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Prevalence of serological markers of transfusion and sexually transmitted infections and their correlation with clinical features in a large cohort of Brazilian sickle cell disease patients

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Abstract

BACKGROUND—Sickle Cell Disease (SCD) patients often require red blood cell (RBC) transfusion for clinical complications, so may be exposed to transfusion-transmitted infections (TTI). The prevalence of markers for Human Immunodeficiency Virus (HIV), hepatitis C (HCV) and B (HBV), Human T-cell Lymphotropic Virus (HTLV-1/2), Chaga disease and syphilis in a SCD cohort in Brazil were studied.

STUDY DESIGN AND METHODS—Clinical history, interview data, blood samples, and medical chart review data were collected during cohort enrollment from November 2013 to May

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2015. Serological markers of infection were assessed. Standard measures of statistical association were calculated, and multivariable models were developed for the most prevalent infections to identify associated factors.

RESULTS—Infection markers were evident in 5.2% (144/2,779) of the enrolled cohort. Anti-HCV was detected in 69 (2.5%), syphilis antibodies in 34 (1.2%), anti-HTLV-1/2 in 17 (0.6%), Hepatitis B surface antigen (HBsAg) in 13 (0.5%), Chagas' disease antibodies in 13 (0.5%) and anti-HIV in 8 (0.3%) of participants. Factors associated with increased odds of being anti-HCV reactive were older age, illegal drug use, increasing number of RBCs, >3 pain crises in the previous year, and geographic location. Syphilis was associated with older age, females, and smoking history.

CONCLUSION—HCV infection was more common in older patients who may have received RBCs before testing was performed on donations, suggesting possible historic TT. The cohort showed decreasing rates of infections and a reduction in TT markers in younger patients compared to historical literature except for syphilis, indicating contemporary reduced risk of TTI.

Keywords

Sickle Cell Disease; Infectious Disease Markers; Hepatitis C; syphilis; HIV; Transfusion

INTRODUCTION

Sickle Cell Disease (SCD) patients frequently require red blood cell (RBC) transfusion to prevent or ameliorate severe complications associated with the disease, such as stroke, acute chest syndrome, splenic sequestration and aplastic anemia. Patients may therefore be exposed to transfusion-transmitted infections (TTI) and other transfusion-associated adverse reactions.[1] Previous studies from the USA have demonstrated higher rates of serological markers of infectious diseases in SCD patients compared to the general population, especially for Hepatitis B and C viruses (HBV and HCV) and Human T-cell Lymphotropic virus types 1 and 2 (HTLV-1/2) virus[2, 3]. Human immunodeficiency virus (HIV) prevalence is lower among SCD patients compared to other patient populations, for reasons not completely understood[2–7].

The objective of this study was to evaluate the prevalence of serological markers for HIV, HCV, HBV, HTLV-1/2, Chagas' disease (*T. cruzi*), and syphilis among participants of a large SCD cohort in Brazil, and to assess the impact of these infections on the prevalence of SCD complications within the cohort. Although syphilis is not easily transfusion transmitted under current blood component preparation, storage, and transfusion practices, blood donation screening for syphilis is still mandated, testing for this infection allowed us to gain broader insights into infection risks in the SCD patient population.

MATERIALS AND METHODS

Study design and setting:

This study is part of the Brazil component of the multi-center Recipient Epidemiology and Donor Evaluation (REDS-III) program funded by the National Heart Lung and Blood

Institute (NHLBI) of the USA National Institutes of Health. The REDS-III program conducted research focused on blood safety and availability, and the impact of transfusion in recipients in the USA, Brazil, China and South Africa[8]. The REDS-III Brazil SCD cohort study was designed to assess SCD pathogenesis and the impact of transfusion on disease outcomes and is a collaboration between Vitalant Research Institute (VRI) in San Francisco, CA and participating healthcare centers in Brazil. Research Triangle Institute, International (RTI), served as the data coordinating center. Details of the cohort study procedures and enrollment findings have been described previously[9]. Briefly, randomly selected SCD patients were enrolled at routine patient care visits in six centers in Brazil from November 2013 to May 2015. The participating centers are Hemope, located in the Northeast of Brazil; Hemorio, in Rio de Janeiro, Hemominas in the cities of Belo Horizonte (BH), Montes Claros (MC) and Juiz de Fora (JF); and Instituto da Criança-Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HdC) in São Paulo. The latter five centers are in the Southeast of the country. The participating centers collectively treat almost 10,000 SCD patients. Approximately half of the patients actively under care (patients with at least 1 clinical encounter in the past 3 years) were randomly selected for recruitment in strata proportional to each center's overall SCD population based on distribution of gender, age (children <18 years and adults 18 years) and SCD genotype. All patients 18 years or older were asked questions related to drug and alcohol use as part of the enrollment interview. The questions regarding potentially stigmatizing behaviors such as drug and alcohol use were based on validated questions developed for the US CDC National Health Interview Survey and have also been used in large population-based studies in Brazil as part of the Pesquisa Nacional de Saude conducted by the Brazilian Institute of Geography and Statistics in partnership with the Ministry of Health[10–12]. In addition, all questions were asked by trained research staff in a private setting to maintain confidentiality.

Measurement (laboratory methods):

Blood samples collected at the enrollment visit into the REDS-III cohort were tested for the following infections: HIV, HCV, HBV, HTLV-1/2, Chagas' disease, and syphilis. These infections were chosen because they align with the panel of infectious disease screening performed on all blood donations in Brazil. The specific tests used, and the testing approach varied by infection (Table 1). A patient was considered reactive if second or third tests confirmed reactivity detected on first test for all infections except for HBV. For HBV, both surface antigen (HBsAg) and anti-HB core (Anti-HBc) were performed. Anti-HBc is known to have relatively poor specificity and no confirmatory assay for anti-HBc was available; most patients with reactive anti-HBc demonstrated low levels of reactivity without HBsAg. Due to concern for potential false positives, which would overestimate transfusion transmitted infection rates, HBV status in this study was determined solely by confirmed reactivity of HBsAg. For syphilis, we used antibody assays that detect the presence of IgM or IgG as first and secondary test, followed by treponemal testing (VDRL). The antibody assays do not differentiate active from previous syphilis.

Analysis:

The prevalence (number positive/number tested) of each infection in the cohort is reported. Bivariate analysis was used to identify potentially significant variables associated with each

infection and across all infections. Categorical variables were analyzed using Chi-Square or Fisher exact test where counts were sparse. Continuous variables were compared using T-test or Mann-Whitney U test, as appropriate. Two-sided p-values <0.05 were considered statistically significant. Multivariable models were developed for prevalent infections to identify factors independently associated with reactive serology results. For two infections, HCV and syphilis, all variables meeting the bivariate screening criteria for significance were included in multiple logistic regression analysis using backward elimination with an exit criterion of p>0.06. Interactions between selected predictors were included in the initial models but none were significant. Odds ratios and corresponding 95% confidence intervals were obtained for variables remaining in the final models. All statistical analyses were performed using SAS 9.4.

Ethical considerations:

Local ethical committee approval was obtained at all participating sites and from the National Ethics Committee in Brazil (CONEP approval number 02790812.0.1001.0065). Institutional Review Board approval in the USA was obtained from UCSF, the IRB of record for VRI, and the RTI IRB. Consent was obtained for all adult participants and age-appropriate assent was obtained for participating children in addition to parental consent for participation by minors.

RESULTS

Of the 9,676 SCD patients actively treated by participating centers, 3,029 were approached for recruitment and 2,793 (92% of recruited and 29% of the active patient population) were enrolled in the cohort. Of these, 2,779 (99.4%) had enrollment visit plasma samples available for serological testing (1,307 males and 1,472 females). There were no significant differences between the demographics of the centers' patients who were included in the cohort or not.

One-hundred forty-four (5.2%) of the study participants (4.4% males and 5.9% females) had reactive results for at least one of the tested infections. Overall, anti-HCV was the most prevalent marker, detected in 69 (2.5%) patients, followed by positive ELISA testing for syphilis in 34 (1.2%) patients; VDRL was 1/8 in 10 out of the 34 (29,4%) ELISA reactive patients. Anti-HTLV-1/2 was detected in 17 (0.6%), HBsAg in 13 (0.5%), anti-*T. cruzi* in 13 (0.5%), and anti-HIV in 8 (0.3%) participants (Table 1-Supplement). Ten patients showed evidence of multiple infections: one patient had markers of HCV, HIV and HTLV-1/2; two patients had markers for HBV (HBsAg) and HTLV-1/2, two were HCV and syphilis reactive; one patient each was reactive for HBV and HIV; HCV and HTLV; HCV and *T. cruzi*; syphilis and HTLV-1/2.

Clinical manifestations and treatments were associated with serological markers of HCV infection in the cohort (Table 2), but less so for the other infections. Among the patients who were anti-HCV reactive, 45 (65%) received 11 or more RBC units, and 46 (67%) reported previous surgeries. Transfusion history, previous surgeries, number of hospital admissions in the previous year, use of analgesics, use of antidepressants, avascular necrosis, leg ulcers and

current iron overload were all highly associated with anti-HCV reactive results (each p<0.001).

Table 3 describes the association of drugs, alcohol and smoking with positive serological markers in adults. Among the 68 HCV positive patients, 4.4% disclosed illegal drug use ever (p<0.05), 51.5% of the 34 Syphilis reactive patients disclosed ever smoking (p<0.05) and 18.2% out of these were currently smoking (p<0.05).

Multivariable analyses were estimated only for the two most prevalent infections, HCV and syphilis, and were restricted to the adult population (>18 years old) as only 5 patients <15 years were reactive for an infectious disease. We found site specific differences with patients at Hemorio [OR = 5.0; 95% CI (2.1–13.7); p<0.001] and Hemope [OR = 3.4; 95% CI (1.3–9.9); p<0.010] demonstrating higher odds of HCV compared to Hemominas Belo Horizonte, the site with lowest HCV prevalence. Patients in the oldest age stratum (50+ years) had a very high odds ratio for HCV when compared to the youngest stratum (15–24 years) [OR = 112.4; 95% CI (18.7->999.9); p<0.001]. In addition, the test for trend by age group was highly significant (p<0.0001). Any history of transfusion was associated with HCV. The highest odds ratio was observed for patients reporting 21–60 lifetime transfusions [OR = 21.5; 95% CI (4.0–402.8); p<0.001] when compared to SCD patients without history of transfusion. The trend for the association between increasing number of transfusions and HCV was significant (p=0.03). Disclosure of ever using illegal drugs was also associated with HCV markers [OR = 7.4; 95% CI (1.4–30.1); p<0.02]. Reporting three or more hospitalizations for pain during the previous year was associated with the odds of having HCV [OR = 5.2; 95% CI (1.9–14.5); p=0.002] (Table 4).

The multivariable analysis for syphilis showed that patients   50 years of age compared to 15–24 years old had higher odds of syphilis [OR = 5.8; 95% CI (1.5–22.3); p=0.013], and females had higher odds than males [OR = 2.3; 95% CI (1.0–5.5); p=0.041]. Ever smoking was associated with syphilis [OR = 2.7; 95% CI (1.3–5.8); p=0.008].

DISCUSSION

In this study, approximately 1 out of 20 SCD patients had reactive serological markers for the infections for which we tested. HCV, HBV, HTLV-1/2, *T. cruzi*, syphilis and HIV infections were detected in the cohort. For the two most common infections in the cohort, HCV and syphilis, the results suggest two different possible routes of infection acquisition. HCV was the most common marker detected, with those who are older and received higher numbers of lifetime RBC transfusion having highest odds of HCV. Serological testing for HCV was implemented as a routine screening at blood centers in Brazil in 1993. Syphilis was the second most common infection in our cohort. Our study did not assess sexual risk behaviors that could have contributed to the transmission of infectious diseases, but modern methods of collection and processing of components (mainly cold temperature storage of RBCs) are effective in neutralizing spirochetes, thus impeding the transmission of the disease through blood transfusion.[13] Therefore, the mostly likely route of acquisition is through sex in the adult members of the SCD cohort.

The overall HCV prevalence of 2.5% within our SCD cohort suggests a low risk of acquiring this infection through transfusion today. However, the results show evidence of geographic differences in risk as the range of HCV seroprevalence varied from 0.6 to 4.9% among the sites with adult SCD patients. Previous studies of HCV prevalence report a rate of 1.4–2.5% seropositivity within the Latin America general population[14], and 0.9% among 4,245 sex workers in 12 cities in Brazil in 2016.[15] A previous study with 1,415 sickle cell adult patients conducted between 1995 and 2009 in Bahia, Brazil, demonstrated HCV prevalence of 13.4% in patients.[3] After the introduction of serology and nucleic acid testing (NAT) in 2012, the rates of transfusion-transmitted HCV significantly declined.[16] The site specific differences we observed are in accord with the last Hepatitis bulletin published by the Brazil Ministry of Health in 2018[16] which describes cases of Hepatitis in the general Brazilian population and reported the highest rate of Hepatitis C incidence in the Southeast region of the country, and a previous REDS-II study[17] published in 2013 that demonstrated the prevalence of HCV antibodies among blood donors was higher in Recife compared to Belo Horizonte. Illegal drug use (ever) was not frequent in our cohort but was a significant risk factor associated with being HCV positive. Even so, much stronger associations with increasing age and transfusion history were evident, suggesting a larger role for historical transfusion transmission of HCV.

Another interesting aspect in our study was the increased association between pain hospitalizations and HCV infection. Previous studies have demonstrated chronic pain affecting 40 to 70% of patients infected by HCV, mainly due to the combination of peripheral neuropathies, arthritis, fibromyalgia and also autoimmune mechanisms.[18, 19] Our findings are consistent with these increased pain rates in persons with HCV.

Estimates of syphilis prevalence in Brazil widely varies based on risk group and population studied; from 8.5% active syphilis among sex workers in the southern region of the country[15], 13% seropositivity among homeless people in Sao Paulo[20] to 6% seropositivity in the general population from State of Para[21]. The study from Bahia including 1,415 Brazilian adult SCD patients in 2011 reported a 0.4% prevalence of syphilis, although this study did not describe the tests used for diagnosis.[3] We found serological evidence of exposure to syphilis in our population, but could not completely differentiate between the patients who had past or were actively infected with the bacteria. Our prevalence of 1.2% among SCD patients is higher than described previously, and may reflect that Brazil has recently being experiencing increased transmission of syphilis due to an increase in unprotected sexual exposures[22]. The odds of being syphilis reactive was 2 times higher among female patients and almost 3 times higher among ever smokers, consistent with previous studies suggesting that behaviors such as smoking may be co-factors or surrogate markers of higher risk groups who may have unprotected sexual relationships and higher number of sexual partners[23–25].

In our study, SCD patients had a similar HIV prevalence (0.3%) compared to the general Brazilian population (0.4%).[26] A small number of patients in all age strata had HIV, likely reflecting sexual, parenteral, and vertical transmission of the disease. Other studies have shown HIV prevalence rates of 0–11% in the SCD population.[4, 27] There is scarce literature discussing the reciprocal effects of SCD and HIV, though lower HIV associated

morbidity and mortality has been reported in case series including small numbers of HIV infected SCD patients. One study detected an increased frequency among SCD of the mutant CCR5 32 allele that protects against HIV infection,[28] while others discuss the possible delayed sexual initiation and reduced risk exposure among the SCD population as a changing factor for acquiring HIV, as well as possible innate immunological defense against the HIV infection and progression[2, 27]. A recently published study also suggested the impact of different iron metabolism and reduced intracellular iron in SCD patients as a mechanism to protect against HIV infection and replication in those patients.[29] While the exact mechanisms remains unclear, our findings of low HIV infection rates in SCD patients, yet relatively high HCV infection rates, continue to provide indirect evidence of low risk of transfusion transmission of HIV to SCD patients.

HTLV-1/2 was most frequently found in Hemope in the Northeast of the country, and this area is recognized as endemic for these viruses.[30] Chagas' detection was highest in Hemominas Montes Claros, an endemic area with ongoing infestation by the vector Triatomine bugs (Reduviidae) that transmit the *Trypanosoma cruzi* parasite, causative agent of Chagas disease.[31, 32] Much lower prevalence was observed in other locations for both HTLV and Chagas. Hepatitis B was detected in 0.5% of our SCD cohort, similar to a recent estimate of HBsAg positivity between 0.5 –1.8% in the general population among the regions where the participating SCD patient care centers are located.[33] HBV was detected mainly among older patients, most likely reflecting risk before HBV universal infant vaccination started in 1998 in Brazil.[34]

Our study has limitations. One of the more important limitations is the inability to definitively confirm infections that could be caused by transfusion. It would be ideal to be able to better estimate the year of infection and correlate it with known dates of RBC transfusion in the SCD patients and the adoption of blood screening tests in Brazil. However, the specific year of infection transmission is not known among our patients and cannot be ascertained with enough precision to know whether infection preceded transfusion. Another limitation is that Hepatitis C treatment was not specifically queried in case report forms, therefore we could not include HCV therapies in our analysis and correlate HCV treatment and clinical complications. In addition, we could not differentiate between active and treated/resolved syphilis infection. Therefore, our estimates of syphilis prevalence are not a direct measure of current active syphilis infection in the SCD patient population in Brazil. One other limitation is important. Our assessment of transmission routes and risk factors for infection acquisition was not exhaustive. For example, although general risk behavior information was obtained by face to face interview, we did not obtain a detailed sexual history from the adult patients enrolled in the study or use an interview technique, such as audio-computer assisted structure interview, to elicit potentially stigmatizing behaviors. Therefore, the behavioral risks we evaluated in this analysis are subject to the possibility of response bias.

The prevalence of most serological markers of transfusion-transmissible infections in the SCD patients in this study are similar to the general population in Brazil. The exception is HCV where prevalence is higher in SCD patients in some areas of the country, and strong associations with transfusion and other medical procedures was evident. HCV prevalence in

adult SCD patients is associated with age and increased RBC transfusion while few infections were found in minors, suggesting a historical risk of transfusion-transmission and an increasingly safe blood supply in Brazil. Taken altogether these findings for all the agents we assessed suggest local epidemiological patterns driving the prevalence of these infections in SCD patients and do not specifically suggest evidence of current transfusion-transmission.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Testing approach and tests used to define infection status in the cohort.

Infection	First test	Second test (if positive on first)	Third test (if positive on second)
HIV	Architect Ag/Ab Combo (CMIA) Abbott	Genscreen ultra HIV Ag/ Ab EIA BIORAD	HIV BLOT 2.2 Western Blot- MP Biomedicals Asia Pacific Pte Ltd
HCV	Anti HCV II (ECLIA) Cobas Roche	Architect HCV (CMIA) Abbott	
HBV	Architect HBsAg Qualitative II (CMIA) Abbott	Architect HBsAg neutralization (CMIA) Abbott	
	Architect Anti-HBc II (CMIA) Abbott		
HTLV	Architect rHTLV-I/II (CMIA) Abbott	GOLD ELISA HTLV I/II	
Chagas	Architect Chagas (CMIA) Abbott	Teste Elisa Chagas III Grupo Bios S.A. – Diasorin	
Syphilis	Architect Syphilis TP (CMIA) Abbott	Syphilis (ECLIA) Cobas Roche	Syphilis Wiener - Wiener lab (VDRL). 2000 Rosario – Argentina

Table 2.

Clinical Characteristics Associated with Positive Serological Markers among a Sickle Cell Disease Cohort in Brazil (n=2,779)

	HCV + n=69 n (%)	Syphilis + n=34 n (%)	HTLV + n=17 n (%)	HBV + n=13 n (%)	Chagas+ n=13 n (%)	HIV + n=8 n (%)	Any infectious disease marker n=144 n (%)	Negative for these markers n=2,635 n (%)
Transfusion history Transfused RBC Units at Hemocenter	*		†				*	
0	1 (0.2)	6 (1.2)	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	10 (1.9)	512 (98.1)
1–5	8 (1.0)	7 (0.9)	1 (0.1)	2 (0.2)	3 (0.4)	1 (0.1)	21 (2.5)	805 (97.5)
6–10	7 (1.9)	4 (1.1)	5 (1.3)	4 (1.1)	3 (0.8)	1 (0.3)	21 (5.4)	369 (94.6)
11–20	15 (5.2)	2 (0.7)	2 (0.7)	1 (0.4)	4 (1.4)	2 (0.7)	23 (7.7)	275 (92.3)
21–60	20 (6.8)	6 (2.2)	4 (1.4)	3 (1.1)	0 (0.0)	0 (0.0)	32 (10.5)	272 (89.5)
61+	10 (4.7)	3 (1.4)	4 (1.9)	1 (0.5)	1 (0.5)	2 (1.0)	19 (8.5)	204 (91.5)
Missing/ Unknown	8 (0.1)	6 (0.2)	1 (0.1)	1 (7.7)	1 (7.7)	1 (12.5)	18 (12.5)	198 (7.51)
Previous surgeries	46 (3.9)*	24 (2.1)†	11 (1.0)	10 (0.9)†	10 (0.9)†	6 (0.5)	99 (8.1)*	1,125 (91.9)
Missed days of school/ work in past month (>6=years old)								
0 days	41 (2.5)	17 (1.1)	10 (0.6)	11 (0.7)	10 (0.6)	6 (0.4)	87 (5.2)	1,573 (94.8)
1–10 days	21 (3.3)	14 (2.2)	7 (1.1)	1 (0.2)	2 (0.3)	1 (0.2)	44 (6.6)	622 (93.4)
>10 days	7 (5.5)	3 (2.4)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	12 (9.1)	120 (90.9)
Missing/ Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (0.4)
Number of hospital admissions in Previous Years	*							
0	41 (2.2)	27 (1.4)	12 (0.6)	7 (0.4)	10 (0.5)	6 (0.3)	98 (5.1)	1,836 (94.9)
1–2	17 (2.5)	6 (0.9)	5 (0.7)	6 (0.9)	3 (0.4)	2 (0.3)	35 (4.9)	674 (95.1)
3+	11 (8.1)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (8.1)	124 (91.9)
Missing/ Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.04)
Number of vaso-occlusive pain hospitalizations in previous year	*						†	
0	43 (2.0)	29 (1.4)	13 (0.6)	10 (0.5)	10 (0.5)	8 (0.4)	107 (4.9)	2,093 (95.1)
1–2	16 (3.3)	4 (0.9)	4 (0.9)	3 (0.6)	3 (0.6)	0 (0.0)	27 (5.5)	462 (94.5)
3+	10 (11.1)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (11.1)	80 (88.9)
Analgesics> 30 days	21 (6.6)*	7 (2.3)	4 (1.3)	1 (0.3)	0 (0.0)	2 (0.7)	31 (9.4)†	299 (90.6)
Antidepressants	12 (11.1)*	2 (2.0)	1 (1.0)	0 (0.0)	0 (0.0)	1 (1.0)	16 (14.3)	96 (85.7)
Avascular Necrosis	20 (8.8)	6 (2.8)	2 (1.0)	3 (1.4)	2 (1.0)	0 (0.0)	32 (13.4)*	207 (86.6)

	HCV + n=69 n (%)	Syphilis + n=34 n (%)	HTLV + n=17 n (%)	HBV + n=13 n (%)	Chagas+ n=13 n (%)	HIV + n=8 n (%)	Any infectious disease marker n=144 n (%)	Negative for these markers n=2,635 n (%)
Leg Ulcers	20 (9.5)[*]	7 (3.5)[†]	7 (3.5)[†]	5 (2.6)[†]	1 (0.5)	0 (0.0)	38 (16.6)[*]	191 (83.4)
Current iron overload	17 (6.0)[*]	5 (1.9)	4 (1.5)	1 (0.4)	0 (0.0)	2 (0.8)	28 (9.6)	264 (90.4)

[*] $p<0.0001$

[†] $p<0.05$

Table 3.

Behavioral Factors Associated with Positive Serological Markers among a Sickle Cell Disease Cohort in Brazil Adults Only (n=1,231), by column percentage

	HCV	Syphilis	HTLV	HBV	Chagas (*T. cruzi*)	HIV	Any infectious disease marker	Negative for these markers
	n=68 (%)	n=33 (%)	n=16 (%)	n=11 (%)	n=13 (%)	n=7 (%)	n=138 (%)	n=1,093 (%)
Illegal drug use (ever) [*]	3 (4.4)[†]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	12 (1.1)
Marijuana (ever)	5 (7.3)	2 (6.1)	1 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	8 (5.8)	68 (6.2)
Alcohol use (ever)	43 (63.2)	26(78.8)	12(75.0)	8 (72.7)	10 (76.9)	5 (71.4)	99 (71.7)	739 (67.6)
Current Alcohol use	9 (13.2)	8 (24.2)	5 (31.2)	3 (27.3)	2 (15.4)	1 (14.3)	27 (19.6)	256 (23.4)
Ever smoking	24 (35.3)	17(51.5)[†]	4 (25.0)	1 (9.1)	8 (61.5)[†]	3 (42.8)	53 (38.4)	279 (25.5)
Current Smoking	6 (8.8)	6(18.2) [†]	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	12 (8.7)	68 (6.2)

[*] Excludes marijuana. Includes crack, cocaine, and intravenous drug use.

[†] $p<0.05$

p value was calculated comparing individuals positive and negative for each infection.

Table 4.

Multivariable logistic models for factors associated with HCV infection and syphilis showing Odds Ratios (OR) and 95% Confidence Intervals (CI) – Models include only the factors significantly associated with infection status for patients 15 years of age or older.

Predictor	Adult patients with Hepatitis C infection: Positive (n=68); Negative (n=1,088)[*]	Adult patients with Syphilis infection: Positive (n=33); Negative (n=1,090)[**]
	OR (95% CI)	OR (95% CI)
Blood Center		
Hemominas BH	Reference	
Hemominas JF	1.6 (0.3–6.3)	
Hemominas MO	2.1 (0.3–10.0)	
Hemope	3.4 (1.3–9.9)	
Hemorio	5.0 (2.1–13.7)	
Transfusion history		
0	Reference	
1–5 units	4.1 (0.6–78.7)	
6–10 units	6.8 (1.1–133.2)	
11–20 units	17.8 (3.1–338.3)	
21–60 units	21.5 (4.0–402.8)	
61 or more units	16.5 (2.7–323.5)	
Missing	11.7 (1.9–228.6)	
Marital Status		
Single	Reference	
Living together/ not married or married	1.8 (0.9–3.5)	
Separated/ Divorced/ Widower	6.0 (2.4–15.0)	
Illegal drug use (ever)		
No	Reference	
Yes	7.4 (1.4–30.1)	
Pain Hospitalizations in previous year		
0	Reference	
1–2	1.7 (0.8–3.4)	
3 or more	5.2 (1.9–14.5)	
Age Strata		
18–24	Reference	Reference
25–34	10.9 (2.1–199.8)	1.4 (0.4–4.2)
35–44	32.7 (6.3–603.0)	4.1 (1.5–13.0)
45–54	51.1 (9.3–956.7)	2.1 (0.5–8.3)
55+	112.4 (18.7->999.9)	5.8 (1.5–22.3)
Gender		
Male		Reference

Predictor	Adult patients with Hepatitis C infection: Positive (n=68); Negative (n=1,088)[*]	Adult patients with Syphilis infection: Positive (n=33); Negative (n=1,090)[**]
	OR (95% CI)	OR (95% CI)
Female		2.3 (1.0–5.5)
Ever smoked cigarettes in lifetime		
No		Reference
Yes		2.7 (1.3– 5.8)

[*] For the HCV multivariable analysis the following variables were considered for inclusion: blood center, age, marital status, transfusion history, illegal drug use (ever), previous surgeries, number of hospital admissions in previous year, vaso-occlusive hospitalizations in previous year, number of vaso-occlusive hospitalizations during the previous year, analgesics and antidepressants use during the last 30 days, current iron overload, avascular necrosis, leg ulcers.

[**] For the syphilis multivariable analysis the following variables were considered for inclusion: gender, age, ever smoking, current smoking, previous surgeries, leg ulcers.