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Total de artigos publicados em 2024: 17

DOENÇAS TRANSMISSÍVEIS POR TRANSFUSÃO E TRANSPLANTE (4 artigos)

1- Transfusion Medicine, 34(1): 46-53, 2024.

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Prevalence, incidence, risk factors and residual risk associated with viral infections among eligible Brazilian blood donors

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Knowledge regarding the profile of eligible blood donors presenting positive results in laboratory screening is essential for reducing transfusion-transmitted human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV). Our study aimed to evaluate the prevalence, incidence, predictor variables and residual risk (RR) of HIV/HBV/HCV in blood bags donated in Minas Gerais, Brazil. This study analysed data retrieved from the records of a large blood bank relating to donations collected at multiple centres within the period 2012-2018, during which 1 991 120 blood bags were screened using immunoassays and nucleic acid tests (NATs). Multilevel modelling was used to investigate the association between sex, civil status and age group with HIV/HBV/HCV. RR was estimated from the incidence values (restricted to negative and positive tests within the study period) and window periods for infections. The prevalence in first time donors, incidence and RR of HCV (223.73 cases per 100 000; 54.84 per 100 000 persons-year and 1.6527 per 100 000, respectively) were higher than those of HIV (172.65 cases per 100 000; 28.25 per 100 000 persons-year and 0.8514 per 100 000) and HBV (168.17 cases per 100 000; 18.54 per 100 000 persons-year and 0.5588 per 100 000). The odds of acquiring infection were greater in male, single and older donors. Sixteen donors were identified as seronegative and NATs+ during the 7-year span of the study. Our study has clarified some spatiotemporal trends regarding

HIV/HBV/HCV infections in donated blood in Brazil. The results will contribute to the formulation of directives addressed to high-risk donors.

2- Vox Sanguinis, 119: 257–264, 2024.

https://doi.org/10.1111/vox.13577

The importance of confirmatory assays in testing blood donors for human T-cell lymphotropic virus

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Background and objectives: Serological HTLV-1/2 screening is mandatory for blood donor candidates in Brazil. Our objective was to analyse HTLV test results in blood donors submitted for screening and confirmatory assays in a Brazilian blood bank.

Materials and methods: Retrospective analysis (2017-2022) results of chemiluminescence immunoassays and confirmatory tests for HTLV-1/2 in reactive donors were performed. During the analysed period, three sets of assays were used: (1) Architect rHTLV-I/II + HTLV Blot 2.4 (Western blot [WB]); (2) Alinity s HTLV I/II Reagent Kit + INNO-line immunoassay (LIA) HTLV I/II Score (LIA); (3) Alinity + WB.

Results: The analysed period comprised a total of 1,557,333 donations. The mean percentage of HTLV reactive donors using the Architect assay was 0.14%. With the change to the Alinity assay, that percentage dropped 2.3-fold (0.06%). The reactivity rate in the confirmatory tests (1064 samples) ranged from 13.5% to 30.2%, whereas 58.3%-85.9% of samples were non-reactive. The highest rates of positive (30.2%) and indeterminate (11.5%) results were seen using LIA. Considering all analysed samples, those with signal/cut-off ratio (S/CO) >50 were positive in confirmatory tests (positive predictive value, PPV = 100%), whereas samples with S/CO ≤6 are very unlikely to be truly positive (PPV = 0).

Conclusion: The use of the Alinity assay reduced the frequency of false-positive results. Confirmatory tests are important to identify true HTLV infection in blood donors, because more than 58% of initially reactive individuals are confirmed as seronegative. Categorizing S/CO values is useful for assessing the likelihood of true HTLV-1/2 infection.

3- AIDS Research and Human Retroviruses, 40(6): 401-407, 2024.

https://doi.org/10.1089/AID.2023.0072

High Ratio of Human T-Cell Lymphotropic Virus Transmission and Prevalence of Human T-Cell Lymphotropic Virus Type 1-Associated Diseases in Brazilian Family Groups Followed up by the GIPH Cohort

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A silent spread of human T-cell lymphotropic virus type 1 (HTLV-1) has been occurring for thousands of years, with a high prevalence in some regions due to the sexual and vertical transmission and formation of family clusters. The time from HTLV-1 infection until the onset of virus-associated diseases is extremely long, approximately one to three decades. In this study, we evaluated intrafamilial HTLV-1 transmission and associated diseases in 1,204 individuals enrolled and followed up by the GIPH cohort between 1997 and 2017. The family groups (n = 43) were composed of 279 individuals who were tested for HTLV-1/human T-cell lymphotropic virus type 2 (HTLV-2) and were classified as two groups according to the index case: blood donor (blood donors referred to the GIPH cohort) and nondonor (individuals referred to the GIPH cohort by other health services). The observed rates of HTLV-1 transmission and associated diseases among the relatives were high. Of 236 family members and sexual partners tested for human T-cell lymphotropic virus (HTLV), 104 (44.1%) were confirmed as having HTLV infection, with 36.7% of relatives whose index case was blood donors and 56.9% of relatives with nondonor index cases. At least one case of HTLV-1-associated myelopathy was observed in 42.9% of the families with intrafamilial transmission of HTLV-1. Brazil is an endemic area for HTLV-1/2 and has implemented mandatory universal screening of blood donors for HTLV-1/2 since 1993. However the lack of public health services offer diagnosis for HTLV to the general population and pregnant women in the country makes it difficult to identify infected people, and contributes to the silent spread of the virus.

4- Brazilian Journal of Infectious Disease, 28(6):104480, 2024. Nov 14

https://doi.org/10.1016/j.bjid.2024.104480

Perceived levels of social stigma following HIV notification: Insights from Brazilian blood centers

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Background: HIV/AIDS remains a highly stigmatizing disease worldwide, preventing people with risk or infection from testing to learn their HIV status, accessing supportive services, or taking antiretroviral therapy. Despite many studies of HIV in blood donors, no studies have evaluated the factors that contribute to stigma surrounding this illness following notification process and counseling provided by blood centers.

Methods: A cross-sectional questionnaire-based survey was conducted between 2016 and 2017. Persons with HIV were invited to return to the blood center for an audio computer-assisted interview after participation in an HIV risk factor assessment study conducted from 2007 to 2016. The questionnaire was based on HIV risk interviews developed by the US CDC, with modifications appropriate to the Brazilian setting which aimed to evaluate their follow-up activities, perceptions of HIV stigma and discrimination, and the quality of counseling and notification after the donation that tested positive for HIV. Response frequencies and adjusted odds ratios from multivariable logistic regression analyses are reported.

Results: 268 HIV-positive blood donors agreed to participate in the study. Almost all participants, 262 (97 %), rated as very important or important the blood center counseling experience in their decision to seek health care. One-hundred-five (39 %) participants reported none to low levels of stigma, and 163 (61 %) participants moderate stigma. Individuals reporting heterosexual orientation (OR=2.13, 95 % CI [1.08–4.22]) and healthcare-seeking behavior (OR=2.46, 95 % CI [1.10–5.48]) had significantly increased odds of reporting moderate levels of stigma.

Conclusions: Our study provides information about perceived stigma and discrimination in the Brazilian blood donor population and reinforces the importance of the counseling process in linkage to care and reducing HIV-related stigma.

HEMOGLOBINOPATIAS (5 artigos)

1- Brazilian Journal of Medical and Biology Research, 57: e12879, 2024. Jan 22.

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CETP gene polymorphisms and haplotypes are explanatory variables for HDL cholesterol level in sickle cell disease

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Variations in lipid profile have been observed in sickle cell disease (SCD) and understanding their relationship with disease severity is crucial. This study aimed to investigate the association of polymorphisms of the CETP gene and laboratory markers of disease severity with lipid profile in a pediatric population with SCD. Biochemical and anthropometric analyses and CETP and alpha-thalassemia genotyping were performed. The study included 133 children and adolescents with sickle cell anemia (SCA) or hemoglobin SC disease (SCC), in steady-state. The SCA and no hydroxyurea (no HU) groups had higher values of ApoB, total cholesterol, low-density lipoprotein cholesterol (LDL-C), and non-high-density lipoprotein cholesterol (non-HDL-C) compared to the SCC and HU groups. However, there were no significant differences in ApoA1 and HDL-C levels between the groups based on genotype. Furthermore, the groups with altered levels of ApoA1, HDL-C, and the triglyceride/HDL ratio exhibited lower hemoglobin (Hb)

levels and higher white blood cell counts. Hb level was associated to HDL-C levels. Analysis of CETP gene variants showed that the minor alleles of rs3764261 (C>A), rs247616 (C>T), and rs183130 (C>T), as well as the TTA haplotype, are explanatory variables for HDL-C levels. These findings suggested that dyslipidemia in SCD, specifically related to HDL-C levels, may be influenced by individual genetic background. Additionally, further investigation is needed to determine if clinical manifestations are impacted by CETP gene variants.

2- Hematology, Transfusion and Cell Therapy, 46(1): 67-71, 2024.

https://doi.org/10.1016/j.htct.2024.01.001

Consensus of the Brazilian Association of Hematology, Hemotherapy and Cellular Therapy (ABHH) and the Brazilian Ministry of Health - General management of blood and blood products on the tests necessary for the release of exceptional medicines for sickle cell disease

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To date, hydroxyurea is the only effective and safe drug that significantly reduces morbidity and mortality of individuals with Sickle cell disease. Twenty years of real-life experience has demonstrated that hydroxyurea reduces pain attacks, vaso-occlusive events, including acute chest syndrome, the number and duration of hospitalizations and the need for transfusion. The therapeutic success of hydroxyurea is directly linked to access to the drug, the dose used and adherence to treatment which, in part, is correlated to the availability of hydroxyurea. This consensus aims to reduce the number of mandatory exams needed to access the drug, prioritizing the requesting physician's report, without affecting patient safety.

3- Molecular Genetics and Metabolism Report, 39: 101086, 2024.

https://doi.org/10.1016/j.ymgmr.2024.101086

Association of ZBTB38 gene polymorphism (rs724016) with height and fetal hemoglobin in individuals with sickle cell anemia

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Objectives: Our study evaluated the association of the polymorphism rs724016 in the ZBTB38 gene, previously associated with height in other populations, with predictors of height, clinical outcomes, and laboratory parameters in sickle cell anemia (SCA).

Methods: Cross-sectional study with individuals with SCA and aged between 3 and 20 years. Clinical, laboratory, molecular, and bone age (BA) data were evaluated. Levels of IGF-1 and IGFBP-3 were adjusted for BA, target height (TH) was calculated as the mean

parental height standard deviation score (SDS), and predicted adult height (PAH) SDS was calculated using BA.

Results: We evaluated 80 individuals with SCA. The homozygous genotype of the G allele of rs724016 was associated with a lower height SDS ($p < 0.001$) and, in a additive genetic model, was negatively associated with HbF levels ($p = 0.016$). Lower adjusted IGF-1 levels were associated with co-inheritance of alpha-thalassemia and with the absence of HU therapy. Elevated HbF levels were associated with a lower deficit in adjusted growth potential (TH minus PAH).

Conclusion: Our analysis shows that SNP rs724016 in the ZBTB38 is associated with shorter height and lower HbF levels, an important modifier of SCA.

4- British Journal of Haematology, 205(5): 1974-1984, 2024.

https://doi.org/10.1111/bjh.19758

Genetic variants associated with white blood cell count amongst individuals with sickle cell disease

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Background: Sickle cell disease (SCD) is a Mendelian disorder characterized by a point mutation in the β-globin gene that leads to sickling of erythrocytes. Several studies have shown that absolute neutrophil count is strongly associated with clinical severity of SCD, suggesting an apparent role of white blood cells (WBC) in SCD pathology. However, the mechanism by which genetic variants lead to WBC count differences in SCD patients remains unclear.

Methods: Genome-wide association (GWA) analyses were carried out amongst a cohort of 2409 Brazil SCD participants. Association of WBC count and genetic markers were

investigated in homozygous sickle cell anaemia participants and compound heterozygous sickle cell haemoglobin C participants.

Results: GWA analysis showed that variants in genes TERT, ACKR1, and FAM3C are associated with WBC count variation. The well-studied association between WBC count and Duffy null phenotype (variant in ACKR1) in healthy populations was replicated, reinforcing the influence of the SNP rs2814778 (T>C) in WBC count.

Conclusion: Genetics plays an important role in regulating WBC count in patients with SCD. Our results point to possible mechanisms involved in WBC count variation and as increased WBC count is associated with more severe SCD, these results could suggest potential therapeutic targets for individuals with SCD.

5- Blood Advances, 8(2): 365-368, 2024.

https://doi.org/10.1182/bloodadvances.2023011765

Natural history of albuminuria in a large cohort of children and adolescents with sickle cell anemia from Brazil

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No abstract available

COAGULOPATIAS (6 artigos)

1- Pediatric Hematology and Oncology, 41(1): 74-80, 2024.

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Changing recombinant factor VIII to plasma-derived factor VIII during immune tolerance induction

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No abstract available

2- Journal of Thrombosis and Haemostasis, 22(9): 2426-2437, 2024.

https://doi.org/10.1016/j.jtha.2024.05.017

Prediction of inhibitor development in previously untreated and minimally treated children with severe and moderately-severe hemophilia A using a machine-learning network

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Background: Prediction of inhibitor development in patients with hemophilia A (HA) remains a challenge.

Aim: To construct a predictive model for inhibitor development in HA using a network of clinical variables and biomarkers based on the individual similarity network.

Methods: Previously untreated and minimally treated children with severe/moderately-severe HA, participants of the HEMFIL Cohort Study, were followed-up until reaching 75 exposure days (ED) without inhibitor (INH-) or upon inhibitor development (INH+). Clinical data and biological samples were collected before the start of factor VIII (FVIII) replacement (T0). A predictive model (HemfilNET) was built to compare the networks and potential global topological differences between INH- and INH+ at T0, considering the network robustness. For validation, the "leave-one-out" cross-validation technique was employed. Accuracy, precision, recall, and F1-score were used as evaluation metrics for the machine-learning model.

Results: We included 95 children with HA (CHA), of whom 31 (33%) developed inhibitors. The algorithm, featuring 37 variables, identified distinct patterns of networks at T0 for INH+ and INH-. The accuracy of the model was 74.2% for CHA INH+ and 98.4% for INH-. By focusing the analysis on CHA with high-risk F8 mutations for inhibitor development, the accuracy in identifying CHA INH+ increased to 82.1%.

Conclusion: Our machine-learning algorithm demonstrated an overall accuracy of 90.5% for predicting inhibitor development in CHA, which further improved when restricting the analysis to CHA with a high-risk F8 genotype. However, our model requires validation in other cohorts. Yet, missing data for some variables hindered more precise predictions.

3- Research and Practice in Thrombosis and Haemostasis, 8(4): 102427, 2024.

https://doi.org/10.1016/j.rpth.2024.102427

Hypocoagulability in severe yellow fever infection is associated with bleeding: results from a cohort study

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Background: Severe yellow fever infection (YFI) may be complicated by a hemorrhagic diathesis. However, the hemostasis profile of YFI has rarely been reported.

Objectives: The aim of this study was to characterize the hemostatic features of YFI by using a rotational thromboelastometry (ROTEM).

Methods: We evaluated clinical, laboratory, and ROTEM parameters in adults with severe YFI and their correlation with hemostatic variables according to bleeding and death.

Results: A total of 35 patients were included (median age, 49 years). ROTEM was performed in 22 patients, of whom 21 (96%) presented bleeding and 4 (18%) died. All patients who died had major bleeding. Patients who died presented prolonged clotting time (CT; median, 2326 seconds; IQR, 1898-2986 seconds) and reduced alpha angle (median, 12°; IQR, 12°-15°) in comparison with patients who had minor (median CT, 644 seconds; IQR, 552-845 seconds and alpha angle, 47°; IQR, 28°-65°) and major (median CT, 719 seconds; IQR, 368-1114 seconds and alpha angle, 43°; IQR, 32°-64°) bleeding who survived. In patients who had bleeding, CT showed a strong negative correlation with factor (F)V (r = -.68), FIX (r = -.84), and FX (r = -.63) as well as alpha angle showed a strong negative correlation with FIX (r = -.92). In patients who died, the correlations were even stronger. A total of 19/21 (90%) patients presented hypocoagulability assessed by ROTEM.

Conclusion: Hypocoagulabitity is the hallmark of the bleeding diathesis of severe YFI. Abnormal CT and alpha angle associated with death and could be used as potential predictors of adverse outcome in severe YFI.

4- Research and Practice in Thrombosis and Haemostasis, 8(4): 102436, 2024.

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High levels of anti-factor VIII immunoglobulin G4 and immunoglobulin G total are associated with immune tolerance induction failure in people with congenital hemophilia A and high-responding inhibitors

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Background: Immune tolerance induction (ITI) is the treatment of choice to eradicate neutralizing anti-factor (F)VIII alloantibodies (inhibitors) in people with inherited hemophilia A. However, it is not successful in 10% to 40% of the cases. The biological mechanisms and biomarkers associated with ITI outcome are largely unknown.

Objectives: The aim of this study was to investigate the association of plasma cytokines (interferon-γ, tumor necrosis factor, interleukin [IL]-2, IL-4, IL-5, IL-6, IL-10, and IL-17A), chemokines (IL-8/CXCL8, RANTES/CCL5, MIG/CXCL9, MCP-1/CCL2, and IP-10/CXCL10), and anti-FVIII immunoglobulin (Ig) G total, IgG1, and IgG4 with ITI outcome.

Methods: In this cross-sectional analysis of the Brazilian Immune Tolerance Study, we assessed plasma levels of anti-FVIII IgGs using an enzyme-linked immunosorbent assay with plasma-derived FVIII and recombinant FVIII as target antigens, immobilized in microplates.

Results: We assayed 98 plasma samples of moderately severe and severe (FVIII activity, <2%) people with hemophilia A after completion of a first ITI course. Levels of anti-recombinant FVIII IgG total and IgG4 were higher in people with hemophilia A who failed ITI (IgG total optical density [OD], 0.37; IQR, 0.15-0.73; IgG4 OD, 2.19; IQR, 0.80-2.52) than in those who had partial (IgG total OD, 0.03; IQR, 0.00-0.14; IgG4 OD, 0.39; IQR, 0.09-1.11; $P < .0001$ for both) or complete success (IgG total OD, 0.04; IQR, 0.00-0.07; IgG4 OD, 0.07; IQR, 0.06-0.40; $P < .0001$ for both). Plasma cytokines, chemokines, and anti-FVIII IgG1 were not associated with ITI outcome.

Conclusion: Our results show that high levels of plasma anti-FVIII IgG4 and IgG total are associated with ITI failure.

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Large deletions and small insertions and deletions in the factor VIII gene predict unfavorable immune tolerance induction outcome in people with severe hemophilia A and high-responding inhibitors

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Introduction: Hemophilia A is an inherited bleeding disorder caused by pathogenic variants in the factor VIII gene (F8), which leads to factor VIII (FVIII) deficiency. Immune tolerance induction (ITI) is a therapeutic approach to eradicate alloantibodies

(inhibitors) against exogenous FVIII in people with inherited hemophilia A. Few studies have evaluated the role of F8 variants on ITI outcome.

Material and methods: We included people with severe hemophilia A (FVIII < 1 international units/dL) and high-responding inhibitors (≥ 5 Bethesda units/mL lifelong) who underwent a first course of ITI. Socio-demographic, clinical and laboratory data were collected. ITI outcomes were defined as total, partial successes, and failure. Detection of intron 1 and 22 inversions was performed by polymerase-chain reaction, followed by F8 sequencing.

Results: We included 168 people with inherited hemophilia A and high-responding inhibitors, median age 6 years at ITI start. Intron 22 inversion was the most prevalent variant (53.6 %), followed by nonsense (16.1 %), small insertion/deletion (11.3 %), and large deletion (10.7 %). In comparison with intron 22 inversion, the odds of ITI failure were 15.5 times higher (odds ratio [OR] 15.50; 95 % confidence interval [95 % CI] 4.59-71.30) and 4.25 times higher (95 % CI, 1.53-12.3) among carriers of F8 large deletions and small insertions and deletions, respectively.

Conclusion: F8 large deletions and small insertions/deletions predicted ITI failure after a first course of ITI in patients with severe hemophilia A and high-responding inhibitors. This is the first study to show F8 large deletions and small insertions/deletions as predictors of ITI failure.

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HLA variants and inhibitor development in hemophilia A: results from the HEMFIL study group

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Evaluation of blood cell count using an automatic hematology analyzer to optimize collection of peripheral blood progenitor cells by leukapheresis

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Background: Autologous stem cell transplantation is a treatment modality for several diseases. Prediction of successful mobilization may be useful to optimize hematopoietic stem cell collection.

Study design and methods: This was a retrospective study with data from transplantation candidates between September 2015 and December 2021 being analyzed. The medical record of each patient was reviewed to mine mobilization information. The laboratory data analyzed were CD34+ cell enumeration and pre-collection peripheral blood cell count. The primary outcome, good mobilization, was defined as a CD34+ cell count ≥20/μL.

Results: This study included 807 patients. Increased patient weight, low mean corpuscular volume, high nucleated red blood cells, peripheral blood mononuclear cell and immature granulocyte counts were significantly associated with good mobilization. In addition, patients diagnosed with multiple myeloma were two times more likely to be good mobilizers than patients with lymphoma. The model was applied to a validation set to identify patients who underwent apheresis (CD34+ cell count ≥10 μL), resulting in a sensitivity of 69 %, a specificity of 95 %, positive predictive value of 98 %, and a negative predictive value of 50 %.

Conclusion: Success in mobilization was greater in patients who underwent the first mobilization cycle and who had a diagnosis of multiple myeloma. Furthermore, higher body weight, and nucleated red blood cells, immature granulocytes and mononuclear

cell counts, as well as low mean corpuscular volumes, were associated with successful mobilization.

LINHA DE PESQUISA: PSICOLOGIA E EDUCAÇÃO EM SAÚDE (1 artigo)

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Educational technologies for the self-care of children with sickle cell anemia: an integrative review

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Objective: To identify the educational technologies used to help children with sickle cell anemia in their self-care. Method: an integrative review carried out in six consecutive phases, between June and July 2023, with no time frame, in the following information resources: Public/published Medline, Virtual Health Library, Scientific Electronic Library Online, and Web of Science and Cumulative Index to Nursing and Allied Health Literature. Results: Five studies were found, of which the following stood out: a game, two electronic applications, a coloring book, and a guided image for pain relief. All the educational technologies reflect the child's better understanding of self-care. Conclusion: The selected studies allowed us to understand that educational technologies help children with sickle cell anemia to understand the disease and take actions that improve its signs and symptoms, favoring selfcare, but it is essential to create new educational technologies since most of the findings are old and do not match the current reality.