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1- BMC Public Health, 25(1): 60, 2025.

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Syphilis reactivity among blood donors in Brazil: associated factors and implications for public health monitoring

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Background: Increasing syphilis infection rates are a concerning issue worldwide. Blood donation screening is an opportunity to monitor the burden of asymptomatic infections, providing information on contemporary factors associated with infection and public health insights into transmission.

Methods: Blood donations collected at five Brazilian blood centers between January 2020 and February 2022 were screened with treponemal or non-treponemal assays according to local protocols, followed by alternate Enzyme-Linked Immunosorbent

Assay (ELISA); samples with reactive or indeterminate results in the alternate ELISA were further tested with the rapid plasma reagin (RPR), and categorized as RPR-positive or RPR-negative. RPR-positive donations were also grouped according to RPR titers (< 1:8 or ≥ 1:8). We report the prevalence of syphilis in first-time donors (FTD) and repeat donors (RD), as well as incidence in RD. Multivariable models were used to assess factors associated with RPR-positive syphilis. Additionally, we explored the relationship between syphilis positivity in FTD and syphilis cases registered by the Brazilian public health surveillance system from 2012 to 2022.

Findings: Of 862,146 donations, 10,771 (1.3%) were reactive or indeterminate on screening; 7,541 available samples underwent additional testing. Of those, 5,876 (77.9%) tested positive or indeterminate on the alternate ELISA; 907 (12.0%) were RPR-negative, 2,980 (39.5%) were RPR-positive < 1:8, and 1,989 (26.4%) were RPR-positive with titers ≥ 1:8. The prevalence of syphilis including RPR-positive and RPR-negative cases was 2.5% among FTD and 0.6% among RD. The incidence of syphilis in RD was $90/10^5$ person-years (95% CI 86-95), with younger age, male gender, Black and Mixed race (relative to White) and lower education associated with incident syphilis in RD. Blood donors had lower rates of syphilis compared to the general population, with correspondence between numbers in blood donors and congenital syphilis rates registered by the Brazilian surveillance system between 2012 and 2022.

Conclusion: The prevalence of syphilis was < 3% among FTD and < 1% among RD. We found wide variability according to donor characteristics, with gender, age, race, and schooling significantly associated with prevalent and incident RPR-positive syphilis in multivariable models. Syphilis occurrence among blood donors can be used to assess disease patterns in low-risk populations.

2- PLoS One, 20(2): e0315933, 2025.

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Syphilis seroprevalence and risk factors among first-time blood donors in Brazil: A comprehensive repeated cross-sectional analysis spanning a decade

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Background: Syphilis remains a global health challenge, with rising incidence rates worldwide. Prevalence surveys conducted in Brazil over extended periods of time are scarce. This study examines the secular trends and risk factors for syphilis seroprevalence among first-time blood donors in Brazil.

Methods: A retrospective analysis was conducted as part of a multicenter, repeated cross-sectional survey of blood donors from four major Brazilian blood centers, covering the period from 2007 to 2020. First-time donors who had undergone valid treponemal screening tests were included in the final dataset. Demographic characteristics and serological results were analyzed to identify risk factors for syphilis seroprevalence using multivariate Poisson models. An interaction term between age group and donation year was added to the final model. Model comparisons were performed using Likelihood Ratio Tests (LRT) and Akaike Information Criterion (AIC).

Results: 1,424,850 donations from first-time donors were included during the study period. The overall syphilis seroprevalence was 2.19%, with significant heterogeneity across centers. Risk factors for increased seroprevalence included male gender, older age, lower education level, and self-reported black or mixed skin color. Notably, an increasing trend in syphilis seroprevalence was observed among younger donors and those born after 1990. Interaction analyses revealed significant effects between visit period and key demographic variables (age group, gender, education, and ethnicity), with the interaction between age group and donation year indicating higher seroprevalence among younger age groups in recent years.

Conclusion: The study highlights a high syphilis seroprevalence among first-time blood donors in Brazil, which has significant implications for blood safety and public health. The increasing trend among younger donors suggests a shift towards newer infections, warranting continued surveillance in this demographic.

3- Transfusion, 65(4): 685-695, 2025.

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Assessing HIV trends among blood donors in five Brazilian blood centers: The impact of individual donor assessment

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Background: In many countries, including Brazil, time-based blood donation deferral policies for gay, bisexual, and other men who have sex with men (gbMSM) have been replaced by individual donor assessment (IDA). We examined HIV prevalence and incidence among first-time (FTD) and repeat donors (RD), comparing data from ~3.5 years before and after the IDA policy implementation in 2020.

Study design and methods: The Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric (REDS-IV-P) Brazil component collects blood donor screening data from five public centers. From January 2017 to December 2023, we report frequencies, rates, and 95% confidence interval (CI) of confirmed HIV-positive donations among FTD, HIV NAT-yield rates for FTD and RD, and the incidence of confirmed HIV among RD before and after the policy change. We also report multivariable regression analysis results.

Results: Confirmed HIV prevalence in FTD was 79 per 100,000 (95% CI 72-87) before and 100 per 100,000 (95% CI 90-109) after the policy change, with differences between centers. HIV NAT-yield rates decreased for RD (p = .0025), with no change for FTD (p = .3). HIV incidence in RD did not increase (12.4 [95% CI: 11.1-13.9] vs. 10.3 [95% CI: 9-11.7] per 100,000 person-years).

Discussion: Our findings showed no significant difference in HIV incidence among RD. Although HIV prevalence among FTD increased, there was no rise in HIV NAT-yield donations. The analysis highlights challenges in interpreting changes within specific groups and blood centers, underscoring the importance of multicenter monitoring of transfusion-transmitted infections.

4- Journal of Virology Methods, 336: 115170, 2025.

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Strictly screening of HTLV-1/2 peptides can drive the development of rapid point-of-care tests

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The Human T-cell lymphotropic virus (HTLV-1/2) cause neglected infections that drives life-threatening diseases and the numbers of infected people around the world are underestimated. Point-of-care tests (POCT) are useful to identifying carriers, to controlling the infection's spread with timely and cost-effectiveness, to include the most affected areas and susceptible populations, and the establishment of public health policies, including the control of vertical transmission. After in silico analysis of Env, Gag and Tax proteins of HTLV-1 and HTLV-2, we synthetized and characterized peptides to screening antibodies anti-HTLV-1/2 with high sensitivity and specificity. The 173 peptides chosen were screened by immunoblot, and by indirect in-house ELISA. Peptides that had best performed in recognize both, HTLV-1 or HTLV-2 sera from infected individual, were Gag-HTLV-1 and Gag-HTLV-2 showing to be very good candidates for screening tests. Peptides of Tax-HTLV-1, and Env-HTLV-2 had discriminated sera from HTLV-1 and HTLV-2 with high sensitivity and specificity. The screening of HTLV-1/2 peptides showed here, including the use of sera from HIV-infected individuals along with seronegative ones were crucial to avoid the use of peptides with unspecific reaction in the final pilot tests, and to reach the Point-of-care test that is under registration at regulatory Brazilian agency.

5- Hematology, Transfusion and Cell Therapy, 47(3): 103863, 2025

https://doi.org/10.1016/j.htct.2025.103863

Risk factors associated with HIV infection in four large Brazilian blood centers: A multicentric case-control study (2009-2017)

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Background: Strategies to reduce contamination by transfusion-transmissible infections are constantly evolving. Over the years, HIV residual risk has decreased in several countries. However, in Brazil a recent study showed that the residual risk remains substantially higher than in other countries. Continuous surveillance of risk behaviors for infection in donors can help in pre-donation screening to reduce the risk of HIV in blood transfusions.

Methods: This analysis evaluated risk factors related to HIV infection among blood donors from four large Brazilian blood centers located in São Paulo, Rio de Janeiro, Belo Horizonte and Recife, from 2009-2017. A binary logistic model was used to evaluate any association between risk characteristics and behaviors and the occurrence of HIV. The significant variables were included in a saturated model, to which the backward strategy was applied to arrive at the final model. The analyses were carried out using the R program version 4.1.2 and p-value <0.05 was considered significant.

Results: A total of 1507 blood donors were included in the study, 716 were HIV positive and 791 were uninfected controls. Demographics significantly associated with infection were: Male sex, incomplete secondary education, separated/divorced/widowed, and bisexual/homosexual orientation. Behaviors most strongly associated with infection were: workplace exposure, intravenous drugs and men who had sex with other men.

Conclusion: The risk factors identified suggest that the blood donor screening process in Brazilian blood centers does not adequately identify donors at increased risk for HIV and further studies should be carried out to support changes to improve the process.

6- PLoS Negleted Tropical Disease, 19(12):e0013770, 2025.

https://doi.org/10.1371/journal.pntd.0013770

FC-duplex IgG1 (HTLV-1/2): Qualifying the flow cytometry IgG1 duplex assay for differential diagnosis of HTLV-1 and HTLV-2 infections

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Human T-lymphotropic virus (HTLV) infection has been implicated in a broad spectrum of clinical conditions, encompassing both neoplastic and inflammatory-degenerative disorders, associated with relevant immunological dysfunctions. Given the distinct epidemiological profiles and clinical manifestations associated with HTLV-1 and HTLV-2 infections, establishing an accurate differential diagnosis is of critical importance. The serological/molecular approaches currently available for differential diagnosis are expensive, time-consuming, and require multiple complementary assays, and still lead to inconclusive results. In this context, the development of a single-platform assay referred to as FC-Duplex IgG1 (HTLV-1/2) assay represented a valuable advance for the differential diagnosis of HTLV infections in clinical settings, while counseling HTLV-seropositive patients and/or conducting seroepidemiological surveys. The present study aimed at qualifying the FC-Duplex IgG1 (HTLV-1/2) kit prototype for differential serodiagnosis of HTLV-1 and HTLV-2 infections. A biorepository library, composed of serum samples from four HTLV reference centers (HTLV-1(+)/n = 225; HTLV-2(+)/n = 80 and HTLV1/2(-)/n = 55), was tested for anti-HTLV-1 and anti-HTLV-2 IgG1 reactivity using three classification criteria. Discriminant performance analysis supported the high accuracy of FC-Duplex IgG1 (HTLV-1/2) with elevated proportion of correct classification according to PCR & Western Blot reference standards (Criterion 3 = 89%; Criterion 2 = 90% and Criterion 1 = 99%). Decision tree accuracy and Leave One Out Cross-Validation re-enforced the robustness, confirming the minimal overfitting of our findings. Kappa agreement indices further confirmed the substantial to near perfect agreement of FC-Duplex IgG1 (HTLV-1/2) with reference standard methods (Criterion 3 = 0.72; Criterion 2 =

0.75 and Criterion 1 = 0.97). Altogether, these findings qualified the FC-Duplex IgG1 (HTLV-1/2) assay for differential diagnosis of HTLV-1/2 infections.

7- Vox Sanguinis, 2025 Dec 17.

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Dengue, chikungunya and Zika virus surveillance in blood donors in Brazil, 2019-2021

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Background and objectives: Arbovirus infections are a major public health concern in Brazil and an ongoing blood safety concern. Periodic outbreaks of such infections are common in the general population. This study aimed to establish the rates of dengue, chikungunya and Zika virus (DENV, CHIKV, ZIKV) RNAemia among blood donors at six public blood centres during the 2019-2020 and 2020-2021 outbreak seasons.

Materials and methods: Residual minipool samples from nucleic acid testing (NAT) screening for human immunodeficiency virus, hepatitis B virus and hepatitis C virus were further pooled to form pools of 18 donation samples and tested using a Grifols research-use-only triplex transcription-mediated amplification assay for DENV, CHIKV and ZIKV RNA to establish the rates of RNAemia and infection incidence. We used these rates and estimated the durations of RNAemia, juxtaposed with public health reporting of cases.

Results: A total of 5,616 minipools representing 101,088 donations were tested. During both outbreak seasons, the highest rates of DENV RNAemia were observed in Ribeirão Preto, at 122/100,000 donations (95% confidence interval [CI]: 66-224) and 100/100,000 (95% CI: 52-189), respectively, with DENV RNAemia also detected in São Paulo, Recife and Manaus in the 2019/2020 season and in the latter two during the 2020/2021 season. CHIKV RNAemia was detected in Recife and ZIKV RNAemia in Manaus during the 2020/2021 season. The estimated numbers of DENV, CHIKV and ZIKV RNAemic components released for transfusion over the study period were 338, 22 and 6, respectively.

Conclusion: Surveillance for arbovirus RNAemia in blood donors is a useful adjunct to public health surveillance, particularly when surveillance systems are under strain, and has implications for transfusion safety.

TRANSPLANTES, ENXERTOS E TERAPIA CELULAR (2 artigos)

1- HLA, 105(2): e70051, 2025.

https://doi.org/10.1111/tan.70051

Common, Intermediate and Well-Documented HLA Alleles in the Brazilian Population: An Analysis of the Brazilian Bone Marrow Donor Registry (REDOME)

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This study investigates the HLA allele diversity in Brazil, a reflection of the country's unique history of population admixture. The international comparison of findings emphasises the importance of incorporating underrepresented populations into global HLA databases. We present a comprehensive analysis of HLA alleles within the Brazilian population, utilising high-resolution sequencing data from 298,000 unrelated haematopoietic stem cell volunteer donors registered with the Brazilian Bone Marrow Donor Registry (REDOME). Our research encompasses donors from all regions of Brazil, identifying HLA alleles that are catalogued as common, intermediate or well-documented (CIWD Version 3.0). We evaluated the alleles of HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DQA1, HLA-DQB1, HLA-DPA1 and HLA-DPB1. At a two-field resolution, we identified 1969 alleles: 418 were classified as common, 358 as intermediate and

1193 as non-CIWD in Brazil. Notably, we report HLA alleles that, while not classified as common or intermediate in the CIWD 3.0 catalogue, are prevalent within the Brazilian population. A detailed list of alleles from the registry, presented at a two-field resolution and supplemented with grouped ARD levels, including three- or four-field resolution when available, serves as an essential reference for HLA typing frequencies specific to the Brazilian population.

2- Cell and Tissue Banking, 26(3): 31, 2025.

https://doi.org/10.1007/s10561-025-10181-4

10-years analysis of cryobag fracture in a large inventory of cellular therapy products: rates and risk factors

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Cryobags play a critical role in freezing, storing, and transporting cellular therapy products but are prone to fractures, which can disrupt patient outcomes and facility workflows. This study evaluated the incidence, risk factors, and impact of cryobag fractures in a large inventory of cellular therapy products in Brazil. A retrospective cohort study included 4514 cryobags from 2262 peripheral blood stem cell collections processed between 2015 and 2024 at a single center supporting nine transplant facilities. Cryobags were frozen at -80°C and stored in nitrogen tanks. Fractures and leaks were identified through routine visual inspections. Among the cryobags, 15 (0.3%) fractured, with 12 detected at processing facility and 3 after release. The fracture rate was 0.37 per 100 bag-years, with a cumulative incidence of 1% at 3.62 years. Of these, 8 were discarded, and 7 were salvaged and infused into six patients. Two salvaged cryobags underwent bedside recovery, while five were recovered aseptically in the processing facility. Positive bacterial cultures were commonly found in salvaged products. In multivariate analysis, a higher total nucleated cell count per cryobag remained an independent risk factor for fracture (OR=1.005; 95% CI: 1.0002-1.0099; p=0.046). Following implementation of quality improvement initiatives based on root cause analysis, no further fractures were observed. These findings highlight the importance of monitoring cell concentration and adjusting cryopreservation protocols to mitigate risks. Adding overwraps may provide additional protection for cryobags at higher risk, reducing the likelihood of microbial contamination and improving the safety and reliability of cellular therapy products.

HEMOGLOBINOPATIAS (6 artigos)

1- World Journal of Clinical Pediatrics, 14(1): 97537, 2025.

https://doi.org/10.5409/wjcp.v14.i1.97537

Importance of neonatal screening: A case study of sickle cell disease and cystic fibrosis coexistence

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Background: Neonatal screening (NS) is a public health policy to identify genetic pathologies such as cystic fibrosis (CF), sickle cell disease, and other diseases. Sickle cell disease is the comprehensive term for a group of hemoglobinopathies characterized by the presence of hemoglobin S. CF is an autosomal recessive multisystemic disease with pathophysiology involving deleterious mutations in the transmembrane regulatory gene that encodes a protein that regulates the activity of chloride and sodium channels in the cell surface epithelium. NS is crucial for early diagnosis and management, which ensures a better quality of life.

Aim: To report a case of the coexistence of sickle cell anemia (SCA) and CF and perform an integrative literature review.

Methods: This is an observational study and a review of the literature focusing on two rare genetic pathologies identified simultaneously in NS from the perspective of a clinical case. The authors identified only 5 cases of SCA associated with CF. No clinical trials or review articles were identified considering the rarity of the coexistence of these two pathologies.

Results: Herein, the authors reported the case of a girl who after undergoing NS on day 8 of life was diagnosed with SCA with an alteration in the dosage of immunoreactive trypsin. The diagnosis of CF was confirmed by the Coulometry Sweat Test. The rarity of the co-occurrence of these two severe genetic pathologies (CF and SCA) is a challenge for medical science.

Conclusion: This study adds to the few case reports present in the literature that highlight the identification of two severe diseases via NS.

2- Transfusion, 65(5): 992-1000, 2025.

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Clinics and genetics of hyperhemolysis syndrome in patients with sickle cell disease

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Background: Hyperhemolysis syndrome (HHS) is a severe transfusion-related complication with a complex immune pathophysiology, primarily affecting individuals with sickle cell disease (SCD). Limited research has investigated the clinical and molecular risk factors for HHS, which could help identify at-risk patients. This study aimed to assess clinical factors associated with HHS and identify genetic variations that increase susceptibility using a candidate-gene approach.

Methods: Data were obtained from the REDS-III SCD cohort, comprising 2793 patients who underwent whole-genome sequencing as part of the Trans-Omics for Precision Medicine (TOPMed) program. Clinical and laboratory data were retrospectively collected. Patients with HHS were compared to matched controls (1:4) based on clinical variables and the frequency of single nucleotide variations (SNVs) associated with HHS, autoimmunity, and red blood cell (RBC) alloimmunization.

Results: HHS was identified in 13 patients (prevalence: 1.13%), the majority of whom had the HbSS genotype (69.2%). The most affected age group was 11-20 years (46.2%), and 61.5% of patients had RBC alloantibodies. Pain crisis was the most common indication for transfusion leading to HHS (41.7%). Three significant genetic variants were identified: rs10748663 (C > T) on chromosome 10 (BLNK gene), rs936469 (G > A) on chromosome 11 (PHRF1 gene), and rs6503691 (C > T) on chromosome 17 (STAT5B gene).

Conclusion: HHS primarily affects adolescents and young adults with RBC alloantibodies, often following episodic transfusions. Genetic variations in STAT5B and the IRF7-PHRF1 region suggest that the B-cell receptor signaling pathway, which is essential for B-cell differentiation, may play a critical role in HHS pathophysiology.

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Mortality from sickle cell disease in Brazil

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Despite early diagnosis through neonatal screening and improved access to vaccines, antibiotics, and disease-modifying therapies, many individuals with sickle cell disease (SCD) die before age 60. This study evaluated causes and independent predictors of mortality in a Brazilian SCD population using data from the multicenter REDS-III cohort [2013-2018], which included six centers. Eligible patients were randomly enrolled during routine visits. Clinical and laboratory data were abstracted from medical records, and deaths were confirmed via chart review and linkage to the national death certificate database. Key variables were compared between deceased and surviving adults using Chi-square and Mann-Whitney tests. A multivariable Cox regression model identified independent predictors of mortality. Children were excluded from regression analysis due to low pediatric mortality. Among 2,793 participants, 1,558 (55.8%) were under 18. By the end of follow-up, 159 (5.7%) had died-142 adults and 17 children. Median life expectancy was 65.7 years. Infection was the leading cause of death (33.3%), followed by non-infectious pulmonary conditions (25.2%) and neurologic disease (14.5%). Cause of death was unknown in 3.1% of cases. In adults, independent predictors of mortality were older age [HR 1.03; 95% CI 1.01-1.04], iron overload [HR 1.68; 95% CI 1.09-2.60], and prior hospital admissions [HR 1.68; 95% CI 1.10-2.56]. The mortality burden in SCD is shifting toward adults, particularly in the third and fourth decades of life. Individuals with SCD in Brazil die about 10 years earlier than the general population. The main causes of death in our cohort were infections, acute chest syndrome and stroke, highlighting the need for prompt recognition and treatment of these complications. Screening and treatment for iron overload and closer monitoring and

consideration of disease modifying therapies for patients with frequent hospital admissions are important as both were identified as independent predictors of mortality.

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Genetic modifiers of frequent vaso-occlusive hospitalizations among individuals with sickle cell disease (SCD)

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Sickle cell disease (SCD) is characterized by painful vaso-occlusive crises (VOC), which occur due to the adhesion of sickled erythrocytes and leukocytes to the endothelium, leading to vascular obstruction and tissue ischemia. Recurrent VOC increases SCD morbidity, reduces quality of life, and results in frequent hospitalizations. While factors like HbF levels and alpha-thalassemia co-occurrence are known to influence the risk of VOC, the genetic basis of this phenotype remains underexplored. To address this, we conducted a Genome-Wide Association Study (GWAS) to identify genetic predictors of frequent VOC in SCD patients. The study focused on patients with the SS genotype, analyzing those who experienced three or more pain crisis hospitalizations annually. To account for population substructure, the top 10 principal components were included. The GWAS was performed using ENCORE and the Saige Logistic Mixed Model, adjusted for hydroxyurea treatment as a covariate, with a genome-wide significance threshold of 5×10^{-8}. The study included 125 cases and 1670 controls, revealing 9 significant SNPs. 8 were associated with the CTNNA2 gene (p-value = 7.77×10^{-9}), and 1 with METTL4 (p-value = 3.39×10^{-8}). These findings highlight the role of CTNNA2 and METTL4 in VOC hospitalizations, providing insights into the genetic underpinnings of SCD pain.

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Clinical, laboratory and genetic factors associated with smoking in a Brazilian Sickle Cell Disease (SCD) cohort

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Background: Smoking is associated with increased morbidity among individuals with sickle cell disease (SCD). While genetic factors influencing smoking behavior have been identified in other populations, they have not been studied in individuals with SCD. This study aimed to assess the impact of smoking on clinical and laboratory parameters in a large SCD cohort and to identify genetic variants potentially associated with smoking behavior in this population.

Methods: The Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) Brazil SCD cohort was established across six Brazilian cities to investigate clinical outcomes in individuals with SCD. Adult participants were interviewed and asked whether they had ever smoked more than 100 cigarettes in their lifetime. Those who responded "yes" were classified as ever smokers, while those who responded "no" were classified as never smokers. Clinical and laboratory data were compared between the two groups. All participants were genotyped using a customized array, and a genome-wide association study (GWAS) was conducted to identify single nucleotide variants (SNVs) associated with smoking status.

Results: Of the 1,231 adults with available smoking data, 332 (27%) were classified as 'ever smokers' and 899 (73%) as 'never smokers'. 'Ever smoker' status was associated with male sex, age ≥ 40 years, lower educational attainment, and hemoglobin levels above the 75th percentile. In the GWAS, no SNVs reached genome-wide significance ($p< 5 \times 10^{-8}$). However, several SNVs demonstrated nominal significance ($p< 1 \times 10^{-7}$), including rs11087854 and a variant at position

1059991 on chromosome 20 within the gene AL110114.1, as well as rs701023 in the NCOR2 gene, suggesting a potential association with smoking behavior.

Conclusion: Biological sex, age, and educational level are associated with smoking status among adults with SCD, and tobacco use appears to correlate with elevated hemoglobin levels in this population. Although no genome-wide significant associations were identified, our findings highlight potential genetic loci-particularly within AL110114.1 and NCOR2-that warrant further investigation in relation to smoking behavior in individuals with SCD.

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UHRF2 as a genetic correlate of hospitalization in sickle cell disease

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No abstract available

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Cost of immune tolerance induction according to its outcome in people with hemophilia A and inhibitors: results from the Co$tIT study

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Background: Immune Tolerance Induction (ITI) is indicated for people with hemophilia A (PwHA) with inhibitors. It is not known whether the costs differ among ITI outcomes.

Aim: To assess the costs of clotting factor concentrates (CFC) according to ITI outcomes.

Methods: This retrospective cohort study included 91 PwHA who completed a first course of ITI. We evaluated the costs with CFC 12 months before (pre-ITI), during and 12 months after ITI (post-ITI), according to ITI outcome. We compared costs in each period, between pre- and post-ITI, and evaluated the determinants of costs during ITI.

Results: A total of 32%, 38% and 30% of PwHA achieved complete (CS), partial success (PS), and failed ITI, respectively. The mean cost per PwHA during ITI was US$1.18 million; US$355,838 in CS, US$724,986 in PS, and US$2,653,217 in the failure group. During ITI, approximately 65% of the variability of the mean cost/kg was explained by the outcome of ITI (failure or PS), duration of ITI, use of prophylactic bypassing agents, and use of incremental FVIII regimen. In post-ITI, we observed about 50% and 22% reduction of mean cost/kg in CS and PS, respectively, while failing ITI resulted in increased costs of over 100% compared with pre-ITI. Regardless of the outcome, in post-ITI, the annualized bleeding rate reduced when compared with pre-ITI.

Conclusions: Costs with CFC during ITI were the lowest with CS, followed by PS and failure. In comparison with pre-ITI, successful ITI was associated with reduced costs, already noticed in the first year post-ITI.

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Genomic ancestry, F8 variants, and immune tolerance in hemophilia A patients with inhibitors: exome sequencing insights

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Abstract Not available.

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Longitudinal Evaluation of Immunological Biomarkers in Previously Untreated/Minimally Treated Patients With Severe and Moderately Severe Haemophilia A During Exposure to Factor VIII: Results From the HEMFIL Study

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Background: Haemophilia A (HA) is an inherited bleeding disorder due to Factor VIII (FVIII) deficiency. Treatment with FVIII can activate immune mechanisms, which may lead to inhibitor development.

Objectives: This study aimed to perform a longitudinal and exploratory analysis of immunological biomarkers during replacement with FVIII concentrate and after immune tolerance induction (ITI) in patients who developed a high-responding inhibitor.

Methods: Biological samples and clinical data from severe and moderately severe persons with HA (PwHA; FVIII < 0.02 IU/mL) were obtained before any or after minimal exposure (≤5 days) to FVIII (T0), at inhibitor development (INB+), at 75 exposure days (ED) without inhibitor (INB-) (T1) and at end of ITI (T2). Biomarkers were assessed at T0, T1 and T2.

Results: One hundred patients were analysed, of whom 32 (86.5%) developed high-responding inhibitor and underwent ITI. We found no difference in the plasma concentration of the 15 immunological biomarkers at T0 or at T1 versus T2 in INB+ compared with INB-. However, at T1, PwHA INB+ who failed ITI had higher median concentration of interleukin (IL)-2 (3.50 vs. 0.85 pg/mL; p = 0.016), IL-10 (3.46 vs. 0.74 pg/mL; p = 0.035), tumour necrosis factor (TNF) (11.18 vs. 0.93 pg/mL; p = 0.016), interferon-gamma (INF-γ) (98.57 vs. 3.57 pg/mL; p = 0.035) and CCL5 (5245.11 vs. 3107.86 pg/mL; p = 0.037) compared with those who achieved complete response, respectively.

Conclusions: Patients who failed ITI had higher concentration of IL-2, IL-10, TNF, INF-γ and CCL5 in comparison with complete responders, suggesting that these biomarkers could be potential predictors of ITI outcome.

4- Hematology, Transfusion and Cell Therapy, 47(3): 103849, 2025.

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Efficacy, safety and satisfaction of using emicizumab in hemophilia A patients without factor VIII inhibitors: A systematic review

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Background: Hemophilia A is a genetic disorder characterized by deficiency or dysfunction of the factor VIII clotting protein, leading to serious bleeding disorders. Conventional treatment involves the exogenous administration of factor VIII. However, this therapy faces significant challenges, including the development of inhibitors and the need for frequent intravenous administration. Emicizumab, a recombinant bispecific monoclonal antibody that can be administered subcutaneously, offers a novel therapeutic alternative by mimicking the action of factor VIII.

Methods: This systematic review evaluates the efficacy, safety, and patient satisfaction with emicizumab in patients with hemophilia A without inhibitors. A comprehensive literature search was conducted using the MEDLINE, SciELO, and LILACS databases. The included studies were original articles on the use of emicizumab in hemophilia A patients without inhibitors and reviews, short communications, expert comments, and case reports were excluded. Data extraction and analysis were performed using predefined criteria.

Results: A total of 471 articles were identified, with 28 meeting the inclusion criteria. Studies demonstrated robust evidence of the efficacy of emicizumab in reducing bleeding episodes, with significant reductions in the Annualized Bleeding Rate and Annualized Joint Bleeding Rate. Safety profiles were favorable, with mainly minor adverse events reported. High patient satisfaction scores highlighted improvements in quality of life and treatment adherence.

Conclusion: Emicizumab represents a significant advancement in hemophilia A treatment, offering superior efficacy, safety, and patient satisfaction compared to traditional therapies. Future research should focus on long-term outcomes and specific subpopulations to further validate these findings.

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Deleterious variants cluster in the A3 domain of factor VIII in people with severe hemophilia A and inhibitors

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Background: Hemophilia A (HA) is an X-linked disorder due to deleterious variants in the factor VIII (FVIII) gene (F8). Few studies from large cohorts have explored F8 genotype in people with HA with origins other than North American and European.

Objectives: We aimed to evaluate the spectrum of F8 variants and haplotypes and affected FVIII domains and chains in the context of inhibitor development in people with severe hemophilia A.

Methods: We performed genotyping of intron 1 and intron 22 inversions (Inv22) and F8 sequencing using a customized gene panel and whole exome sequencing.

Results: We included 265 people with severe hemophilia A. We identified deleterious variants in 98.1% of them, totaling 97 unique mutations, of which 32 (33.0%) are novel. Inv22, nonsense, small insertion/deletion, large deletion, and missense variants accounted for 48.3%, 14.7%, 11.3%, 9.8%, and 7.5% of the variants identified. Variants clustered in the FVIII A3 domain were more often associated with people with HA with inhibitors (INH+) than those without inhibitors (INH-) (21.0% vs 0.0%; P < .001); variants clustered in the A1 domain were more often associated with INH- than with INH+ individuals (33.3% vs 7.7%; P < .001). Inv22 was associated with a 4.8-fold increased risk of developing inhibitors in previously untreated patients (odds ratio, 4.81; 95% CI, 2.02-12.01). Conversely, missense variants protected against inhibitor development (odds ratio, 0.09; 95% CI, 0.01-0.50).

Conclusion: These findings highlight the role of F8 genotype and specific FVIII domains in inhibitor development in an admixed population of people with HA. This could help engineer therapeutic approaches targeting FVIII molecules with reduced immunogenicity.

LINHA DE PESQUISA: DOAÇÃO DE SANGUE E COMPONENTES (2 artigos)

1- Transfusion Medicine, 35: 312-321, 2025.

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Performance of a large Brazilian network of blood banks during the COVID-19 pandemic: Impact assessment and time series analysis (2016–2023)

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Background: During the COVID-19 pandemic, blood banks faced the risk of shortages of blood components and adopted measures to mitigate this threat. The present study aims to describe the influence of the pandemic on a large hemotherapy centre, including data from 21 regional blood centres (Hemominas-Minas Gerais/Brazil). Methods: Time series for the blood donor attendance were constructed covering 8 years (2016–2023). Blood centre performance indicators from the pandemic period (2020–2023) were compared with the pre-pandemic period (2016–2019). Results: During the pandemic, a 11.6% decline in the production of blood components was observed (Semiannual average of 355 511 vs. 402 528 units). The first half of 2022 was the period with the highest number of COVID-19 cases (third wave) and the lowest production. The drop in the number of candidates for blood donation was more pronounced in the most populated cities. An increase in returning donors was observed, as well as a decrease in the deferral rate. The time series analysis indicated a strong downward trend in blood donors during the pandemic period but with a tendency to recover from the second half of 2023. Conclusion: The COVID-19 pandemic significantly affected the hemotherapy system in Minas Gerais, resulting in a drop in the production of blood components. The operation of Hemominas as a network of blood centers contributed to mitigating the effects of the pandemic, alleviating the scarcity of blood components, especially in the most populated cities, where blood donation was very affected and where the largest and most complex hospitals are located.

2- Revista Médica de Minas Gerais, 35: e-35112, 2025

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Post-blood donation screening for acute infectious diseases at a regional blood center

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Introduction: While blood transfusion is a relatively safe procedure, it is not without inherent risks. Adverse events may occur at any stage of the procedure. Hemovigilance is a set of monitoring protocols that accompany the entire cycle of blood use. The objective of hemovigilance is to collate and disseminate data on adverse events with a view to preventing their occurrence or recurrence, enhancing the quality of processes and products, and guaranteeing the safety of both donors and recipients. An indispensable element of hemovigilance is post-donation reporting. This encompasses the identification and removal of stored blood components that may be contaminated, in addition to the monitoring of recipients for the early detection of potential transfusion transmission. Objective: To analyze post-donation information on acute infectious diseases at the Montes Claros Regional Blood Center – Fundação Hemominas from January 2020 to December 2023. Methods: This is a documentary, analytical and quantitative epidemiological study in which data from the post-donation

information report reported at the blood center were analyzed. The following variables were extracted from the instruments: total donors screened, total collections, cause of notification, year of notification, whether the blood component was distributed, whether the blood component was transfused, and the type of blood component transfused. Results: There were 76 post-blood donation reports of acute infectious diseases in the period studied, with an average of 19 ±6.4 notifications/year and an average of 1.6 notifications/month ±1.7. Of the 76 notifications, 35 (46.05%) were for conditions consistent with those associated with the novel coronavirus and influenza, 32 (42.11%) were for other unspecified acute infectious diseases, and nine (11.84%) were for arboviruses. The number of notifications for the coronavirus/flu syndrome exhibited an upward trend in 2022, followed by a decline in 2023. Concurrently, there was a notable surge in arbovirus notifications, rising from 0% in 2020 to 43.80% in 2023. Conclusion: It is imperative that blood centers adopt strict criteria for donor screening, especially for arboviruses, particularly in tropical countries such as Brazil, and it is essential to explore viable alternatives to ensure transfusion safety.

LINHA DE PESQUISA: IMUNOHEMATOLOGIA (1 artigo)

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Anti-M induced severe Hemolytic Disease of the Fetus and Newborn: The role of the Monocyte Monolayer Assay in elucidating the clinical relevance of alloantibodies in pregnancy

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Introduction: Hemolytic Disease of the Fetus and Newborn (HDFN) is associated with the induction of fetal anemia. Usually, the occurrence of this disease is associated with alloantibodies directed to Rh and K antigens, while severe or fatal cases involving anti-M are rare, especially in non-Asian populations. The Monocyte Monolayer Assay (MMA) is a cellular assay that has been shown to be useful in defining the clinical importance of antibodies.

Case description: Severe fetal anemia induced by anti-M was observed in a pregnant 32-year old white Brazilian woman. The immunohematological investigation revealed the presence of two other alloantibodies in the maternal serum. The use of the MMA contributed to elucidating the case, associating only anti-M with the evidenced outcome.

Discussion: The presence of anti-M in pregnant women is generally not a concern, as it is commonly identified as a benign IgM antibody of natural origin. However, it can also be present

in its IgG isoform of immune origin, which is associated with both destruction of fetal red cells and suppression of erythropoiesis. There is still no consensus among professionals for the monitoring of pregnant women through the titration of anti-M. In this context, MMA may be useful to clarify the unfavorable outcomes observed in pregnancies of alloimmunized women.

Conclusion: The present report describes a rare case of severe fetal anemia associated with maternal anti-M in a Brazilian woman and how MMA assisted to elucidate the clinical relevance of the alloantibodies detected.