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Authors

Moreira, Carlos

Salomon, Tassila

Alencar, Cecília

et al.

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HIV primary drug resistance and associated HIV risk factors among HIV positive blood donors in Brazil from 2007 to 2017.

Carlos Henrique Valente Moreira[1,2], **Tassila Salomon**[2], **Cecília S. Alencar**[3], **Thelma T. Gonçalez**[4], **Ester C. Sabino**[2], **Liliana Preiss**[5], **Paula Loureiro**[6], **Maria Esther Lopes**[7], **Carolina Miranda Teixeira**[8], **Mariana Mundim**[7], **Anna Barbara Carneiro-Proietti**[8], **Cesar de Almeida-Neto**[9,10,*], **Brian Custer**[4,11,*]

[1.]Instituto de Infectologia “Emílio Ribas”, São Paulo, SP, Brazil

[2.]Instituto de Medicina Tropical de São Paulo, Faculdade de Medicina (FMUSP) da Universidade de São Paulo São Paulo, SP, Brazil

[3.]Laboratório de Medicina Laboratorial LIM 03- HCFMUSP, São Paulo, SP, Brazil

[4.]Vitalant Research Institute, San Francisco, CA, USA

[5.]RTI – Research Triangle Institute, Durham, NC, USA

[6.]Fundação HEMOPE, Recife, PE, Brazil.

[7.]Fundação HEMORIO, Rio de Janeiro, RJ. Brazil.

[8.]Fundação HEMOMINAS, Belo Horizonte, MG, Brazil

[9.]Departamento de Aféreses, Fundação Pró-Sangue, Hemocentro de São Paulo, Sao Paulo, Brazil.

[10.]Disciplina de Ciências Médicas, Faculdade de Medicina da Universidade de São Paulo, São Paulo, SP, Brazil

[11.]Department of Laboratory Medicine, UCSF, San Francisco, CA, USA

Abstract

Background: Acquisition of HIV primary drug-resistant (PDR) infection can lead to poor virologic and clinical outcomes in individuals and hampers public health efforts in epidemic control. Monitoring PDR in HIV-positive blood donors can be used to inform nationwide trends in the spread of drug-resistant HIV strains.

Methods: We conducted a cross-sectional study using genetic sequence analysis to assess HIV pol sequences, PDR, and risk factors for infection using audio computer-assisted structured interviews (ACASI) in four large blood centers in Brazil from 2007 to 2017.

Corresponding author: Carlos Henrique Valente Moreira, carloshvmoreira@gmail.com.
*These authors share the senior authorship for this paper.

AUTHORS CONTRIBUTIONS

CHVM, CAN, BC, ECS, and TTG designed the study. TS, CSA, PL, MEL, CMT, MM, and ABC participated in data collection. CSA participated in laboratory procedures. LP participated in the data analysis. CHVM, TS, ECS, CAN, and BT wrote the manuscript. All authors revised and approved the final version of the manuscript.

The authors declare that they have no conflict of interest

Results: Of 716 HIV-positive blood donors, 504 (70.4%) were successfully sequenced. HIV clade B (73.2%) was the most prevalent subtype, followed by a mix of non-B (21.2%) sub-types. A two-fold increase (from 4% to 8%) in recombinants prevalence was observed during the study period. Sixty-four (12.7%) presented PDR. Overall, HIV PDR prevalence remained stable during the study period. Drug resistance mutations for non-nucleoside reverse transcriptase inhibitors were found in 39 (7.7%) donors, while for nucleoside reverse transcriptase inhibitors were found in 26 (5.1%), and for protease inhibitors in 24 (4.8%) of HIV-infected donors. We did not find statistically significant differences in demographics, behavioral risk factors, or HIV genotypes when comparing volunteers with and without PDR.

Conclusion: The HIV PDR rate among donors remained stable during the study period. HIV-positive blood donors can be an informative population to monitor primary HIV resistance and ultimately may help to increase the knowledge and awareness of HIV risk factors and PDR.

Keywords

HIV drug resistance; primary HIV drug resistance surveillance; transfusion safety; blood donors; Brazil

INTRODUCTION

The increasing prevalence of pretreatment drug resistance and high rates of resistance-associated mutations found in many countries primarily, among specific populations, is the price for the widespread availability of the HIV treatment programs (1,2).

HIV drug resistance (HIVDR) is due to changes in the genetic structure of the virus, affecting the ability of particular drugs or drug classes to block its replication effectively. There are two main categories: acquired HIV drug resistance, that occurs over time due to viral replication in individuals receiving antiretroviral therapy (ART), and transmitted HIV drug resistance or primary HIV drug resistance (PDR), that arises in people with no previous history of ART exposure, who were infected with an already drug-resistant strain HIV (3).

PDR may lead to suboptimal viral suppression, followed by immunologic failure, poor clinical outcomes in individual patients, adding risk for communities from viremic patients (4). Continued use of an already failed treatment will positively select for resistance mutations decreasing the efficacy of viral suppression by ART, favoring the risk of sexual and perinatal HIV transmission, and threaten the effectiveness of subsequent regimens.

The frequency and types of HIVDR are greatly dependent on the variety of drug classes currently proposed in each country, and according to the WHO, pretreatment HIVDR rates for non-nucleoside reverse transcriptase inhibitors (NNRTI) had increased worldwide from 11% to 29% since the global rollout of ART since 2001 (5). Also, the prevalence of NNRTI PDR is higher, notably in specific subpopulations, such as women, 11.8%, comparing to 7.8% among men initiating ART between 2014 and 2018 (3).

In Brazil, HIVDR mutations have evolved over the past 20 years, with an overall rate of 6.6% in 2001 (6), followed by 8.1% in a survey dated from 2007–2008 (7), and 16,3% was documented more recently in the year of 2017 (8). The prevalence of HIVDR varies across

the country, ranging from 6.8%, in the Midwest, up to 11.2%, in the Southeast of Brazil (9). Most HIVDR studies address newly diagnosed and before ARV onset (9).

HIV infected blood donors are a readily accessible population that may, by proxy, act as a sentinel population for surveillance and monitoring drug-resistance trends. Although these donors may not represent the overall HIV population, we can infer that persons with a variable range of risk behaviors perform blood donation and can provide a picture of the currently circulating HIV strains, including genotypes, and the rates of PDR.

Our primary study aim was to evaluate the frequency of PDR among Brazilian blood donors from among a ten-year time frame (2007 to 2017), and secondarily to assess if PDR was associated with HIV different genotypes and donors behavioral risk factors.

MATERIALS AND METHODS

Study design and population

In this cross-sectional study, serologically confirmed HIV infection blood donors, during two phases of the NHLBI, NIH REDS program (Retrovirus Epidemiology Donor Study (II) and Recipient Epidemiology and Donor Evaluation Study (III) - International Component, Brazil REDS-II (2007–2012) and REDS-III (2012–2017) (10) were recruited to participate in molecular surveillance and behavioral risk factor assessments. Following the analysis of the work previously done, we extended that by describing in a more detailed and comprehensive narrative.

Settings

HIV infected blood donors from four large Brazilian blood centers were included in the study. Fundação Pró-Sangue (FPS) is located in the state of São Paulo, Fundação Hemominas in Belo Horizonte, Minas Gerais; Fundação Hemorio, Rio de Janeiro; all in the southeastern part of Brazil which is the most densely populated, and Fundação Hemope in the state of Pernambuco, in the northeastern part of the country (Figure 1). In 2016, 3,796,776 blood donations were collected in Brazil, and 593,949 (15%) of these blood units were collected in these participating blood centers.

In Brazil, HIV infected donors are asked to return to the blood center for notification of the routine donation testing results, and for the collection of additional samples for new confirmatory testing (11). In our study, all blood donors who returned to the blood bank were invited to participate.

A consecutive and sequentially convenience sample of HIV diagnosed blood donors enrolled in the research study. The participants collected blood samples for molecular surveillance and completed an audio computer-assisted structured interview (ACASI) (12). The ACASI instrument included questions on demographics, previous blood donation, motivational factors for donation, blood testing, HIV knowledge, and HIV behavior risk factors (occupational, non-occupational and sexual exposure). Details of the study recruitment, HIV behavior risk factor questionnaire, and HIV genotyping methods have been previously described (11,13).

Laboratory methods

HIV-1 Clade Typing and Drug Resistance Testing—Subtype and resistance analyses were performed at Fundação Pro-Sangue, São Paulo (14). In brief, an HIV genome fragment encompassing the protease gene and approximately 700 base pairs of the reverse transcriptase gene were amplified and sequenced using the ABI PRISM Big Dye Terminator Cycle Sequencing Ready Reaction kit (Applied Biosystems Foster City, CA) following the manufacturer's protocol. Subsequently, the products of this reaction were analyzed by an ABI3500 automated sequencer (Applied Biosystems). Only partial HIV pol sequences were obtained. The calibrated population resistance tool version 5.0 beta (available through the Stanford University HIV Drug Resistance Database http://cpr.stanford.edu/cpr.cgi) and Bennett et al., 2009, were used to identify transmitted drug-resistant mutations (15). Mutations listed as causing or contributing to resistance are non-polymorphic in untreated persons and apply to all HIV-1 subtypes according to the World Health Organization (WHO) report (3). Sequences from this study were submitted to GenBank under the numbers JQ237931–JQ238236, and KC834581–KC834601.

HIV Drug Resistance definition—HIV drug resistance was defined as the presence of ≥1 surveillance drug resistance mutations (SDRM) (15) and classified for one or more of the following drugs: nevirapine, efavirenz, any NRTI, atazanavir, darunavir or lopinavir. NNRTI resistance was defined as resistance to nevirapine or efavirenz; NRTI resistance was defined as resistance to any nucleoside reverse transcriptase inhibitor drug; and protease inhibitor resistance was defined as resistance to atazanavir, darunavir or lopinavir (5,16).

Statistical analysis—Variables with continuous distributions were reported as median (interquartile range) or means (standard deviations), depending on the distribution, while categorical variables were summarized as absolute numbers and percentages. When appropriate, 95% confidence intervals were calculated. Differences between patients with and without PDR were assessed using chi-square, or Fisher's exact test for categorical variables and T-test or Mann-Whitney U test, as appropriate, for continuous variables. All statistical analysis was performed using SAS 9.4, with a 2-sided p-value of < 0.05 considered to be significant. Missing data are shown in the tables for informative purposes but were excluded from the statistical comparisons. Statistical comparisons with HIV risk factors and PDR included all patients who reported each behavior risk. We did not classify behavior risk ordinarily, such as higher or lower risk exposures or calculate counts of total reported risks. HIV subtypes were treated as an outcome in the analysis alongside PDR.

Ethical issues—Study protocols were approved by the Federal Committee on Human Subjects (CONEP) of the Ministry of Health in Brazil as part of the REDS-II/III International Program, local ethics committees from each of the participating blood centers, IRB of record for Vitalant Research Institute and from the Research Triangle Institute. Written informed consent for all the procedures was obtained from each participant after recall to perform confirmatory HIV test and before the sample collection. As the finding can directly impact clinical care, all laboratory results were returned to the participants.

RESULTS

A total of 716 HIV infected blood donors were enrolled in the study: 341 from REDS-II (2007 to 2012) and 375 from REDS-III (2012 to 2017). Of these, 212 HIV donors were excluded from the analysis; 124 (17.3%) for reporting prior whatever ART use; 11 (1.5%) due to lack of information on ART use, and in 77 (10.7%) the HIV sequences were not successfully amplified due to low or undetectable viral load.

Thus, five hundred and four HIV infected donors (70.5% of enrolled cases) were included in the study, 304 from REDS II and 200 from REDS III. HIV case participation varied across the blood centers; 181 (35.9%) were from HEMOPE-Recife; 160 (31.7%) from HEMORIO-Rio de Janeiro; 95 (18.8%) from Fundação Pró-Sangue-São Paulo and 68 (13.5%) from HEMOMINAS-Belo Horizonte. There was a predominance of men 408 (81%), and most of the participants had more than 31 years old, 266 (52.8%).

Primary Drug Resistance (PDR)

Overall, 64 (12.7%) of the 504 HIV infected blood donors had PDR. The PDR prevalence varied across the blood centers. The highest PDR prevalence (17.9%) was observed at São Paulo, followed by Belo Horizonte (16.2%), Rio de Janeiro (13.1%), and the lowest (8.3%) was found in Recife. No demographic and regional differences were observed between HIV-positive participants with or without PDR (Table 1).

Primary Drug Resistance and HIV Behavior Risk Factors

PDR and sexual risk exposures—PDR frequency rates varied according to sexual exposure. Of 408 men, 195 (47.8%) reported sex with other men over the course of a lifetime; of these, 26 (13.3%) presented PDR. One hundred sixty-two (39.7%) men reported sex with other men in the last 12 months; of these, 27 (16.7%) had PDR.

Sex with a person who injects drugs or non-prescription substances (PWID) in the last 12 months was reported by 29 (5.8%) study participants; of these, four (13.8%) had PDR. Also, PDR was found in seven out of 51 (13.7%) blood donors that reported sex with a person under potential biological risk due to job exposure throughout the lifetime.

No significant statistical association was observed between reported sexual risk exposures, the number of sexual partners' lifetime, nor in the last 12 months, and PDR.

PDR and Occupational and non-Occupational exposures—Overall, 67 (13.3%) of the HIV infected blood donors reported occupational exposure to needle or body fluid throughout a lifetime; of these, six (9.0%) had PDR. For non-occupational exposures, the highest PDR frequency was found among those reporting blood transfusions throughout a lifetime in which, out of 19 (3.8%) study participants, three (15.8%) presented PDR. Besides, 125 (24.8%) study participants reported tattoo, and of these, 19 (15.2%) had PDR. PWID ever was reported by 79 (15.7%); of these, 11 (13.9%) had PDR.

The remaining risk non-occupational exposures, such as body piercing, acupuncture, surgery, and endoscopic/colonoscopic corresponded to 12.6%, 12.5%, 13.4%, and 12.6%

case of PDR, respectively. No subjects who had been an inmate, throughout a lifetime presented PDR. The prevalence of PDR by disclosed risk factors is represented in table 2.

Virologic HIV-1 characteristics during the period of donation

During the ten years study period, HIV subtype B was the most prevalent genotype, 369 (73.2%), followed by non-B sub-types 107 (21.2%), and 28 (5.6%) of recombinants. Also, small increases in subtype D (from 0.3% to 2%) and recombinant subtypes (from 4% to 8%) were observed. Subtype A was identified among one (0.3%) participant during REDS-II and was not detected during REDS-III. In the opposite direction, subtype G was not present among participants from REDS-II; however, it was detected in two (1%) participants during REDS-III. HIV subtype differences were not significant throughout the period studied. Table 3 shows the HIV genotype characteristic during the donation period.

A decrease in the frequency of drug resistance mutation for protease inhibitor from 5.9% to 3%, followed by a modest increase for NRTI (4.9% to 5.5%) and NNRTI (7.6% to 8%) was observed. Considering drug class mutations, frequencies for PIs, NRTI, and NNRTI did not change between the different analyzed periods (Figure 2). NNRTI resistance was observed in 39 (7.7%) donors, while NRTI was found in 26 (5.1%) and protease inhibitors, 24 (4.7%) (Supplemental figure 1).

HIV subtype and association with HIV risk factors and behavior

The frequency of HIV subtypes varied according to the HIV risk factors and sexual behavior. For each subtype, more than half had surgery (ever), more than 20% had tattoos (ever), and more than 14% had body piercing (ever). Being a sexual partner of MSM during their lifetime was the more frequent sexual behavior reported, and was found among 41.5% participants with B subtype, 40.2% with Non-B subtypes, and 32.1% with recombinant subtypes. The majority of participants (69.5%) reported having had one to three sexual partners in the last 12 months independent of the subtype. There was no statistically significant difference among risk exposures, sexual behaviors, and HIV subtypes (Table S1).

DISCUSSION

We evaluated more than five hundred HIV-positive blood donors at four large Brazilian blood centers across a ten-year timeframe. The highest PDR was found in male donors who reported being sexual partners of MSM during the last 12 months. Our data suggest that the drug resistance mutations remained stable over the study period among the blood donation centers.

The overall PDR prevalence found in our study was consistent with PDR found in previous reports among recently diagnosed ART-naïve people living with HIV in Brazil between 2013 and 2015 (9), and among broader populations of HIV positive blood donors in Brazil, China and Spain (17,18).

We did not find significant differences in demographics, HIV behavior risk factors, or HIV genotypes when comparing persons with and without PDR. Additionally, the HIV PDR rate

remained stable during the study period, when compared with the previous study report, in which 11.8% of PDR was found (13).

Blood centers located in the Southeast part of the country had accounted for a two-fold higher PDR prevalence compared to the Northeast (Recife). Currently, São Paulo state is responsible for more than 40% of patients receiving antiretroviral treatment in Brazil, and nearly a quarter of the people living with HIV on ART live in this city (9). The city of São Paulo, the capital of the most populous state in the country, was the first to introduce ART treatment in the 90s (9). Therefore, due to the sequential use of ART and broader use of unboosted protease inhibitors in the earliest years of the national HIV treatment program, it would be expected that a higher proportion of patients experiencing virological failure, and consequently transmitting HIV drug resistance would be found (9,19). However, the PDR rate was similar to 19.4% previously reported (13). Except for the Central-West region where the PDR prevalence in ART-naïve population was found to be lower (6.8%), the PDR rates found in our sample were somewhat similar to the overall 9.5% PDR prevalence observed in a nationwide observational study (9).

In line with previous Brazilian studies (9), genotype B was the most prevalent clade, reflecting the foundation of the HIV epidemic in the Brazilian population (20). We observed an increased frequency among the recombinant clades over the study period that potentially can reflect what is happening in the general population, as a result of lower ART adherence, mainly among young adults (19). In Brazil, there has been an increase in the genetic diversity of the epidemic when compared with other regions worldwide. In our country, unique recombinants were described in addition to the co-circulation of different HIV-1 clades (21).

Continuous surveillance of genotypes is needed to corroborate our findings (19). Overall, mutations leading to resistance appear to be similar among subtypes. Still, certain mutations seem to occur more frequently in non-B subtypes, in particular, consequently influencing first-line ART treatment choices (22).

Contemporary information on genotyping, drug resistance and the spread of HIVDR strains trends is difficult to obtain, particularly in low/middle-income countries, and the World Health Organization (WHO) suggested several monitoring activities to improve surveillance (2,23). Additionally, preventive measures such as post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) may have their efficacy jeopardized by drug resistance. As test-and-start ART strategies are considered, data to support optimal first-line therapy are needed worldwide (2). Supplementary resistance data extracted from variable samples and analysis of their associated HIV risk factors for PDR are lacking, although necessary to show a reliable picture of the current HIV epidemic status and strict public policies to mitigate HIV epidemics.

This study was completed before PrEP was offered as a Brazilian public health strategy in December 2017 and may serve as a baseline to understand the impact of this policy on drug resistance soon. In Brazil, PrEP is freely available for MSM and transgender women, and

there are concerns that it may decrease the capacity of the tests used in the blood centers to identify infected individuals, and HIV breakthrough infection should occur (24).

We recognize some limitations. First, our convenience sample represents a population that came for blood donation, with an expected low HIV-risk self-perception, not entirely typical of the general population or high-risk key populations. However, given the diversity and relative proportions of the range of self-disclosed risk behaviors, the sample may be, by proxy, characteristic of the HIV infected population in the communities in Brazil where the hemocenters are located. Second, we did not successfully amplify one out of ten HIV-positives samples, representing a gap in our understanding of subtypes and drug resistance. Unamplifiable samples are likely to have lower viral loads, and we were not able to define the specific reasons why samples where unsuccessfully amplified. We did not run a multi-variate analysis to better approach associations. We considerer that our study did not present the right design, sample size, nor power for this purpose. We assessed previous ART exposure by a self-reported questionnaire. If persons stated there were on ART, we did not include their samples in the PDR group, but we could not substantiate the treatment status of any participant. Finally, we did not evaluate mutations of resistance for integrase inhibitor class among these naive HIV infected blood donors. However, this drug class, represented mainly by dolutegravir, was approved for experienced patients since the end of 2015, and as first-line therapy since 2017.

We conclude that ongoing efforts to conduct molecular surveillance on HIV infections in the blood donor population can contribute to an improved understanding of HIV genotype and drug resistance distributions in Brazil. HIV positive blood donors are an informative source of samples for drug resistance monitoring, and the diversity of risks suggests that donor data can be used to gain an impression of what is happening in the broader population as a whole (25). The role of blood donors for HIV surveillance will vary in different jurisdictions by epidemiology and donor criteria compliance. For public health, donor data merged with other surveillance national-wide databases can be employed for phylogenetic/phylodynamic analyses to understand better epidemics trends, dynamics of drug-resistance spread relative to current primary ART regimens and to provide insights into the success of policies to control HIV epidemics. This may be particularly important with the advent of the widespread availability of PEP and PrEP, and our data serve as a baseline in blood donors before the availability of PrEP. Blood center networks can share information about the national distribution of HIV infection through the different regions of Brazil, which may potentially improve the public health measures on HIV prevention and control.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ART	Antiretroviral therapy
ACASI	Audio computer-assisted structured interview
DRMs	Drug resistance mutations
HAART	Highly active antiretroviral treatment
HIVDR	HIV drug resistance
PDR	Primary HIV drug resistance
PI	protease inhibitors
NRTI	nucleoside reverse transcriptase inhibitor
NNRTI	non-nucleoside reverse transcriptase inhibitor
PEP	Post-exposure prophylaxis
PrEP	Pre-exposure prophylaxis

REFERENCES

1. Gupta RK, Gregson J, Parkin N et al. HIV-1 drug resistance before initiation or re-initiation of first-line antiretroviral therapy in low-income and middle-income countries: a systematic review and meta-regression analysis. Lancet Infect Dis 2018;18:346–355. [PubMed: 29198909]
2. Godfrey C, Thigpen MC, Crawford KW et al. Global HIV Antiretroviral Drug Resistance: A Perspective and Report of a National Institute of Allergy and Infectious Diseases Consultation. J Infect Dis 2017;216:S798–S800. [PubMed: 28973412]
3. Organization WH. HIV Drug Resistance Report, 2019. (WHO/CDS/HIV/19.21). License: CC BY-NC-SA 3.0 IGO. ed, 2019.
4. Hamers RL, Schuurman R, Sigaloff KC et al. Effect of pretreatment HIV-1 drug resistance on immunological, virological, and drug-resistance outcomes of first-line antiretroviral treatment in sub-Saharan Africa: a multicentre cohort study. Lancet Infect Dis 2012;12:307–17. [PubMed: 22036233]

5. Organization WH. HIV drug resistance report 2017. License: CC BY-NC-SA 3.0 IGO. ed. Geneva, 2017.
6. Brindeiro RM, Diaz RS, Sabino EC et al. Brazilian Network for HIV Drug Resistance Surveillance (HIV-BResNet): a survey of chronically infected individuals. AIDS 2003;17:1063–9. [PubMed: 12700457]
7. Inocencio LA, Pereira AA, Sucupira MC et al. Brazilian Network for HIV Drug Resistance Surveillance: a survey of individuals recently diagnosed with HIV. J Int AIDS Soc 2009;12:20. [PubMed: 19765271]
8. Ferreira ACG, Coelho LE, Grinsztejn E et al. Transmitted drug resistance in patients with acute/recent HIV infection in Brazil. Braz J Infect Dis 2017;21:396–401. [PubMed: 28539254]
9. Arruda MB, Boullosa LT, Cardoso CC et al. Brazilian network for HIV Drug Resistance Surveillance (HIV-BresNet): a survey of treatment-naive individuals. J Int AIDS Soc 2018;21.
10. Kleinman S, King MR, Busch MP et al. The National Heart, Lung, and Blood Institute retrovirus epidemiology donor studies (Retrovirus Epidemiology Donor Study and Retrovirus Epidemiology Donor Study-II): twenty years of research to advance blood product safety and availability. Transfus Med Rev 2012;26:281–304, 304.e1–2. [PubMed: 22633182]
11. de Almeida-Neto C, Goncalez TT, Birch RJ et al. Risk factors for human immunodeficiency virus infection among Brazilian blood donors: a multicentre case-control study using audio computer-assisted structured interviews. Vox Sang 2013;105:91–9. [PubMed: 23517235]
12. Blatyta PF, Custer B, Gonçalez TT et al. Undisclosed human immunodeficiency virus risk factors identified through a computer-based questionnaire program among blood donors in Brazil. Transfusion 2013;53:2734–43. [PubMed: 23521083]
13. Alencar CS, Sabino EC, Carvalho SM et al. HIV genotypes and primary drug resistance among HIV-seropositive blood donors in Brazil: role of infected blood donors as sentinel populations for molecular surveillance of HIV. J Acquir Immune Defic Syndr 2013;63:387–92. [PubMed: 23507660]
14. Barreto CC, Nishyia A, Araujo LV, Ferreira JE, Busch MP, Sabino EC. Trends in antiretroviral drug resistance and clade distributions among HIV-1--infected blood donors in Sao Paulo, Brazil. J Acquir Immune Defic Syndr 2006;41:338–41. [PubMed: 16540943]
15. Bennett DE, Camacho RJ, Otelea D et al. Drug resistance mutations for surveillance of transmitted HIV-1 drug-resistance: 2009 update. PloS one 2009;4:e4724. [PubMed: 19266092]
16. Liu TF, Shafer RW. Web resources for HIV type 1 genotypic-resistance test interpretation. Clin Infect Dis 2006;42:1608–18. [PubMed: 16652319]
17. Bes M, Piron M, Casamitjana N et al. Epidemiological trends of HIV-1 infection in blood donors from Catalonia, Spain (2005–2014). Transfusion 2017;57:2164–2173. [PubMed: 28681400]
18. Zeng P, Liu Y, He M et al. The infection staging and profile of genotypic distribution and drug resistance mutation among the human immunodeficiency virus-1 infected blood donors from five Chinese blood centers, 2012–2014. PLoS One 2017;12:e0179328.
19. Diaz RS, Inocêncio LA, Sucupira MC et al. The Virological and Immunological Characteristics of the HIV-1-Infected Population in Brazil: From Initial Diagnosis to Impact of Antiretroviral Use. PLoS One 2015;10:e0139677.
20. Soares MA, De Oliveira T, Brindeiro RM et al. A specific subtype C of human immunodeficiency virus type 1 circulates in Brazil. AIDS 2003;17:11–21. [PubMed: 12478065]
21. Sabino EC, Shpaer EG, Morgado MG et al. Identification of human immunodeficiency virus type 1 envelope genes recombinant between subtypes B and F in two epidemiologically linked individuals from Brazil. J Virol 1994;68:6340–6. [PubMed: 8083973]
22. Taylor BS, Hammer SM. The challenge of HIV-1 subtype diversity. N Engl J Med 2008;359:1965–6. [PubMed: 18971501]
23. Jordan MR, Bennett DE, Wainberg MA et al. Update on World Health Organization HIV drug resistance prevention and assessment strategy: 2004–2011. Clin Infect Dis 2012;54 Suppl 4:S245–9. [PubMed: 22544182]
24. Seed CR, Yang H, Lee JF. Blood safety implications of donors using HIV pre-exposure prophylaxis. Vox Sang 2017;112:473–476. [PubMed: 28370177]

25. Riemenschneider M, Hummel T, Heider D. SHIVA - a web application for drug resistance and tropism testing in HIV. BMC Bioinformatics 2016;17:314. [PubMed: 27549230]

Figure 1 -
Locations of REDS-Brazil participating blood centers

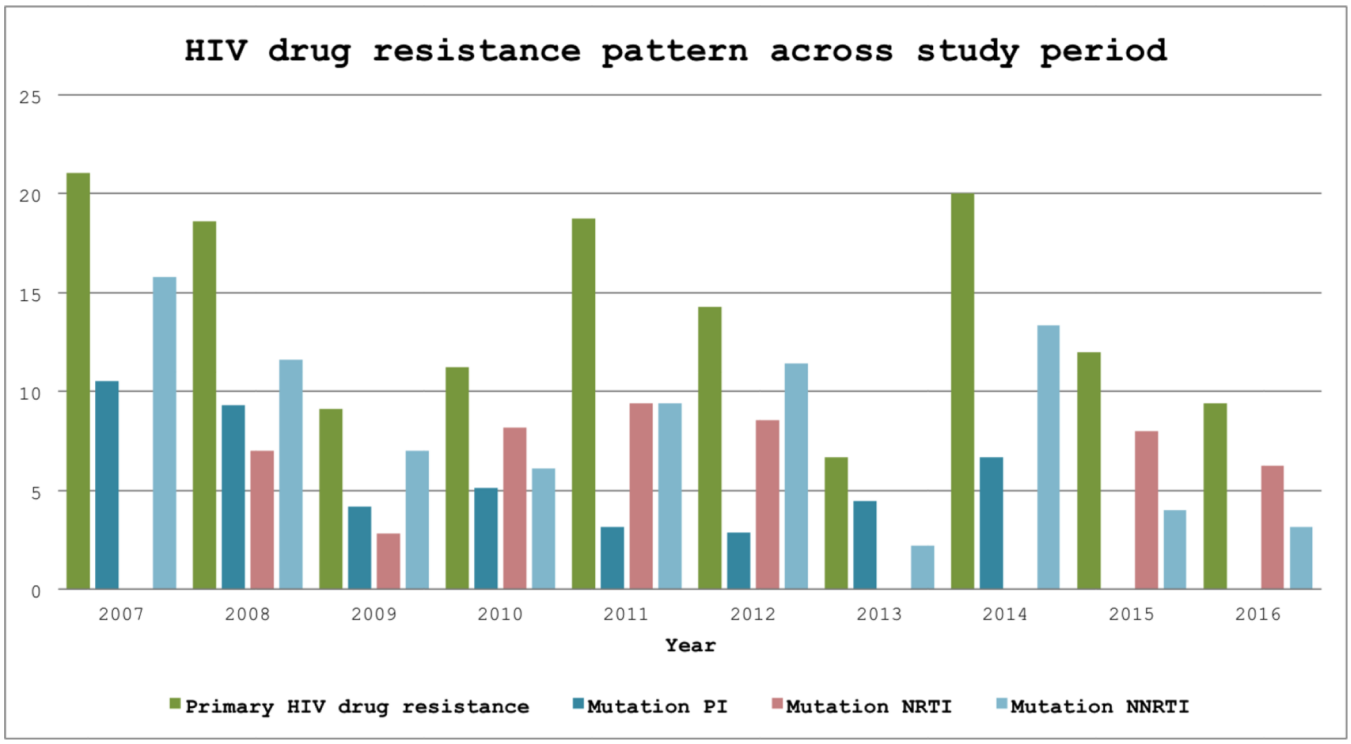

Figure 2 -
Histograms of drug classes resistance by year

Table 1.

Demographic characteristics, sexual orientation and marital status among 504 blood donors from 2007 – 2017

Demographic characteristics, sexual orientation, and marital status	REDS (2007 – 2017) HIV infected blood donors n=504	HIV infected donors with resistance n=64	p-value
	n (%)	n (%)	
Site			
Hemope	181 (35.9)	15 (23.4)	
Hemominas	68 (13.5)	11 (17.2)	0.1
FPS	95 (18.8)	17 (26.6)	
Hemorio	160 (31.7)	21(32.8)	
Donor Status *			
First Time	220 (43.7)	26 (40.6)	
Repeat	260 (51.6)	33 (51.6)	0.7
Unknown	24 (4.8)	5 (7.8)	
Donation Type *			
Community	303 (60.1)	39 (60.9)	
Replacement	176 (34.9)	20 (31.3)	0.5
Unknown	25 (5.0)	5 (7.8)	
Gender			
Male	408 (81.0)	53 (82.8)	0.7
Female	96 (19.0)	11 (17.2)	
Age (years)			
18 – 25	130 (25.8)	19 (29.7)	
26 – 30	108 (21.4)	14 (21.9)	0.3
31 – 39	149 (29.6)	22 (34.4)	
40 +	117 (23.2)	9 (14.1)	
Education level			
Never been to school	3 (0.6)	1 (1.6)	
Elementary school	154 (30.6)	18 (28.1)	
High/Technical school	248 (49.2)	29 (45.3)	0.3
College or more	97 (19.2)	16 (25.0)	
Dońt know/ refused	2 (0.4)	0 (0.0)	
Education level B			
≤ Elementary School	157 (31.2)	19 (29.7)	
> Elementary School	345 (68.5)	45 (70.3)	0.8
Don‘t know/ refused	2 (0.4)	0 (0.0)	
Sexual Orientation *			
Heterosexual	286 (56.7)	32 (50.0)	
Bisexual	96 (19.0)	14 (21.9)	0.3
Homosexual	107 (21.2)	17 (26.6)	
Refused/Don’t know	15 (3.00)	1 (1.5)	

Demographic characteristics, sexual orientation, and marital status	REDS (2007 – 2017) HIV infected blood donors n=504	HIV infected donors with resistance n=64	p-value
	n (%)	n (%)	
Marital status			
Single, never married	276 (54.8)	39 (60.9)	0.4
Living together, not married	105 (20.8)	14 (21.9)	
Married	74 (14.7)	5 (7.8)	
Divorced/Widowed/Separated	49 (9.7)	6 (9.4)	

*Self-reported

Table 2.

General exposure, sexual and behavior risks among blood donors with evidence of HIV-1 primary antiretroviral resistance

HIV REPORTED RISKS	Total	Primary HIV resistance[†] n=64	p-value[*]
	n	n (%)	
Occupational Exposure			
exposure to needle or body fluids, ever	67	6 (9.0)	0.4
Non Occupational Exposure			
Body piercing,ever	111	14 (12.6)	0.9
Tattoos,ever	125	19 (15.2)	0.3
Acunpuncture,ever	32	4 (12.5)	0.9
Surgery procedure, ever	328	44 (13.4)	0.4
Endoscopic/colonoscopic procedure, ever	103	13 (12.6)	0.9
PWID[‡] ever (injected any drugs or non-prescription substances)	79	11 (13.9)	0.7
Blood transfusion, ever	19	3 (15.8)	0.7
Inmate, ever	11	0 (0.0)	0.4
Sexual exposure			
SEX with			
Inmate, ever	31	4 (12.9)	0.8
blood transfusion recipient, ever	24	2 (8.3)	0.8
HIV positive partner, ever	42	4 (9.5)	0.6
HIV positive partner taking ART, ever	42	4 (9.5)	0.6
PWID ever	29	4 (13.8)	0.7
person with potential job exposure, ever	51	7 (13.7)	0.8
Sexual partner of MSM[§] - males[*]	162	27 (16.7)	0.1
Sexual partner of MSM[§] - females[*]	3	0 (0.0)	0.9
MSM[§], ever	195	26 (13.3)	0.8
Lifetime number of sex partners			
0	5	1 (20.0)	
1	21	1 (4.8)	
2 – 3	53	6 (11.3)	
4 – 6	104	14 (13.5)	0.6
7 – 10	71	11 (15.5)	
11 – 20	80	15 (18.8)	
21+	69	6 (8.7)	
Number of sex partners, in the last 12 months			
0	20	4 (20.0)	
1	182	17 (9.3)	0.2
2 – 3	168	26 (15.5)	
4 – 6	61	9 (14.8)	

HIV REPORTED RISKS	Total	Primary HIV resistance† n=64	p-value*
	n	n (%)	
7 – 10	23	2 (8.7)	
11+	16	0 (0.0)	

*Last 12 months

†From the sequenced samples n=275 (71.2%)

‡Person who injected drugs or non-prescription substance (PWID)

§Men who have sex with men (MSM)

‖Totals must be less due to missing values

Table 3.

Virologic HIV-1 characteristics by period of donation

Characteristics	REDS-II (2007 – 2011)		REDS-III (2012 – 2017)		Total	p-value**
	n (%)	95% CI	n (%)	95% CI	n	
Genotypes						
B	229 (75.3)	(70.5 – 80.2)	140 (70.0)	(63.6 – 76.4)	369	
Non-B	63 (20.7)	(16.2 – 25.3)	44 (22.0)	(16.3 – 27.7)	107	
A	1 (0.3)	(0.0 – 1.0)	-	-		
C	14 (4.6)	(2.3 – 7.0)	8 (4.0)	(1.3 – 6.7)		0.13
D	1 (0.3)	(0.0 – 1.0)	4 (2.0)	(0.06 – 3.9)		
F/F1	47 (15.5)	(11.4 – 19.5)	30 (15.0)	(10.0 – 19.9)		
G	-	-	2 (1.0)	(0 – 2.4)		
Recombinants	12 (4.0)	(1.8 – 6.1)	16 (8.0)	(4.2 – 11.8)	28	
Resistance						
To NRTI *	15 (4.9)	-	11(5.5)	-	26	0.8
To NNRTI †	23 (7.6)	-	16 (8.0)	-	39	0.8
To PI ‡	18 (5.9)	-	6 (3.0)	-	24	0.1
Any antiretroviral mutation						
SDRMs §	37	12.2%	27	13.5%	64	0.6

*Nucleoside Reverse Transcriptase Inhibitor

†Non-Nucleoside Reverse Transcriptase Inhibitor

‡Protease Inhibitors

§Surveillance Drug Resistance Mutations

**p-value for genotype B, non-B, recombinant by REDS-II/III