Prevalence of HIV-1 infection and associated characteristics in a Brazilian indigenous population: a cross-sectional study

Erica C. S. Schnaufer,[a,i] Marcelo S. Barbosa,[a,i] Michele F. R. Marques,[a] Gabriel T. Brito,[a] Tiago S. Ferreira,[a] Anny D. C. Ribeiro,[a] Anna C. Valiente,[a] Indianara R. Machado,[b,h] Crhistinne C. M. Gonçalves,[c,d] Tayana S. O. Tanaka,[c] Monick L. Guimarães,[g] Suzana M. Ribeiro,[a] Julio Croda,[e,f] and Simone Simionatto[a,*]

[a]Laboratório de Pesquisa em Ciências da Saúde, Universidade Federal da Grande Dourados (UFGD), Dourados, Mato Grosso do Sul, Brazil
[b]Distrito Sanitário Especial Indígena (DSEI), Dourados, Mato Grosso do Sul, Brazil
[c]Universidade Federal do Mato Grosso do Sul (UFMS), Campo Grande, Mato Grosso do Sul, Brazil
[d]Secretaria Estadual de Saúde (SES), Campo Grande, Mato Grosso do Sul, Brazil
[e]Fundação Oswaldo Cruz (FIOCRUZ), Campo Grande, Mato Grosso do Sul, Brazil
[f]Faculdade de Medicina (FAMED), Universidade Federal do Mato Grosso do Sul, Campo Grande, Mato Grosso do Sul, Brazil
[g]Laboratório de AIDS e Imunologia Molecular, Instituto Oswaldo Cruz, Fundação Oswaldo Cruz (FIOCRUZ), Rio de Janeiro, Rio de Janeiro, Brazil
[h]Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil

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Summary

Background Despite significant progress in the areas of prevention, diagnosis, and treatment, HIV continues to result in a substantial number of fatalities on a global scale each year. Gaining insights from epidemiological data can prove instrumental in the development of health promotion strategies, particularly within vulnerable populations, such as indigenous groups. Consequently, our study aimed to investigate the prevalence of HIV infection within the indigenous population residing in the second-largest region of Brazil. Additionally, we sought to explore the subtypes of HIV-1 and detect any drug-resistance mutations present within this population.

Methods In this cross-sectional study, we aimed to evaluate the prevalence of HIV-1 infection and explore its associated characteristics within the indigenous population residing in the villages of Jaguapiru and Bororó, located in the Dourados area of Mato Grosso do Sul (MS), Brazil. Blood samples were collected for rapid HIV screening, serological tests, nucleic acid amplification, and HIV subtyping. Additionally, the HIV-1 viral load and CD4+ T lymphocyte count of the people living with HIV (PLHIV) were assessed at the time of recruitment and 24 weeks later.

Findings Out of the 2190 invited individuals, 1927 (88%) were included in this study. The average age of the participants was 34.2 (±13.8) years, with a majority of 74% being female. Moreover, 68.44% of the participants identified themselves as belonging to the Guarani-Kaiowa ethnic group. HIV seroprevalence was 0.93% (18/1927), and 73.22% (1411/1927) were unaware of their serological status. The prevalence of HIV-1 was higher in single indigenous people [10/617 (1.62%)], who received government benefits [14/1021 (1.37%)], had less than five years of formal education [11/685 (1.61%)], had sexual intercourse with users of injectable drugs [2/21 (9.52%)], with history of sexually transmitted infections (STIs) [10/62 (16.2%)] and incarceration [3/62 (4.84%)]. Of 18 positive samples, 44.4% (8/18) were successfully amplified, and HIV-1 subtype C was prevalent. Furthermore, we identified HIV-1 drug resistance mutations in four patients, specifically from the classes of Protease Inhibitor, Nucleoside Reverse Transcriptase Inhibitor, and Non-Nucleoside Reverse Transcriptase Inhibitor. Notably, three of these patients exhibited a high viral load even after 24 weeks of undergoing antiretroviral therapy. Out of the 18 PLHIV, 66.66% (12/18) had a viral load below 1000 copies/mL, while 50% (9/18) had a CD4+ T lymphocytes count greater than 350 cells/mL after 24 weeks of treatment.

Interpretation Despite the concerted efforts to control HIV infection, the prevalence observed in the indigenous population under study surpassed that reported in other Brazilian indigenous groups. This disparity highlights the disproportionate impact of the disease on this particular group. The detection of drug-resistance mutations further emphasizes the critical need to expand diagnostic coverage, closely monitor treatment strategies, and maintain ongoing molecular surveillance. These measures are imperative for enhancing HIV management within this vulnerable population.

*Corresponding author. Rodovia Dourados/Itahum, Km 12 - Unidade II, Caixa Postal: 364; Cep: 79.804-970, Brazil.
E-mail address: simonesimionatto@ufgd.edu.br (S. Simionatto).
[i]Both authors have equally contributed to this work.

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Keywords: Human immunodeficiency virus; Vulnerable population; Sexually transmitted infections

Research in context

Evidence before this study

The vulnerability of indigenous populations is well-defined in the literature. However, there is limited documented evidence of the prevalence of HIV and its characteristics in the Brazilian indigenous population. Reliable and comparable estimates over time of HIV prevalence are essential for making public health decisions, defining research priorities, and evaluating the impact of disease prevention and infection control programs. We reviewed articles published in the Web of Science, Medline-PubMed, and SCIELO from January 02, 2000 to May 28, 2023, using a combination of the keywords "HIV in Indigenous," "Factor associated with HIV," "HIV prevalence," and "HIV treatment." Only 14 articles addressing HIV in indigenous people were returned. Evidence suggests that HIV prevalence has substantially increased in the past decades, especially in low- and middle-income countries. HIV transmission seems to be affected by socioeconomic and behavioral factors, including education, living conditions, access to healthcare, and contact with other populations. While limited, evidence suggests that the transmission of HIV may affect other sexually transmitted infections (IST) spread.

Added value of this study

We report the prevalence of HIV infection within the Brazilian indigenous population. We also described the sociodemographic characteristics of this population, HIV-1 subtyping, and drug resistance mutations commonly related to a reduction in the susceptibility to anti-retroviral therapy. Finally, we highlighted that HIV surveillance and diagnosis capability are inadequate, and access to health services is restricted for the indigenous population of Brazil.

Implications of all the available evidence

These findings emphasize the need to expand diagnostic coverage and improve health care in the indigenous population. The evidence might contribute to a better understanding of the viral transmission dynamics and the behavior of these populations in the face of an HIV-1 infection. In addition, the present study allowed us to identify viral diversity and resistance mutations commonly related to a reduction in the susceptibility to anti-retroviral therapy. This helps decision-makers create more effective measures to protect and preserve the indigenous population, which is pivotal for epidemic and pandemic preparedness.

Introduction

Globally, there are 37.7 million individuals living with Human immunodeficiency virus (HIV) or *AIDS*, and 36.3 million people have died from AIDS-related illnesses since the beginning of the epidemic. Despite advancements in prevention, diagnosis, and treatment, HIV continues to cause significant fatalities worldwide.[1] The widespread availability of antiretroviral therapy in Brazilian public health services has contributed to reducing morbidity, mortality, and virus transmission.[2,3] Since 1997, new HIV infections have decreased by 40% globally, and HIV-related deaths have declined by one-third.[4] However, in Brazil, the number of new infections exceeded 40,000 in 2021.[5]

HIV infection predominantly affects marginalized populations due to individual, cultural, and economic factors that render them vulnerable. Indigenous communities are particularly susceptible to HIV exposure and infection.[6] These populations face substantial social, economic, and health disparities compared to the non-indigenous population, often stemming from colonization and delayed economic development.[1] These factors hinder and restrict their access to healthcare services, thus affecting their overall health outcomes.[7] The HIV prevalence among indigenous populations worldwide is three times higher than the general population.[4] In Brazil, the HIV prevalence among indigenous people in the Amazon region was reported as 0.13% in 2012.[8]

The Dourados indigenous area is the second most populous in Brazil.[9] Located near the country's borders, this community experiences significant drug trafficking activities and migratory flows. Most of the population resides in close proximity to the city and is influenced by non-indigenous urban dwellers who have easy access to them. Additionally, indigenous individuals frequently venture into non-indigenous territories, which impacts their community dynamics and exposes them to risks such as alcohol consumption and engagement in sex work.[10] Understanding the epidemiological data on

infectious diseases within indigenous communities can aid in the development of health promotion strategies that consider their cultural and social contexts.[11] Hence, this study aimed to assess the prevalence of HIV infection among the indigenous population in Dourados/MS. Furthermore, we investigated HIV-1 subtyping and the presence of drug-resistance mutations.

Methods

Study setting and population

Mato Grosso do Sul, located in the Central-West region of Brazil, shares its borders with Paraguay and Bolivia. It is home to the second-largest indigenous population in Brazil, comprising 73,181 individuals.[9] The primary ethnic groups within this population are Guarani-Kaiowá, Terena, and Guarani-Nhandeva, accounting for 96% of the indigenous population in the state. Among these, the municipality of Dourados encompasses the largest peri-urban indigenous area in Brazil, housing approximately 15,000 people (Fig. 1). Notably, Bororó and Jaguapirú villages are inhabited by 13,094 individuals, constituting 87.29% of the population in this area.[9]

We performed a cross-sectional study of the indigenous population of Dourados from September 2017 to March 2020. The primary objective of this research was to determine the current HIV prevalence among the indigenous population in Brazil. Additionally, a secondary aim was to perform molecular characterization of HIV-1. To calculate the required sample size, the HIV prevalence rate (0.6%) for the general Brazilian population, a 95% confidence interval (CI), and a precision of 0.35% were considered. This calculation yielded a minimum sample size of 1675 individuals. To account for potential attrition, an additional 20% of participants were recruited, resulting in a total sample size of 2010 individuals.

The study included indigenous individuals aged 18 years or older who provided written informed consent and resided in the indigenous area of Dourados/MS. Participation involved an interview and the provision of a biological sample. The study encompassed ten clusters that covered the two villages, and convenience sampling was employed to select participants (Fig. 1). The clusters were situated in close proximity to primary healthcare units and were subdivided into microregions based on

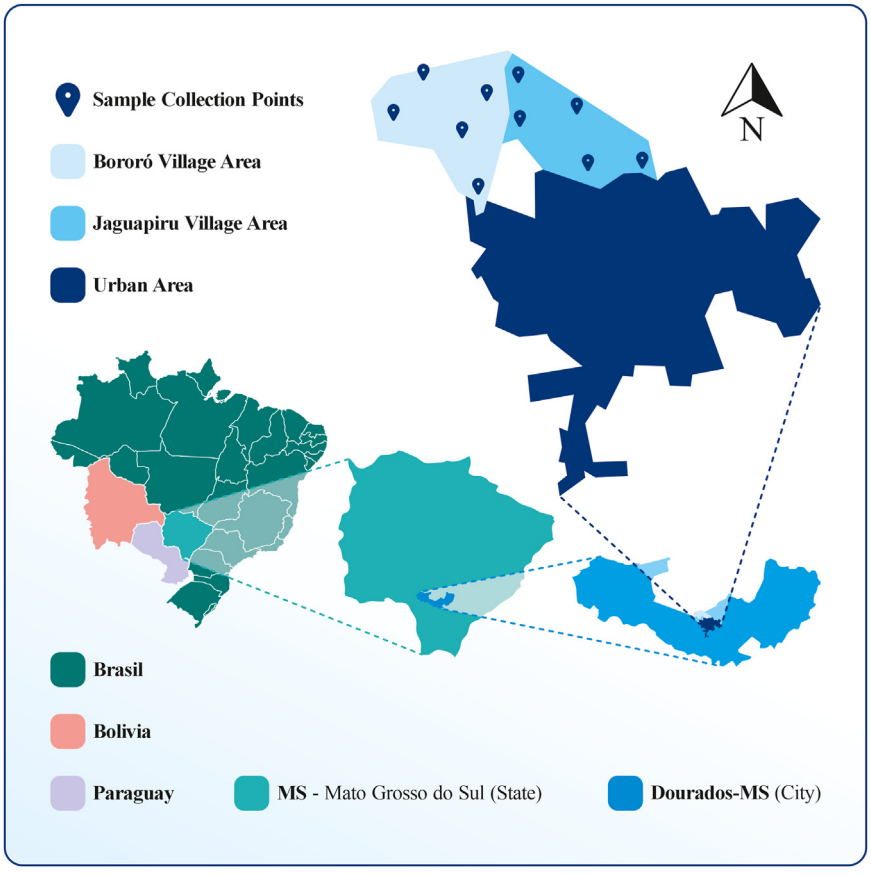

Fig. 1: The geographical position of the indigenous area of Dourados, Mato Grosso do Sul (MS), Brazil. Sample and data collection points are presented. Source: Author compilation (2022).

the number of individuals served. Recruitment was conducted in person through multiple visits to the clusters, with the assistance of indigenous community health teams. To ensure a diverse population, a numeric balance was maintained across each region. A total of 2190 indigenous individuals were invited to participate in the study.

Data and blood collection

The study consisted of the following strategy to collect data: 1) interview with a standardized questionnaire about demographic and sexual behavior, 2) collection of blood samples to perform serological and molecular tests, and 3) medical charts of people living with HIV (PLHIV) to evaluate the treatment outcomes. The participants underwent interviews using a standardized questionnaire that covered various aspects, including age, gender, marital status, educational level, history of drug use, sexual history, previous blood transfusions and STIs, tattoos, prior surgeries, and incarceration. Participants also self-reported their villages (Bororó and Jaguapirú), gender, and ethnicities. To aid in translation, the interviews were conducted with the assistance of health teams consisting of native indigenous individuals. Following the application of appropriate antiseptic measures, peripheral venous blood samples were collected from all participants using a vacuum tube system with a volume of 10 mL. These samples were then stored in refrigerated thermal boxes and transported to the University's Laboratory of Health Sciences Research. Within a maximum of 2 h after collection, the samples were processed to separate the serum and whole blood components and subsequently stored at a temperature of –20 °C.

Serological tests

To determine the serological profile for HIV, rapid tests were employed. For HIV-1, the Rapid Check HIV 1-2TM kit (Federal University of Espírito Santo, Vitória, Brazil) was utilized.[12] Furthermore, for positive samples, the Rapid test Bio-Manguinhos HIV ½^{TM} (Bio-Manguinhos, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil) was conducted, following the recommendations of the Ministry of Health.[12] Positive and undetermined samples were subsequently confirmed through immunoblot analysis, specifically Western blot, using a fresh blood sample.[13] This blood sample was drawn 30 days after the initial collection within the indigenous area. Individual participants received their serological test results in person from a physician who specialized in infectious diseases. If a participant tested positive, appropriate treatment was prescribed. All newly identified HIV cases in the study were reported to the Notifiable Disease Database, and treatment was provided by the HIV/AIDS Specialized Assistance Service (SAE) associated with the municipality of Dourados in the state of Mato Grosso do Sul (MS).

Molecular analysis

At the time of study recruitment, all HIV-positive samples underwent nucleic acid extraction utilizing the QIAamp DNA Blood Mini Kit (Qiagen, Hilden, Germany). The polymerase (*pol*) gene, specifically the protease/reverse transcriptase (PR/RT) gene region, was partially amplified through a nested polymerase chain reaction (Nested-PCR) employing a combination of primers.[14] The resulting amplified products (1261 bp) were subjected to agarose gel electrophoresis (1%) for analysis. To purify the DNA, the ExoSAP-IT PCR Product Cleanup Reagent (Thermo Fisher Scientific, Waltham, MA, USA) was employed according to the manufacturer's recommendations. Subsequently, the purified DNA was subjected to sequencing using the Big Dye Terminator Cycle Sequencing Ready Reaction kit v.3.1 (Applied Biosystems, CA, United States) and processed utilizing Sanger's method in an automated ABI 3130xl sequencer (Applied Biosystems).

The sequences were edited using DNASTAR software and subsequently aligned with sequences from the Los Alamos HIV Sequence Database. This alignment was performed using the Clustal W program, which is implemented in MEGA 7.0 software.[15] To determine the subtypes of the sequences, the REGA HIV Subtyping tool was utilized, and the results were further confirmed through phylogenetic analysis and Simplot v. 3.5.1.[15] The phylogenetic tree was constructed using the Neighbor-Joining (NJ) method,[16] and the evolutionary distances were computed using the Tamura-Nei model.[17] To explore the presence of transmitted and acquired drug resistance, the sequences were submitted to the Stanford HIV Database for Transmitted DRM [TDRM/Calibrated Population Resistance Tool (CPR Tool)] Version 6.0.[18] Additionally, the Genotypic Resistance Interpretation Algorithm (HIVdb algorithm)[19] was employed to provide further insights into drug resistance patterns.

HIV treatment and follow-up

To assess the effectiveness of antiretroviral therapy in individuals living with HIV (PLHIV), we analyzed data on viral load and CD4+ T lymphocyte counts obtained from the HIV/AIDS Specialized Assistance Service (SAE) in the municipality of Dourados, Mato Grosso do Sul state (MS). Viral load was measured using the Abbott real-time assay, while CD4+ T lymphocyte counts were determined by flow cytometry using the Facscalibur-Multitest method.[20] These measurements were taken at the time of recruitment and after 24 weeks of treatment at the HIV/AIDS-SAE healthcare facility. Participants who consistently received ART and attended all follow-up appointments during the 24-week period at the HIV/AIDS-SAE in Dourados, MS were classified as receiving regular treatment.[21,22]

Data analysis

To ensure quality control, the questionnaire data and results of HIV tests underwent a double registration and

verification process. Cases with missing data were excluded from the analysis, as they were deemed questionnaire failures. The collected data were subsequently entered into the Research Electronic Data Capture (REDCap) program. For the univariate analysis, the SAS version 9.2 software (SAS Institute, Cary, NC, USA) was utilized. This involved descriptive analyses of sociodemographic data, behavioral characteristics, and the frequency of HIV. The continuous variable (age) was presented as the median and standard deviation, while patients' demographic data were expressed as percentages with 95% confidence intervals (95% CI). Group comparisons were conducted using Pearson's chi-square or Fisher's exact tests. To assess the association of risk factors with HIV prevalence, univariate odds ratios with corresponding 95% CIs were calculated based on 2 × 2 contingency tables. The Wald method was employed to derive the 95% CIs. For multinomial variables, the reference category was chosen as the first category. Statistical significance was defined as a probability (P) value of 0.05 or less.

Ethics approval

The study involving human participants was reviewed and approved by the Brazilian Research Ethics Committee (CONEP), an ethics Committee on Human Research, protocol number 2.000.496. The participants provided their written informed consent to participate in this study. All experiments were conducted in accordance with the relevant guidelines and regulations, following the guidelines set forth by CONEP. Confidentiality and the right to leave the study at any time were guaranteed to all participants.

Role of funding

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Results

A total of 2190 individuals were invited, and 88% (1927/2190) were included in this study. Of the 2190 indigenous people invited, 8.95% (196/2190) declined, and 3.05% (67/2190) were missing (Fig. 2). The prevalence of HIV-1 infection was 0.93% (18/1927), and 73.22% (1411/1927) of the participants had never tested for HIV, hepatitis, or syphilis. The median age was 34 years; 74.16% (1429/1927) were females, and 53.45% (1030/1927) were from Bororó village. Most of them, 68.41% (1319/1927), stated that they were of Guarani-Kaiowá ethnicity, 52.41% (1021/1927) received government benefits, and 64.45% (1242) had more than four years of education (Table 1).

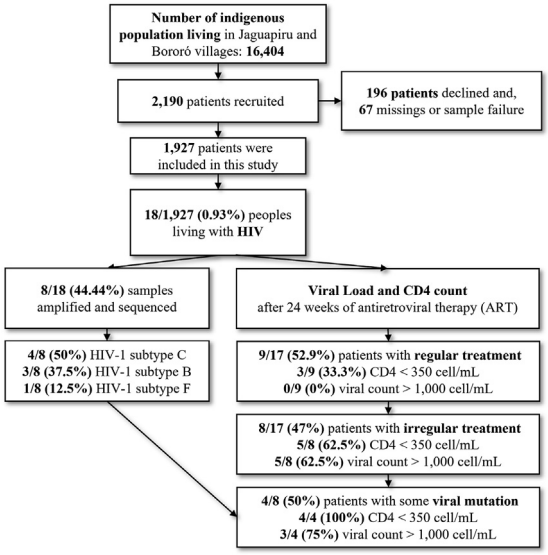

Fig. 2: Flow chart of the study design, screening process, the number of human immunodeficiency virus (HIV) cases detected, and sample subtyping.

In the univariate analysis, several variables were found to be associated with HIV. A history of alcohol use was reported by 27.61% of participants (532/1927), illicit drug use by 4% (77/1927), and STIs by 3.21% (62/1927). Other factors associated with HIV prevalence included being single among indigenous individuals (1.62%) [OR: 2.65 (95% CI: 1.05–6.82)], having a family income between 244 and 488 USD (1.17%) [OR: 2.98 (95% CI: 1.85–5.53)], receiving government benefits (1.37%) [OR: 3.1 (95% CI: 1.02–9.40)], having less than 4 years of formal education (1.61%) [OR: 2.84 (95% CI: 1.11–7.39)], having a history of previous STI testing (2.52%) [OR: 7.26 (95% CI: 2.57–20.48)], a history of incarceration (4.8, 4%) [OR: 6.02 (95% CI: 1.76–22.25)], engaging in sexual intercourse with injectable drug users (9.52%) [OR: 11.34 (95% CI: 2.67–57.88)], and having a history of STIs (16.12%) [OR: 37.6 (95% CI: 14.34–98.54)] (Table 1).

Nested PCR targeting the PR/RT region successfully amplified 44.45% (8/18) of the samples. Among the amplified samples, subtype C was identified in 50% (4/8), subtype B in 37.5% (3/8), and subtype F in 12.5% (1/8) of the patients (Figs. 2 and 3). Notably, seven samples (7/10) that were not amplified had viral loads below 50 copies/mL. HIV-1 recombinant forms were not identified. Seven

Variable	n (1,927)	%	HIV 0.93% (18/1927)	95% CI	OR	95% CI	X^2 P
Age	34.2 (±13.8)		40.2 (±13.8)		–	–	–
Gender							
Male	498	25.84	1.41 (7/498)	0.17–3.65	1.83	0.70–4.76	0.21
Female	1429	74.16	0.77 (11/1924)	0.29–1.96			
Village							
Jaguapiru	897	46.55	1.23 (11/897)	0.62–2.84	1.82	0.70–4.71	0.21
Bororo	1030	53.45	0.68 (7/1030)	0.13–1.24			
Ethnicity							
Guarani-Kaiowa	1319	68.44	1.06 (14/1319)	0.58–2.54	1.62	0.53–4.94	0.39[a]
Others	608	31.56	0.66 (4/608)	0.09–1.42			
Marital status							
Single	617	32.02	1.62 (10/617)	0.74–3.49	2.65	1.05–6.82	**0.03**
Married or cohabited	1310	67.98	0.61 (8/1310)	0.23–1.00			
Steady job							
Yes	649	33.68	0.46 (3/649)	0.06–1.37			
No	1278	66.32	1.17 (15/1278)	0.59–2.08	2.53	0.73–8.74	0.12[a]
Familiar monthly incomes (USD)							
<244	1039	53.92	0.29 (3/1039)	0.07–0.96			
>244–488	761	39.49	1.84 (14/761)	0.86–3.09	2.98	1.85–5.53	**0.00**[a]
>488	127	6.59	0.79 (1/127)	0.02–4.68	0.22	0.06–0.84	
Government benefit (Financial assistance)							
Yes	1021	52.98	1.37 (14/1021)	0.80–2.93	3.1	1.02–9.40	**0.02**[a]
No	906	47.02	0.44 (4/906)	0.11–0.77			
Education level							
<4 years	685	35.55	1.61 (11/685)	0.42–3.12	2.84	1.11–7.39	**0.02**
Most of 5 years	1242	64.45	0.56 (7/1242)	0.16–0.93			
People living in the house							
<2 peoples	279	15	3.46 (10/279)	0.68–7.24			
3–5 peoples	1155	59.94	0.43 (5/1155)	0.16–0.93	0.21	0.14–0.86	**0.000**[a]
>6 peoples	493	25.58	0.61 (3/493)	0.12–1.48	0.23	0.15–0.90	
Previously incarceration							
Yes	62	3.22	4.84 (3/62)	0.14–10.47	6.02	1.76–22.25	**0.01**[a]
No	1865	96.78	0.8 (15/1865)	0.41–1.71			
History of blood transfusion							
Yes	191	9.91	1.57 (3/191)	0.23–3.67	1.82	0.52–6.38	0.26[a]
No	1736	90.09	0.86 (15/1736)	0.52–1.21			
Sexual history							
Steady sexual partner							
Yes	1440	74.73	0.76 (11/1440)	0.39–1.12			
No	487	25.27	1.44 (7/487)	0.31–4.72	1.89	0.73–4.87	0.18
Sexual intercourse with injectable drug user							
Yes	21	1.09	9.52 (2/21)	0.05–6.26	11.34	2.67–57.88	**0.01**[a]
No	1906	98.91	0.84 (16/1906)	0.49–1.28			
Condom use							
Yes	284	14.74	0.7 (2/284)	0.04–2.36			
No	1643	85.26	0.97 (16/1643)	0.60–2.09	1.38	0.32–5.98	0.49[a]
Use drug/alcohol history							
Smoker							
Yes	273	14.17	1.83 (5/273)	1.00–2.67	2.33	0.83–6.65	0.09
No	1654	85.83	0.79 (13/1654)	0.48–1.11			
Alcohol user							
Yes	532	27.61	1.5 (8/532)	1.05–2.96	2.09	0.83–5.39	0.10
No	1395	72.39	0.72 (10/1395)	0.50–0.95			

(Table 1 continues on next page)

Variable	n (1,927)	%	HIV 0.93% (18/1927)	95% CI	OR	95% CI	X^2 P
(Continued from previous page)							
Illicit drug user							
Yes	77	4	1.3 (1//77)	0.17–2.43	1.42	0.18–10.80	0.73[a]
No	1850	96	0.92 (17/1850)	0.72–1.13			
Other risk behaviors							
History of STI							
Yes	62	3.21	16.12 (10/62)	8.07–26.16	37.6	14.34–98.54	**0.000**
No	1865	96.78	0.43 (8/1865)	0.21–0.65			
Previously test for STI							
Yes	516	26.78	2.52 (13/516)	1.72–3.32	7.26	2.57–20.48	**0.000**
No	1411	73.22	0.35 (5/1411)	0.21–0.49			

Familiar income is based in Brazilian Minimal Wage of 2020 (244.00 USD). For multinomial variables ("***Familiar monthly incomes***" and "***People living in the house***", the OR was calculated based on the reference category (category in which the OR and *P* value appear). The 95% confidence interval was performed by Wald method. **OR**: odds ratio; **CI**: confidence interval; **Bold**: variables with *P* values less than 0.05 were considered significant; **Smokers** were defined as those who reported smoking every day, regardless of the amount; **Alcohol users** were defined as those who reported alcohol user, casually or not, regardless of the amount; **Condom use** are participants reported "using condoms in all sexual relations"; **Fixed Sexual Partner** participants who reported having only one sexual partner in the last 2 years; **Occupation** formal employment or unemployment; **Government Benefit** participants who are partially or fully dependent on government financial assistance; **Illicit Drug Users** are participants who reported continuous use of cannabis, crack, or cocaine; **Injectable Drug User** are participants who reported continuous use of injected drugs. [a]Fisher exact test.

Table 1: **Characteristics of the study population with and without HIV.**

different mutations were found in four patients, with four different mutations in the ID-P01 sample. Two concomitant NNRTI mutations were identified in the ID-P03 sample. Drug resistance mutations were detected in samples ID-P01 and ID-P03, which belonged to treatment-naïve patients. In two other samples (ID-P06 and ID-P08), the K103N mutation was identified (Table 2), and these sequences exhibited a high degree of similarity (Fig. 3). Notably, the ID-P06 and ID-P08 samples with drug-resistance mutations were obtained from patients who had previously been diagnosed with HIV prior to their enrollment in this study.

Out of the patients assessed, ten individuals reported being diagnosed with HIV-1 upon enrollment in the study. After 24 weeks of treatment, 66.66% (12/18) patients had a viral load below 1000 copies/mL, and 50% (9/18) showed CD4+ T lymphocytes count above 350 cells/mL. The nine patients with a viral load below 50 copies/mL received regular antiretroviral therapy, and 77.7% (7/9) showed CD4+ T lymphocytes count above 350 cells/mL. Among patients with irregular treatment, 83.33% (5/6) had a viral count above 1000 copies/mL, and 33.3% (2/6) patients had a CD4+ T lymphocytes count greater than 350 cells/mL. Table 2 presents the baseline measurements of CD4+ T lymphocytes (cells/mL) and viral load (copies/mL) for each of the 22 patients.

Discussion

Gaining a more comprehensive understanding of indigenous PLHIV can yield valuable insights for public health systems, leading to improved diagnosis, treatment, and long-term health outcomes. In our study, the prevalence of HIV (0.93%) among indigenous individuals was found to be higher compared to other Brazilian indigenous populations, such as those residing in the Amazon (0.13%).[8] Although the prevalence was similar to indigenous populations in Peru (0.7%)[10] and Colombia (1.02%),[23] it exceeded the prevalence reported for the general Brazilian population (0.6%).[24] The elevated prevalence of HIV within the indigenous population of Dourados/MS may be influenced by various social determinants, including their indigenous status and the subsequent impact on their lives. Indigenous individuals have historically faced stress, social disadvantage, and intergenerational effects on health. Additionally, limited knowledge about HIV has been observed among indigenous communities in Latin America.[25] These factors underscore the vulnerability of this population and can contribute to the higher HIV prevalence observed in our study.

Our findings indicate that the majority of PLHIV had a monthly family income between 244 and 488 USD and less than 4 years of formal education, aligning with reports from other countries.[26] Indigenous individuals experience the consequences of colonialism, widespread racism, and discrimination, which have restricted job opportunities, limited access to education, and resulted in inadequate housing and higher poverty rates.[27] Furthermore, our study suggests that individuals with a history of incarceration were more likely to be infected with HIV compared to indigenous individuals without such a history. A significant proportion of participants in our study reported never having been tested for HIV, which may reflect poor access to public health facilities, stigma, or discrimination. This finding warrants attention since failure to detect, diagnose, treat, and follow up

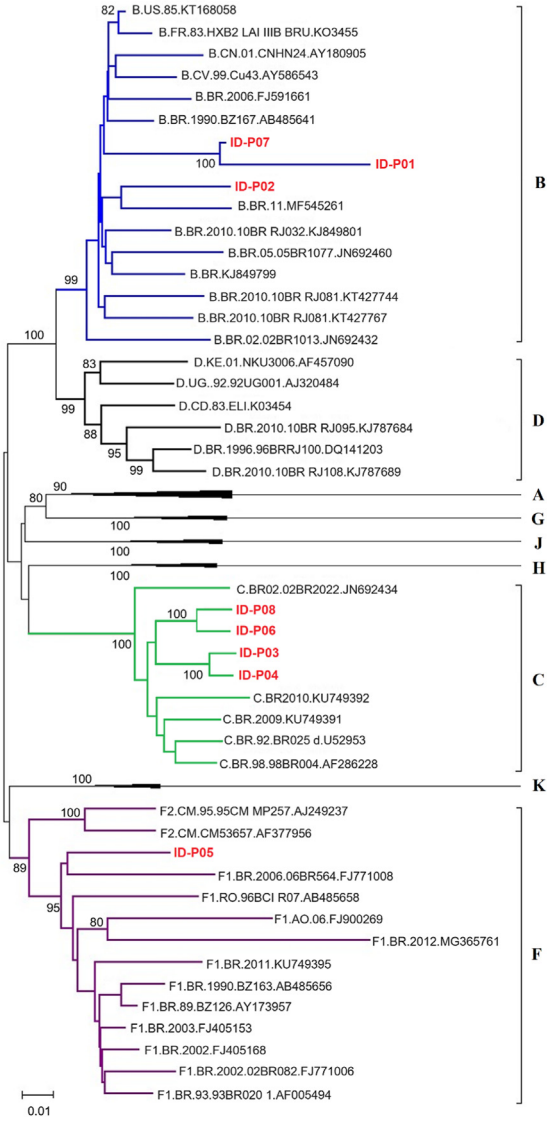

Fig. 3: Phylogenetic tree showing the HIV-1 subtypes from indigenous people and reference sequences in Brazil. Note: The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (1000 replicates) are shown next to the branches. There were 1205 positions in the final dataset. Samples from HIV-1-positive indigenous people are highlighted with triangles. A, B, C, D, F, G, H, J, and K represent the subtypes of HIV-1. Patients who attended the specialized treatment unit for medication withdrawal and follow-up appointments were considered to have regular treatment.

on HIV infections leads to poorer prognoses and increased transmission rates.[28] Therefore, it is crucial to enhance testing opportunities within this population. Additionally, promoting HIV awareness and implementing infection control measures in indigenous communities are vital for increasing testing uptake and monitoring treatment strategies.[29]

Our study revealed that unmarried individuals had a higher HIV prevalence, which may be attributed to risk behaviors associated with a more active sex life.[30] The history of STIs also emerged as a significant factor associated with HIV prevalence, underscoring the importance of addressing the treatment and prevention of these infections as critical strategies for reducing transmission rates. Furthermore, engaging in sexual intercourse with injectable drug users was identified as an additional risk factor. These findings emphasize the necessity of implementing prevention programs that specifically target these issues and promote safe behaviors.

This study presents novel findings regarding the prevalence and characteristics of HIV-1 subtype C in the Midwest region. No HIV recombinant forms were identified in the samples analyzed. However, two patients with high viral load and reduced CD4+ T lymphocyte count after 24 weeks of ART exhibited a resistance mutation (K103N) associated with decreased susceptibility to efavirenz and nevirapine. These findings underscore the importance of molecular surveillance to prevent therapy failures, as these mutations are known to compromise the response to NNRTI-based treatment.[31] Furthermore, the genetic similarity between two samples (ID-P06 and ID-P08) from patients diagnosed with HIV prior to the study's recruitment suggests a possible transmission event between the individuals. Two other treatment-naïve patient samples (ID-P01 and ID-P03) showed drug resistance mutations, indicating transmitted drug resistance. Notably, the presence of different mutations within the same sample (ID-P01) highlights the need to identify HIV mutations in patients experiencing treatment failure to facilitate appropriate therapeutic interventions.

Patients who consistently received regular treatment demonstrated the best therapeutic outcomes, underscoring the efficacy of ART.[32] Although data on viral load and CD4+ T lymphocyte count were lacking for one patient with resistance mutations at recruitment, the remaining patients with drug resistance mutations exhibited CD4+ T lymphocyte counts below 350 cells/mL after 24 weeks of ART. Therefore, investigations into the underlying causes and the determination of alternative treatment strategies are crucial for achieving therapeutic success. Previous studies have described deficiencies in HIV/AIDS treatment among indigenous populations in Colombia.[23] Moreover, patients with CD4+ T lymphocyte counts below 500 cells/mL had a lower likelihood of achieving viral suppression.[6] Notably, a significant decrease in the incidence of STI was observed following treatment among indigenous illicit drug users residing in urban areas.[33] These findings suggest that improved access to healthcare facilities may contribute to overall health improvements.

This study had some limitations. Firstly, there is a possibility of data inaccuracy due to information bias or

Identification	At recruitment of study		24 weeks after recruitment		ART scheme	Regular treatment?	HIV-1 subtype	Drug resistance mutations		
	Viral load (copies/mL)	CD4 count (cells/mL)	Viral load (copies/mL)	CD4 count (cells/mL)				PI	NRTI	NNRTI
ID-P01*	757	303	910	227	Tenofovir + Lamivudine + Efavirenz	Yes	B	G73S**	M184I	V108I/ M230I
ID-P02	Unknown	Unknown	51,282	422	Tenofovir + Lamivudine/Dolutegravir	No	B	–	–	–
ID-P03*	Unknown	Unknown	142	170	Tenofovir + Lamivudine/Dolutegravir	No	C	–	–	Y181C/ H221Y
ID-P04	28,698	98	36,014	149	Tenofovir + Lamivudine/Nevirapine	No	C	–	–	–
ID-P05	406,599	137	336,168	685	Zidovudine + Lamivudine/ Atazanavir/Ritonavir	No	F	–	–	–
ID-P06#	14,407	184	302,236	117	Tenofovir + Lamivudine + Efavirenz	No	C	–	–	K103N
ID-P07	7862	721	<50	796	Tenofovir + Lamivudina/Atazanavir/ Ritonavir	Yes	B	–	–	–
ID-P08#	6710	493	366,483	171	Tenofovir + Lamivudine/Nevirapine	No	C	–	–	K103N
ID-P09	12,927	685	177	227	Tenofovir + Lamivudine/Dolutegravir	No	N/S	N/A	N/A	N/A
ID-P10#	<50	784	<50	496	Tenofovir + Lamivudine/Dolutegravir	No	N/S	N/A	N/A	N/A
ID-P11#	<50	77	<50	22	Tenofovir + Lamivudine/Raltegravir	Yes	N/S	N/A	N/A	N/A
ID-P12#	<50	482	<50	472	Tenofovir + Lamivudine + Efavirenz	Yes	N/S	N/A	N/A	N/A
ID-P13#	<50	579	<50	464	Tenofovir + Lamivudine + Efavirenz/ Tipranavir	Yes	N/S	N/A	N/A	N/A
ID-P14#	<50	315	<50	656	Tenofovir + Lamivudine + Efavirenz	Yes	N/S	N/A	N/A	N/A
ID-P15#	<50	164	<50	425	Tenofovir + Lamivudine + Efavirenz	Yes	N/S	N/A	N/A	N/A
ID-P16#	<50	300	<50	289	Tenofovir + Lamivudine + Efavirenz	Yes	N/S	N/A	N/A	N/A
ID-P17#	<50	476	<50	478	Tenofovir + Lamivudine + Efavirenz	Yes	N/S	N/A	N/A	N/A
ID-P18	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown

Unknown, patient who did not perform the sample collection or did not continue with follow-up. N/S, unamplified sample; N/A, not available; PI, protease inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor **APOBEC mutations; ART, antiretroviral therapy. ART Scheme, antiretroviral therapy used during 24 weeks evaluated in this study. ID-P06#, ID-P08#, ID-P010#, ID-P011#, ID-P012#, ID-P013#, ID-P014#, ID-P015#, ID-P016# and ID-P17, samples from patients with HIV diagnosis before recruitment in this study. ID-P06# and ID-P08#, samples with drug resistance mutations from patients already had a HIV diagnosis before recruitment of this study. ID-P01* and ID-P03*, samples with drug resistance mutations from treatment-naïve patients. Drug resistance mutations analysis was performed with samples collected at recruitment of study. To investigate the presence of transmitted and acquired drug resistance, the sequences were submitted to Stanford HIV Database for Transmitted DRM [TDRM/Calibrated Population Resistance Tool (CPR Tool)] Version 6.0 and to Genotypic Resistance Interpretation Algorithm (HIVdb algorithm), respectively. Patients that received regular antiretroviral therapy and attended all follow-up appointments from Specialized Assistance Service during 24 weeks were considered underwent regular treatment. The results were obtained at the time of recruitment and after 24 weeks of study.

Table 2: **The antiretroviral therapy scheme, HIV-1 viral load, CD4+ T lymphocytes count, HIV-1 subtype, and drug resistance mutations of 18 PLHIV.**

memory loss among the participants. Secondly, certain variables may be influenced by legal and social desirability bias, which can impact the authenticity of the responses. Thirdly, the absence of involvement of indigenous individuals in the development and interpretation of the results should be noted. Moreover, the assessment of adherence to ART relied on medical records or self-reported medication withdrawal by the patients. Additionally, the relatively small number of HIV-positive cases in this study may limit the statistical power of the analysis. Furthermore, the study was unable to establish the previous contact between PLHIV, hindering inferences about possible virus transmission. Despite these limitations, this study represents the first examination of HIV-1 infection prevalence, associated characteristics, and genetic diversity among a Brazilian indigenous population in South America.

In conclusion, this study investigated the prevalence of HIV within the Brazilian indigenous population, revealing a higher prevalence compared to that reported in the general population. Although a limited number of HIV-1 sequences were evaluated, we could detect viral diversity and resistance mutations commonly related to reduced susceptibility to antiretroviral therapy. Furthermore, a considerable number of PLHIV exhibited elevated viral load levels and diminished CD4+ T lymphocyte counts. Considering that many factors are associated with social vulnerability and risky behavior that can cause HIV infections among indigenous populations, public policies need to be implemented to develop culturally appropriate intervention programs. Nevertheless, ensuring improved access to diagnosis and follow-up for HIV-positive individuals among the Brazilian indigenous population remains a significant challenge.

Contributors

Study design: SS, JC, and CCMG. Investigation and data collection: ECSS, MSB, MFRM, GB, TSF, ADCR, ACV, IRM, CCMG, TSOT, MLG, SMR, JC, and SS. Data analysis: MSB, TSOT, and MLG. Writing—original draft: ECSS. Review & editing: MSB and SS. Data curation: SS and JC. Funding acquisition and project administration: SS. All authors provided critical revision of the manuscript and final approval of the version to be published.

Data sharing statement
All data are available from the corresponding authors upon reasonable request.

Ethical approval
The study was approved by the National Research Ethics Commission (number 2.000.496).

Additional information
This study is part of a thesis (Erica Cristina dos Santos Schnaufer). https://repositorio.ufgd.edu.br/jspui/bitstream/prefix/4916/1/EricaCristinadosSantosSchnaufer.pdf.

Editor note
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Declaration of interests
Dr. Julio Croda is a member of the International Advisory Board of The Lancet Regional Health—Americas.

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