently, in Brazil, a mobilization of black communities has been on-going by which they are gradually resuming their former maroon identity and endeavoring to belong to a particular territory and to have their rights as an ethnic group acknowledged, including the right to public health. In the state of Sergipe, the Palmares Foundation identified 23 maroon communities distributed in 14 municipalities, including the Patioba community in the municipality of Japaratuba (SANTOS, 2006) .

In Brazil, people with sickle-cell anemia have a prevalence of heterozygous haplotypes, involving 66 % of Bantu, 32 % Benin and 2 % Senegal haplotypes (STEINBERG; EMBURY, 1986; NAOUM, 1997). In the case of these haplotypes in Brazilian territory, Africans were distributed heterogeneously and are thus more frequent in places where the proportion of black ancestors was largest, as in northeastern Brazil.

The sickle-cell trait (Table 1) characterizes the asymptomatic carrier, heterozygous for HbS, laboratory represented by HbAS. These carriers do not have sickle-cell anemia or they have abnormalities in the number and shape of blood cells, usually discovered by routine analysis (NAOUM, 1999).

The global prevalence of sickle-cell trait is highly diverse and depends on a greater or lesser degree of miscegenation. In Africa, for example, Ghana features a sickle-cell trait in 13.27% of the population, whereas Kenya has an estimated trait of 3% among its population (DINIZ et al., 2009). In Brazil, the HbS gene frequencies vary according to the African influence in each region. One of the largest studies of screening for hemoglobin performed in Brazil evaluated individuals from 48 Brazilian cities and resulted in a 2.2% frequency of carriers of the sickle-cell trait (ALVAREZ FILHO et al., 1995), similar to that observed in the cross-sectional study in the Patioba maroon community.

Other recent serological surveys have indicated the prevalence of even higher HbS: 5.3% in Bahia; 4% in Pernambuco; 4% in Rio de Janeiro; 3% in Minas Gerais (CANÇADO; JESUS, 2007) and 3.23% in the Federal District (DINIZ et al., 2009). Studies on newborns in Rondônia revealed sickle-cell trait frequency of 2.9% by high performance liquid chromatography (HPLC) (SIQUEIRA et al., 2009). In the state of Sergipe, a study was conducted during 2006 on the occurrence of hemoglobin HbS among blood donors at the Hematology Center and abnormal hemoglobin percentages (5.6 and 4.1%) of sickle cell traits were reported (VIVAS et al., 2006).

The frequency of the sickle-cell trait in the Patioba maroon community in Sergipe proves to be similar to the Brazilian average (2%), calculated in the last survey by the Ministry of Health (ZAGO, 2002), albeit lower than the rates in some African countries. The above may be due to the fact that the Brazilian population has heterogeneous miscegenation pattern which reflects the input of about four million slaves from three main groups: Sudanese cultures (Yoruba people from Nigeria, Dahomey, Gold Coast, Ghana and others), Islamized Sudanese Guinea cultures (Peuhl, Mandigas, Hausa, Slap, Borem, Gurunsi and others) and Bantu cultures (Angola, Congo, Mozambique, Kenya and others).

Thalassemias (Table 1) typically result in the development of microcytic and hypochromic anemia (NAOUM, 1999), while alpha-thalassemia has been reported as the most common heritable change of the abnormal hemoglobin synthesis. People with sickle-cell trait (hemoglobin AS) associated with alpha-thalassemia exhibit alterations in the morphology and quantity of erythrocytes, such as hypochromic, microcytic reduced MCV observed in current study (Table 1), usually absent in heterozygotes for this variant hemoglobin. This may be a protective genetic trait for potential and future severe cases of sickle-cell anemia in the Patioba maroon community in Sergipe. The interaction between hemoglobin S and alpha-

thalassemia has been described as one of the factors responsible for the improvement in the clinical conditions of homozygous hemoglobin S (sickle-cell anemia), with a decrease in sickle-cell crisis events (TOME-ALVES et al., 2000).

However, the alpha-thalassemia cases associated with heterozygosity for hemoglobin S (Table 1) should be evaluated to detect suspected iron deficiency by assessment of serum iron and ferritin rates (TOME-ALVES et al., 2000). Beta-thalassemia in the heterozygous form is characterized by elevated HbA2 and / or fetal Hb in classic cases (WEATHERALL, 2001; HARDISON et al., 2002). The increase in HbA2 rates may suggest the individual's genotype. Changes in phenotypic expression have been registered and reveal the ontogeny of the Brazilian population (WEATHERALL, 1997; HÜNEMEIER et al., 2007). P3 and P7 patients presented an association of beta thalassemia with Hemoglobin S heterozygosity (Table 1). The frequency of beta thalassemia reported in the northeastern region of Brazil is 3.95% (DOMINGOS et al., 2009).

Several serological studies have mapped the epidemiological indexes of the sickle-cell syndrome in Brazil by different methodological strategies. The observed variations may be explained by ethnic differences among the studied populations and by selection criteria. In the mid-western region, the migratory target home of Brazilians from several regions of the country, a sample of 404 individuals from 55 cities in the state of Goiás revealed a 10.1% prevalence of hereditary anemia, thalassemia and hemoglobin variants, specifically 5.2% of heterozygous alpha thalassemia, 2.2% of hemoglobin S heterozygosity (HbAS); 1% heterozygosity for hemoglobin C (HbAC); 0.7% of lower beta thalassemia; 0.5% alpha-thalassemia and heterozygous for HbS; 0.3% alpha-thalassemia and heterozygous for HbC; and 0.3% heterozygous for hemoglobin D (HbAD) (MELO-REIS et al., 2006). Similar to the Sergipe study, there were no cases of homozygosis in Goiás.

Molecular studies in different regions of Brazil show an approximately 25% prevalence of alpha thalassemia in Brazilian populations (LERMEN, 2007). High frequency and diversity of carriers in the Brazilian population are due to differences in the ethnic composition of populations in the different regions and the extensive miscegenation which occurred throughout the history of Brazil. Electrophoretic procedures were performed in the UNESP Laboratory of Hemoglobin in São José do Rio Preto, São Paulo State, Brazil, (TOME-ALVES et al., 2000), which confirmed the presence of hemoglobin AS. Further, cytological research also revealed alpha thalassemia in 1,002 blood samples with the sickle-cell trait, among which 1.59% showed the association between hemoglobin AS and alpha-thalassemia, with kinship among some individuals. The erythrocyte morphology of most cases of interaction HbAS - alpha thalassemia (75%) was modified with patterns of microcytic hypochromic ranging between mild and moderate, as in current analysis (Table 1).

Conclusion

The above results demonstrate that the gene flow and profile of patients with sickle-cell trait and thalassemia in the Patioba maroon community in Sergipe State are consistent with the prevalence in the Brazilian national rates, whilst the miscegenation pattern of African descent is restricted to two households.

It should be underscored that the profiles outlined in current study require further studies, comprising the evaluation of hematological profiles of members of Brazilian *quilombo* communities from different regions. Results help characterize the profile of patients with sickle-cell syndrome in Afro-Brazilian descendants to improve early diagnosis in the population and the quality of life of these individuals.

References

ALVAREZ FILHO, F.; NAOUM, P. C.; MOREIRA, H. W.; CRUZ, R.; MANZATO, A. J.; DOMINGOS, C. R. Age and racial geographic distribution of S hemoglobina in Brazil. **Sangre**, v. 40, n. 2, p. 97-102, 1995.

BANDEIRA, F. M. G. C.; PERES, J. C.; CARVALHO, E. J.; BEZERRA, I.; ARAÚJO, A. S.; MELLO, M. R. B.; MACHADO, C. Hidroxiuréia em pacientes com síndromes falciformes acompanhados no Hospital Hemope, Recife-PE. **Revista Brasileira de Hematologia e Hemoterapia** ,v. 26, n. 3, p. 189-194, 2004.

BRASIL. Ministério da Saúde. **Manual de diagnóstico e tratamento de doenças falciformes**. Brasília: Anvisa, 2001a.

BRASIL. Ministério da Saúde. Secretária de Políticas da Saúde. **Manual de doenças mais importantes por, razões étnicas, na população brasileira afro-descendente**. Brasília: Ministério da Saúde, 2001b.

CANÇADO, R. D.; JESUS, J. A. A doença falciforme no Brasil. **Revista Brasileira de Hematologia e Hemoterapia**, v. 29, n. 3, p. 203-206, 2007.

DINIZ, D.; GUEDES, C.; BARBOSA, L.; TAUIL, P. L.; MAGALHÃES, I. Prevalência do traço e da anemia falciforme em recém-nascidos do Distrito Federal, Brasil, 2004 a 2006. **Cadernos de Saúde Pública**, v. 25, n. 1, p. 188-194, 2009.

DOMINGOS, A. L. B.; GRANZOTTO, L. A.; BELINI JÚNIOR E.; OLIVEIRA, T. Y. K.; DOMINGOS, A. C. B.; BONINI-DOMINGOS, C. R. Perfil de beta talassemia heterozigota obtido a partir de análise em banco de dados. **Revista Brasileira Hematologia e Hemoterapia**, v. 32, n. 1, p. 78-79, 2009.

EDELSTEIN, S. J. **The sickled cell**: from myths to molecules. Boston: Harvard University Press, 1986.

HARDISON, R. C.; CHUI, D. H. K.; BELINDA G.; RIEMER, C.; PATRINOS, G. P.; ANAGNOU, N.; MILLER, W.; WAJCMAN, H. HbVar: A relational database of human hemoglobin variants and thalassemia mutations at the globin gene server. **Human Mutation**, v. 19, n. 3, p. 225-233, 2002.

HÜNEMEIER, T.; CARVALHO, C.; MARRERO, R. A.; SALZANO, F. M.; JUNHO PENA, S. D.; BORTOLINE, M. C. Niger-Congo speaking populations and the formation of the Brazilian gene pool: mtDNA and Y-chromosome data. **American Journal of Physical Anthropology**, v. 29, n. 3, p. 203-206, 2007.

LEONELIL, G. G.; IMPERIAL, R. E.; MARCHI-SALVADOR, D. P. Hemoglobinas anormais dificuldade diagnóstica. **Revista Brasileira de Hematologia e Hemoterapia**, v. 22, n. 3, p. 396-403, 2000.

LERMEN, L. Talassemia beta minor: estudo de caso e revisão da literatura. **Estudos de Biologia**, v. 29, n. 68/69, p. 329-334, 2007.

MELO-REIS, P. R.; ARAÚJO, L. M. M.; DIAS-PENA, K. G. B.; MESQUITA, M. M.; CASTRO, F. S.; COSTA, S. H. N. A importância do diagnóstico precoce na prevenção das anemias hereditárias. **Revista Brasileira de Hematologia e Hemoterapia**, v. 28, n. 2, p. 149-52, 2006.

NAOUM, P. C. **Hemoglobinopatias e talassemias**. São Paulo: Sarvier, 1997.

NAOUM, P. C. **Eletroforese, técnicas e diagnósticos**. 2. ed. São Paulo: Editora Santos; 1999.

NAOUM, P. C. Interferentes eritrocitários e ambientais na anemia falciforme. **Revista Brasileira de Hematologia e Hemoterapia**, v. 22, n. 1, p. 5-22, 2000.

NAOUM, P. C.; BONINI-DOMINGOS, C. R. Dificuldades no diagnóstico laboratorial das hemoglobinopatias. **Revista Brasileira de Hematologia e Hemoterapia**, v. 29, n. 3, p. 226-8, 2007.

REIS, P. R. M.; PENNA, K. G. B. D.; ARAÚJO, L. M. M.; MESQUITA, M. M.; CASTRO, F. S.; BALESTRA, F. A. Prevalência de hemoglobinopatias e talassemias em crianças de 6 meses a 7 anos de idade no laboratório escola do Departamento de Biomedicina (CBB)-UCG. **Revista Brasileira de Análises Clínicas**, v. 37, n. 1, p. 3-5, 2005.

SAKAMOTO, T. M.; PERUZZO, G. M.; IVO, M. L.; BRUM, M. A. R.; BONINI-DOMINGOS, C. R. Talassemia β intermediária em gestante. **Revista Brasileira de Hematologia e Hemoterapia**, v. 30, n. 6, p. 498-500, 2008.

SANTOS, R. A. **Território Negro**: lentes e olhares sobre comunidades remanescentes de quilombos em Sergipe. Sergipe: Celacute, 2006.

SIQUEIRA, B. R.; ZANOTTI, L. C.; NOGUEIRA, A.; MAIA, A. C. S. Incidência de anemia falciforme, traço falcêmico e perfil hemoglobínico dos casos diagnosticado na triagem neonatal no estado de Rondônia no ano de 2003. **Saber Científico**, v. 2, n. 1, p. 43-53, 2009.

STEINBERG, M. H.; EMBURY, J. Alpha thalassemia in blacks: genetic and clinical aspects and interactions with sickle hemoglobin gene. **Blood**, v. 68, n. 5, p. 985-990, 1986.

TOME-ALVES, R.; MARCHI-SALVADOR, D. P.; ORLANDO, G. M.; PALHARINI, L.A.; IMPERIAL, R. E.; NAOUM, P. C.; BONINI-DOMINGOS, C. R. Hemoglobinas AS thalassemia alfa: Importância Diagnóstica. **Revista Brasileira de Hematologia e Hemoterapia**, v. 22, n. 3, p. 388-394, 2000.

VIVAS, W. L. P.; REBOUÇAS, D. S.; FABBRO, A. L. D.; CIPOLOTTI, R. Heterozigose para hemoglobinopatias em doadores de sangue do Centro de Hemoterapia de Sergipe. **Revista Brasileira de Hematologia e Hemoterapia**, v. 28, n. 4, p. 284-287, 2006.

WEATHERALL, D. J. The thalassemias. **British Medical Journal**, v. 314, n. 7095, p. 1675-1678, 1997.

WEATHERALL, D. J. Phenotype-genotype relationships in monogenic disease: lessons from the Thalassemias. **Nature Reviews Genetics**, v. 2, n. 4, p. 245-255, 2001.

ZAGO, M. A. Considerações gerais. In: ANVISA-Agência Nacional de Vigilância Sanitária. **Manual de Diagnóstico e Tratamento de Doenças Falciformes**. Brasília: Anvisa, 2002. p. 7-12.

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