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*Original Article*

# Comparison between potential risk factors for cardiovascular disease in people living with HIV/AIDS in areas of Brazil

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## Abstract

Introduction: Coronary heart disease and its risk factors depend on genetic characteristics, behaviors, and habits, all of which vary in different regions. The use of antiretroviral therapy (ARV) has increased the survival of people living with HIV/AIDS (PLWHA), who begin to present mortality indicators similar to the general population. This study aimed to compare the prevalence of factors potentially associated with coronary heart disease in three cohorts of PLWHA from three different regions of Brazil.

Methodology: The study population was composed of participants of the cohorts of Pernambuco, Goiás, and Rio Grande do Sul states. In these sites, adult patients attending reference centers for treatment of HIV/AIDS were consecutively enrolled.

Results: Pernambuco and Goiás had a higher proportion of males and of individuals with high-risk high-density lipoprotein (HDL). Pernambuco also had a greater proportion of individuals with hypertension, elevated triglycerides, and CD4 counts below 200 cells/mm$^3$. Lower education was more frequent in Rio Grande do Sul, and the use of cocaine was higher in this state.

Conclusions: The results confirm the importance of risk factors for coronary heart disease in PLHIV and highlight differences in the three cohorts. Specific measures against smoking and sedentary lifestyle, avoidance of advanced stages of immunosuppression, and appropriate treatment of dyslipidemia and dysglicemia are urgently needed to cope with the disease in Brazil.

**Key words:** HIV; coronary heart disease; prevalence, Brazil.

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## Introduction

Mortality rates among people living with HIV/AIDS (PLWHA) remain higher than those observed in the general population [1], despite the significant decline observed after the large-scale implementation of antiretroviral therapy (ARV) [2,3]. The concern goes beyond the early death of the patient, even in developing countries, and has been focusing on the adverse effects of ARV and co-morbidities not related to HIV. The aging of HIV-infected individuals has brought about the emergence of age-related diseases [4], gradually changing patterns of morbidity and mortality due to increasing incidence of noncommunicable diseases [5], with an emphasis on cardiovascular risk factors and coronary heart disease (CHD) [6].

The evidence indicates that the increasing prevalence of chronic diseases in this population is

related to the metabolic changes associated with the use of ARV and to the increased longevity of individuals [2]. With longer survival, PLWHA have become vulnerable to diseases that affect the general population. Vulnerability increases depending on lifestyle and risk behaviors such as smoking, alcoholism, and illicit drug use, as well as obesity [4]. As the mortality rate among PLWHA remains higher in comparison with the general population [1], further efforts are needed to identify and reduce the prevalence of risk factors associated with AIDS-related mortality as well as mortality not related to AIDS. The latter is responsible for half of the deaths in some countries [5].

Studies have reported a prevalence of dyslipidemia and other risk factors for cardiovascular disease in PLWHA ranging from 20% to 80% [7] both in developed and developing countries [8,9].

In Brazil, the mortality rate from CHD in the general population increased from 46.2 per 100,000 inhabitants in 2000 to 52.4 per 100,000 inhabitants in 2010. However, in 2010, the highest rate of mortality from ischemic heart disease was observed in the South (62/100,000 inhabitants), while the rates for the Midwest and Northeast were 42.6 and 44.9 per 100,000, respectively [10]. As CHD and the associated risk factors depend on genetic characteristics, behavior, and lifestyle, they vary from region to region. With the use of ARVs (and the consequent decline in mortality from opportunistic diseases) and the increased survival of PLWHA, this population has begun to present specific mortality indicators similar to those of the general population. One would assume that the prevalence of CHD in PLWHA varies throughout regions of Brazil, especially if this prevalence depends more on traditional risk factors than on HIV-related factors. This study aimed to describe and compare the prevalence of factors potentially associated with coronary heart disease using baseline data of three well-established cohort studies of people living with HIV/AIDS in the Northeast, Midwest, and South regions of Brazil.

## Methodology

A joint analysis was performed in the baseline data of three well-characterized cohort studies of HIV/AIDS patients living in three metropolitan areas of three Brazilian states: Pernambuco, Goias, and Rio Grande do Sul, located, respectively, in the Northeast, Midwest, and South of the country. Brazil is a continental country (8,500,000 $km^2$) with striking socioeconomic and cultural differences among regions. The states vary not only in geographic location, but also in the Brazilian Human Development Index (IDHM). Rio Grande do Sul, located in the South, has an IDHM of 0.746, which reflects higher socioeconomic status and better distribution. The state of Goiás is located in the Midwest, has an IDHM of 0.735 and intermediate socioeconomic status. The state of Pernambuco, on the other hand, is located in the Northeast, and has a lower level of development, a wealth distribution with higher contrast, and an IDHM of 0.673 [11]. Studies were conducted in the capitals of those states, which have marked differences in the incidence of AIDS. Porto Alegre, capital of Rio Grande do Sul, has the highest rate of AIDS incidence (95 cases per 100,000 inhabitants), being in first place in Brazil, while Recife, capital of Pernambuco, holds the eighth position (35.5 cases per 100,000), and Goiânia, capital of Goiás, is thirteenth (27.5 cases per 100,000 inhabitants). As a whole, the incidence rate of AIDS in Brazil is 20.2 cases per 100,000 population [12]. The states of Pernambuco and Goiás predominantly present HIV subtypes B and F, whereas Rio Grande do Sul presents a predominance of subtype C, which is apparently more virulent and therefore more easily spread [13].

HIV-infected patients attending referral centers for treatment of HIV/AIDS were consecutively enrolled. In Recife, patients seen in two public hospitals (Hospital Universitario Oswaldo Cruz, from Universidade de Pernambuco, and Hospital Estadual Correia Picanço, from Health Secretariat of the state) were between 17 and 74 years of age. The enrollment in Goiania occurred in a public referral center for infectious diseases (Hospital das Clinicas da Universidade Federal de Goias), including patients between 20 and 75 years of age without clinical evidence of active opportunistic infections at baseline. In Porto Alegre, patients 18 years of age and older seen in one of the largest outpatient HIV/AIDS centers (Hospital Sanatorio Partenon, of the Health State Department) were included. In all studies, pregnant women, patients with mental retardation, and patients under restriction of freedom were excluded. Data collection was performed concurrently: 2007–2009 (Recife), 2009–2011 (Goiania), and 2006–2008 (Porto Alegre). All research projects were approved by the institutional review boards of the institutions, which are accredited by the Office of Human Research Protections, and all participants signed informed consent forms.

Patients had standardized blood pressure and anthropometric measurements and were interviewed at the clinics using similar questionnaires regarding demographic and social data, lifestyle, habits, current medical treatments, HIV infection, and related diseases. Additional information on the use of antiretroviral medicine, history of HIV infection, CD4 T-cell count and viral load were obtained from medical records. Central obesity was determined by waist circumference, measured in duplicate, and the average was categorized as ≥ 102/88 cm for men and women, respectively. Weight and height were obtained to calculate body mass index (kg/m$^2$), and were classified into < 25, 25–29, or ≥ 30 kg/m$^2$. In Porto Alegre, there were four standardized measurements of blood pressure in two visits, using an oscillometric monitor OMRON CP-705, (Bannockburn, USA), and blood pressure was classified based on the average. In Recife and Goiania, there were two and three measures of blood pressure, respectively, using a calibrated aneroid sphygmomanometer (WelchAllyn Tycos, Skaneateles Falls, USA), and either the average as ≥ 140/90 mmHg or the use of blood pressure lowering agents was used to determine hypertension. Blood samples were collected after 12 hours of fasting for assaying total cholesterol, high-density lipoprotein (HDL), triglycerides, and blood glucose. Laboratory tests were performed within approximately three months of the date of the interview. Altered values were considered triglycerides ≥ 150 mg/dL and HDL cholesterol < 40 (men) or < 50 mg/dL (women). Diabetes mellitus was diagnosed based on fasting glucose ≥ 126 or the use of anti-diabetic agents. Metabolic syndrome was characterized according to the National Cholesterol Education Program (NCEP-ATPIII), and specific cutoffs were used for fasting glucose ≥ 100 mg/dL and blood pressure ≥ 130/85 mmHg or use of lowering agents, respectively, to determine diabetes mellitus and hypertension [14]

*Statistical analysis*

The statistical analysis consisted of calculating the prevalence of each category of the selected variables (potential risk factors for CHD) and their respective 95% confidence intervals. The frequencies of risk factors among datasets were compared using Chi-square tests, and the means were compared by applying the t test for independent samples.

## Results

Table 1 shows sociodemographic factors and lifestyle habits potentially associated with coronary heart disease in patients with HIV/AIDS, from three states, corresponding to different regions of Brazil. With respect to variables, a greater prevalence of individuals under 50 years of age was observed, and

**Table 1.** Comparison of risk factors for coronary heart disease in persons living with HIV/AIDS in three Brazilian states, corresponding to different regions of the country

| | Recife (Northeast) | | Goiania (Midwest) | | Porto Alegre (South) | | P value |
|---|---|---|---|---|---|---|---|
| | N | % (95% CI) | N | % (95% CI) | N | % (95% CI) | |
| **Patients** | 2,347 | - | 300 | - | 1,240 | - | - |
| *Sociodemographic data* | | | | | | | |
| Age (years) | | | | | | | 0.018 |
| < 40 | 1,237 | 52.7 (50.7–54.7) | 181 | 60.3 (54.8–65.9) | 711 | 57.4 (54.6–60.1) | |
| 40–49 | 768 | 32.7 (30.8–34.6) | 82 | 27.3 (22.2–32.4) | 351 | 28.3 (25.8–30.8) | |
| 50–59 | 282 | 12.0 (10.7–13.3) | 27 | 9.0 (5.7–12.3) | 138 | 11.1 (9.4–12.9) | |
| ≥ 60 | 60 | 2.6 (1.9–3.2) | 10 | 3.3 (1.3–5.4) | 40 | 3.2 (2.2–4.2) | |
| Male sex | 1,467 | 62.5 (60.5–64.5) | 230 | 76.7 (71.9–81.5) | 628 | 50.6 (47.9–53.4) | < 0.001 |
| *Years of schooling* | | | | | | | *< 0.001* |
| Illiterate | 269 | 11.6 (10.3–12.9) | 6 | 2.0 (0.4–3.6) | 40 | 3.2 (2.2–4.2) | |
| 1–9 | 1,098 | 47.4 (45.3–49.4) | 97 | 32.3 (27.0–37.7) | 795 | 64.1 (61.4–66.8) | |
| 10–12 | 688 | 29.7 (27.8–31.5) | 114 | 38.0 (32.5–43.5) | 279 | 22.5 (20.2–24.8) | |
| ≥ 12 | 263 | 11.3 (10.0–12.6) | 83 | 27.7 (22.6–32.8) | 126 | 10.2 (8.5–11.8) | |
| *Lifestyle habits* | | | | | | | |
| Abusive use of alcohol | 534 | 22.8 (21.1–24.5) | 71 | 26.3 (21.0–31.6) | 69 | 5.6 (4.3–6.8) | < 0.001 |
| Current smoker | 572 | 24.4 (22.7–26.1) | 69 | 23.0 (18.2–27.8) | 525 | 42.3 (39.6–45.1) | < 0.001 |
| Physical activity: > 150 min/week | 498 | 21.2 (19.6–22.9) | 77 | 25.7 (20.7–30.6) | 664 | 53.5 (50.8–56.3) | < 0.001 |
| Lifetime use of crack | 159 | 6.8 (5.8–7.8) | - | - | 111 | 8.9 (7.4–10.5) | 0.019 |
| Lifetime use of cocaine | 210 | 9.0 (7.8–10.1) | 32 | 10.7 (7.1–14.2) | 367 | 29.6 (27.1–32.1) | < 0.001 |
| Hypertension | 693 | 29.5 (27.7–31.4) | 60 | 20.0 (15.4–24.6) | 241 | 19.4 (17.2–21.6) | < 0.001 |

patients from the three settings had differences in age distribution. While in the South there was a lower proportion of males, in the Midwest, males represented three-quarters of the population. The study population had a heterogeneous education level, with a higher proportion of individuals with less education (up to 9 years of study) in the South and a higher proportion of individuals with more education (12 years or more) in the Midwest. In relation to lifestyle habits, it was observed that alcohol abuse was less frequent in in the South, while the proportion of current smokers was larger. There was a marked difference in the use of cocaine among patients from the three states, with higher consumption in Porto Alegre and lower consumption in Recife. Participants from Recife and Goiania were more sedentary. Hypertension was prominent in the Northeast.

Regarding the characteristics related to HIV, the Northeast had the highest proportion of participants taking antiretroviral agents and, on average, for a greater length of time; however, these patients had lower CD4 counts (< 200 cells/mm$^3$) (Table 2). Obesity was more prevalent in the South, while normal abdominal circumference was more frequent in the Northeast.

With respect to metabolic profiles, Table 3 shows that diabetes mellitus was more prevalent in the South, high triglycerides in the Northeast, and abnormal cholesterol in the Midwest. Prevalence of metabolic syndrome varied markedly between Recife and Porto Alegre, while the point estimate for Goiania had a wider confidence interval. Framingham score (mean) was higher in the Northeast.

Among PLWHIV with metabolic syndrome, there was a trend to increased enlarged abdominal circumference from the Northeast to the South. In the Midwest, triglycerides were higher and fasting glucose was lower, while abnormal HDL cholesterol was lower in the South (Table 4).

## Discussion

In this analysis, differences in demographic characteristics, socioeconomic status, lifestyle habits, HIV-related factors, anthropometric measurements, diabetes mellitus, hypertension, and lipid profiles of the PLWHIV from Northeast, Midwest, and South Brazil emerged, which were able to express distinct behaviors of the HIV infections. This is the first Brazilian study to detail cardiovascular risk factors in a relatively large population of PLWHIV and to compare data from regions where the disease incidence is increasing and about which information is scarce.

**Table 2.** Comparison of HIV-related and anthropometric measurements associated with coronary heart disease in persons living with HIV/AIDS in three Brazilian states, corresponding to different regions of the country

| | Recife (Northeast) | | Goiania (Midwest) | | Porto Alegre (South) | | P value |
|---|---|---|---|---|---|---|---|
| | N | % (95% CI) | N | % (95% CI) | N | % (95% CI) | |
| **Related to HIV** | | | | | | | |
| Use of ARV | 1,776 | 75.7 (73.9–77.4) | 200 | 66.7 (61.3–72.0) | 815 | 65.7 (63.1–68.4) | < 0.001 |
| Time on ARV (mean ±SD) | 4.4 ± 3.5 years | | 2.7 ± 2.5 years | | 3.8 ± 2.8 years | | < 0.001† |
| *CD4 (cells/mm$^3$)* | | | | | | | *< 0.001* |
| < 200 | 345 | 20.0 (18.2–21.9) | 26 | 8.9 (5.6–12.2) | 181 | 14.8 (12.8–16.8) | |
| 200–349 | 398 | 23.1 (21.1–25.1) | 54 | 18.6 (14.1–23.0) | 295 | 24.1 (21.7–26.5) | |
| 350–499 | 396 | 21.0 (21.0–25.0) | 66 | 22.7 (17.8–27.5) | 317 | 25.9 (23.4–28.3) | |
| ≥ 500 | 582 | 33.8 (31.6–36.1) | 145 | 49.8 (44.0–55.6) | 432 | 35.3 (32.6–37.9) | |
| *Viral load (copies/mL)* | | | | | | | *0.005* |
| < 400 | 603 | 53.8 (50.9–56.7) | 161 | 55.7 (49.9–61.5) | 616 | 50.4 (47.6–53.2) | |
| 400–100,000 | 409 | 36.5 (33.7–39.3) | 115 | 39.8 (34.1–45.5) | 512 | 41.8 (39.1–44.6) | |
| > 100,000 | 109 | 9.7 (8.0–11.5) | 13 | 4.5 (2.1–6.9) | 93 | 7.7 (6.2–9.2) | |
| **Anthropometric measurements** | | | | | | | |
| Body mass index | | | | | | | < 0.001 |
| Eutrophic | 1,597 | 69.2 (67.3–71.0) | 188 | 67.9 (62.3–73.4) | 709 | 57.2 (57.2–60.0) | |
| Overweight | 552 | 23.9 (22.2–25.6) | 74 | 26.7 (21.5–32.0) | 379 | 30.6 (28.0–33.1) | |
| Obese | 160 | 6.9 (5.9–8.0) | 15 | 5.4 (2.7–8.1) | 152 | 12.3 (10.4–14.1) | |
| *Abdominal circumference* | | | | | | | *0.003* |
| Normal | 1,525 | 65.0 (63.1–67.0) | 172 | 57.3 (51.7–63.0) | 737 | 59.4 (56.7–62.2) | |
| Enlarged | 399 | 17.0 (15.5–18.5) | 56 | 18.7 (14.2–23.1) | 244 | 19.7 (17.5–21.9) | |
| Considerably enlarged | 421 | 18.0 (16.4–19.5) | 72 | 24.0 (19.1–28.9) | 259 | 20.9 (18.6–23.2) | |

† Bonferroni test: Statistically significant differences among regions

**Table 3.** Comparison of metabolic profile associated with coronary heart disease in persons living with HIV/AIDS in three Brazilian states, corresponding to different regions of the country

| | Recife (Northeast) | | Goiania (Midwest) | | Porto Alegre (South) | | P value |
|---|---|---|---|---|---|---|---|
| | N | % (95% CI) | N | % (95% CI) | N | % (95% CI) | |
| **Diabetes mellitus** | | | | | | | < 0.001 |
| Normal | 1,983 | 95.2 (94.3–96.2) | 292 | 97.3 (95.5–99.2) | 1,126 | 91.5 (90.0–93.1) | |
| Diabetes | 99 | 4.8 (3.8–5.7) | 8 | 2.7 (0.8–4.5) | 104 | 8.5 (6.9–10.0) | |
| **Metabolic syndrome** | 554 | 27.5 (25.6–29.5) | 52 | 18.6 (14.0–85.9) | 187 | 15.3 (13.2–17.3) | < 0.001 |
| **Laboratory tests** | | | | | | | |
| *Total cholesterol* | | | | | | | < 0.001 |
| Normal | 1,465 | 70.9 (68.9–72.9) | 283 | 94.3 (91.7–97.0) | 845 | 68.9 (66.3–71.5) | |
| Borderline | 392 | 17.3 (17.3–20.7) | 12 | 4.0 (1.8–6.2) | 237 | 19.3 (17.1–21.5) | |
| High risk | 209 | 10.1 (8.8–11.4) | 5 | 1.7 (0.2–3.1) | 144 | 11.7 (9.9–13.6) | |
| *HDL-cholesterol* | | | | | | | < 0.001 |
| Normal | 515 | 21.9 (20.3–23.6) | 29 | 9.7 (6.3–13.0) | 306 | 24.7 (22.3–27.1) | |
| Borderline | 936 | 39.9 (37.9–41.9) | 170 | 56.7 (51.0–62.3) | 685 | 55.2 (52.4–58.0) | |
| High risk | 896 | 38.2 (36.2– 40.1) | 101 | 33.6 (28.3–39.0) | 249 | 20.1 (17.8–22.3) | |
| *LDL-cholesterol* | | | | | | | 0.097 |
| Normal | 1,489 | 79.3 (77.5–81.1) | 247 | 85.5 (81.4–89.6) | 967 | 78.9 (76.6–81.2) | |
| Borderline | 265 | 14.1 (12.5–15.7) | 32 | 11.1 (7.4–14.7) | 171 | 13.9 (12.0–15.9) | |
| High risk | 124 | 6.6 (5.5–7.7) | 10 | 3.5 (1.3–5.6) | 87 | 7.1 (5.7–8.5) | |
| *Triglycerides* | | | | | | | < 0.001 |
| Normal | 1,077 | 52.0 (49.9–54.2) | 189 | 63.0 (57.5–68.5) | 787 | 64.2 (61.5–66.9) | |
| Altered | 439 | 48.0 (45.8–50.1) | 111 | 37.0 (31.5–42.5) | 439 | 35.8 (33.1–38.5) | |
| **Use of hypolipidemic agents** | 49 | 2.1 (1.5–2.7) | 6 | 2.0 (0.4–3.6) | 29 | 2.3 (1.5–3.2) | 0.5 |
| **Framingham score (mean ± SD)** | 1,985 | 4.28 ± 6.10 | 300 | 3.42 ± 6.38 | 1,228 | 3.07 ± 7.82 | < 0.001† |

† Bonferroni test: Statistically significant differences among Northeast and South

**Table 4.** Distribution of metabolic syndrome components among persons living with HIV/AIDS with metabolic syndrome in three Brazilian states, corresponding to different regions of the country

| | Recife (Northeast) | | Goiania (Midwest) | | Porto Alegre (South) | | P value |
|---|---|---|---|---|---|---|---|
| | N | % (95% CI) | N | % (95% CI) | N | % (95% CI) | |
| Enlarged abdominal circumference | 253 | 45.7 (41.5–49.8) | 29 | 55.8 (41.8–69.7) | 131 | 62.1 (55.5–68.6) | < 0.001 |
| Triglycerides ≥ 150 mg/dL | 471 | 85.0 (82.0–88.0) | 50 | 96.1 (90.7–100) | 170 | 80.6 (75.2–86.0) | 0.03 |
| Abnormal HDL-cholesterol | 481 | 86.8 (84.0–89.6) | 48 | 92.3 (84.8–99.8) | 137 | 64.9 (58.4–71.4) | < 0.001 |
| Hypertension | 384 | 69.3 (65.5–73.2) | 41 | 78.8 (67.4–90.3) | 131 | 62.1 (55.5–68.7) | 0.3 |
| Fasting glucose > 100 mg/dL | 247 | 44.6 (40.4–48.7) | 10 | 19.2 (8.2–30.3) | 81 | 43.3 (36.1–50.5) | 0.002 |

Although the South has the highest level of education [15] and income [16] among the three states, most PLWHA with less education belonged to this population. Considering that these participants reflect the overall HIV-infected patients, the results suggest that the process of pauperization of infection is more marked in the South. In those three states, although the rate of men to women is similar in the general population [17], both the results of this study and the data reported in the notification database (SINAN) (Pernambuco: 1.54, Goias: 1.83, Rio Grande do Sul: 1.26) [18] point to a lower male/female ratio in the state of Rio Grande do Sul, suggesting that in the South, the feminization of the infection is more advanced. Differences in sociodemographic characteristics may convert into differences in the risk of CVD. Previous studies in the South indicated an association between fewer years of schooling and metabolic syndrome in men [19]. In the Northeast, an association between male sex and subclinical atherosclerosis [20] and higher velocity of pulse wave was observed, similar to the observations among HIV-negative individuals [21].

In Brazil, the prevalence of smoking has been reduced in the last decades, but it is still higher among those with little or no education. In general, cities in the North and Northeast present lower than average rates [22]. Large cities located in the South and Southeast regions present higher prevalence rates, and Porto Alegre had the highest prevalence rate in the country among women. The prevalence of smoking in the South (42.3%) is similar to smoking rates among PLHIV in Europe [23], ranging from 40% to 50%, while the prevalence of smoking in Pernambuco and Goiás was lower, reflecting a lower prevalence of smoking in the Northeastern and Midwest regions (about 15% in the young adult population). All prevalence rates of smoking were higher among PVHIV than in the general population of the respective states. In addition, in Recife, the use of crack was found to be associated with the irregular use of ARV agents [24], which has implications in the spread of the infection besides CHD.

With regard to HIV infection, CD4 counts below 200 cells/mm$^3$ were higher in Recife than in the other two cities, which may reflect delayed access to diagnosis and treatment in the Northeast. Grangeiro *et al*. [25], analyzing the data of approximately 100,000 HIV-infected individuals who entered into care in Brazil between 2003 and 2006, detected a greater risk of a late entry into HIV care in the Northeast and Midwest in comparison to the South.

Differences in metabolic risk factors, which may reflect the atherogenic profile, described for PLWHIV living in Recife were associated with high cardiovascular risk [26,27]. A previous study in Recife demonstrated an increased prevalence of hyperapolipoprotein B, which was associated with prolonged use of antiretroviral therapy, hypertriglyceridemia, insulin resistance, diabetes, and a past history of hypertension; hyperapolipoprotein B was higher among patients with metabolic syndrome and higher Framingham scores [28]. Interestingly, in the Rio Grande do Sul group, there was a higher proportion of overweight and obese individuals than in the other two states, although there was a smaller proportion of individuals with metabolic syndrome. The differences in lipid profiles were reflected in the components of metabolic syndrome in the participants of each study.

In PLWHIV treated with antiretroviral agents, there is a marked increase in insulin resistance and diabetes mellitus prevalence [29-31], which is more common in ethnic minorities than in the white population [32,33]. In addition, chronic inflammation seems to influence the progression to diabetes in HIV-infected patients. Chronic inflammation in HIV is evidenced by the elevation of systemic inflammatory markers [34]. The frequency of diabetes in the PLWHIV in this study was not higher than those reported to the general population in the same settings [35]. Data from Rio Grande do Sul showed diabetes as one of the strongest predictors of CHD risk in 10 years in PLWHIV [36].

Several alternatives may explain the differences in the lipid profiles in these PLWHIV. The use of lipid-lowering therapy was low and similar among centers, but no dietary intervention had been provided, even though there is evidence of benefit equivalent to lipid-lowering agents [37]. Although the frequency of physical inactivity was much higher in Recife, the effectiveness of physical activity in improving the lipid profile in HIV-infected patients in routine conditions is still unclear [38].

A possible explanation could be related to the ARV treatment. Although a higher proportion of patients were on highly active antiretroviral therapy (HAART) in Pernambuco and the length of time on treatment was higher, the differences were not large. The type of antiretroviral regimen employed, an alternative explanation, was not assessed in this study; however, because antiretroviral treatment is distributed equitably by the Brazilian Health Ministry, which has a specific protocol recommendation for the whole

country [39], there is no reason to suppose that there were great differences between the treatment regimens within the three study sites. This point deserves further investigation. Finally, one aspect to be considered is that in the state of Pernambuco, where patients presented higher levels of immunosuppression, represented by lower levels of CD4, dyslipidemia was more frequent. This association, if real, could be related to the degree of inflammation and the level of circulating cytokines. Analysis of a subsample of the Pernambuco cohort showed an association between high TNF-α levels and having attained a viral load ≥ 100,000 RNA copies/mL and between IL-6 and a current CD4 level < 200 cells/mm3 [40]. The cytokines IL-6 and TNF-α and C-reactive protein have been reported to be higher in PLHIV and in those with previously severe immunosuppression [41], and they are related to the development of atherosclerosis, CHD, immunosenescence, and mortality due to non-HIV-associated co-morbidities [42].

We are aware that comparative studies like ours have inherent limitations. One concern would be about the representativeness of the studied population in each setting. In all settings, patients were equally enrolled in studies in reference centers for HIV/AIDS treatment. In Brazil, all HIV/AIDS patients are treated in the public sector with similar access to treatment throughout the country. Therefore, we may assume that the reference centers give assistance to patients of different socioeconomic levels and that the assembled patients may reflect the characteristics of the infected individuals in each setting. The lack of comparative data of risk factors for cardiovascular diseases among individuals with no HIV infection makes it difficult to judge to which extent the observed differences across the states reflect the distribution of these factors among the general population. However, it was beyond the scope of this study to assess risk factors for cardiovascular disease among individuals with no HIV infection; furthermore, these kind of data are not available nationwide. The selected risk factors herein analyzed were the classical ones, and information about other additional factors such inflammatory markers was not available for the three settings. One of the strengths of our analysis is that data on risk factors were collected using standardized questionnaires or procedures that allowed comparisons among studies.

## Conclusions

The data presented herein confirm the importance of risk factors for CHD in the population of PLWHIV. This risk is even higher in the poorest individuals and in individuals who have reached a higher degree of immunosuppression. Specific measures against smoking and a sedentary lifestyle, the avoidance of advanced stages of immunosuppression, and actions to increase the awareness of cardiologists, endocrinologists, and nutritionists to provide appropriate treatment for dyslipidemia, dysglicemia, and hypertension in special assistance programs are urgently required and must be integrated into the proposals for coping with the disease in Brazil.

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