








Assessment of biochemical and hematological parameters related to aging in people living with HIV

Avaliação dos parâmetros bioquímicos e hematológicos relacionados ao envelhecimento em pessoas vivendo com HIV

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ABSTRACT

Background: HIV infection is a serious public health problem worldwide. The number of elderly people living with HIV has increased rapidly, due to the success of antiretroviral therapy and lifestyle changes. However, the chronic inflammation caused by HIV and the effects of antiretroviral therapy have been associated with the premature aging of these individuals. To date, there is no consensus on the age at which an individual with HIV is considered elderly. In this context, the present study aims to evaluate, through biomarkers, aging in people living with HIV. **Method:** This is a cross-sectional study developed with people living with HIV, attended at the Specialized Care Service of Divinópolis in the state of Minas Gerais, from October 2019 to March 2021. For comparison, a non-HIV group, was selected from the national health survey database. Patients were divided into age groups: 18 to 49, 50 to 59, and over 60 years for some analysis, other analyses were carried out with age groups: over 50 years and over 60 years. The groups were compared in terms of biochemical and hematological variables with each other and with the components of the non-HIV group. **Results:** When analyzing the renal function of the HIV and non-HIV groups of over 60 years old, no differences were found between the groups. When comparing the metabolic profile of the HIV group aged 50 to 59 years and those aged over 60 years, they also did not differ. Finally, when analyzing hematological data, different patterns were shown. For the red blood cell count, the group from 50 to 59 years old was the same as the group over 60 years old; in relation to hematocrit, the group from 50 to 59 years old was the same as the group from 18 to 49 years old. **Conclusions:** This study demonstrates that for renal function and hematocrit, the age cutoff for an individual with HIV to be considered elderly would be 60 years of age or older. In contrast, for the metabolic profile and for the red blood cell count, the ideal age cutoff would be 50 years or older. These results may be of great importance to guide dose adjustment and choice of drugs for people living with HIV at older ages, aiming at better therapeutic control.

Keywords: Aging, HIV, Biochemical marker, Blood cell count, Biomarkers

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RESUMO

Introdução: A infecção por HIV é um grave problema de saúde pública em todo o mundo. O número de idosos que vivem com HIV tem aumentado rapidamente, devido ao sucesso da terapia antirretroviral e mudanças no estilo de vida. Porém, a inflamação crônica causada pelo HIV, e os efeitos da terapia antirretroviral têm sido associados ao envelhecimento precoce desses indivíduos. Até o momento, não existe um consenso sobre a idade em que o indivíduo com HIV é considerado idoso. Nesse contexto, o presente estudo tem por objetivo avaliar, por meio de biomarcadores, o envelhecimento em pessoas vivendo com HIV. **Método:** Trata-se de um estudo transversal desenvolvido com as pessoas que vivem com HIV, atendidas no Serviço de Atendimento Especializado de Divinópolis-MG, no período de outubro de 2019 a março de 2021. Para comparação, utilizou-se um grupo “não HIV”, selecionado a partir do banco de dados da pesquisa nacional em saúde. Os pacientes foram divididos em grupos etários: 18 a 49, 50 a 59 e maiores de 60 anos para algumas análises, outras análises foram realizadas com grupos etários: maiores de 50 anos e maiores de 60 anos. Os grupos foram comparados em termos de variáveis bioquímicas e hematológicas entre si e com os componentes do grupo “não HIV”. **Resultados:** Ao analisar a função renal do grupo HIV e “não HIV”, acima de 60 anos, não foram encontradas diferenças entre os grupos. Ao comparar perfil metabólico do grupo HIV de 50 a 59 anos e acima de 60 anos, estes também não diferiram. Finalmente, ao analisar dados hematológicos, estes apresentaram padrões diferentes. Para a contagem de hemácias o grupo de 50 a 59 anos foi igual ao grupo acima de 60 anos, em relação ao hematócrito, o grupo de 50 a 59 anos foi igual ao grupo de 18 a 49 anos. **Conclusão:** Este estudo demonstra que, para a função renal e hematócrito, o corte de idade para que o indivíduo com HIV seja considerado idoso, seria a partir de 60 anos. Diferentemente, para o perfil metabólico e para contagem de hemácias, o corte ideal quanto à idade, seria a partir de 50 anos. Estes resultados podem ser de grande importância para orientar ajuste de dose e escolha de fármacos para pessoas vivendo com HIV em idades avançadas, visando um melhor controle terapêutico.

Palavras-chave: Envelhecimento, HIV, Marcador bioquímico, Contagem de células sanguíneas, Biomarcadores.

INTRODUCTION

It is estimated that in the year 2020, there were worldwide 37.7 million people living with the human immunodeficiency virus (PLHIV)¹. According to the Centers for Disease Control and Prevention (*Centro de Controle e Prevenção de Doenças - CDC*), more than half of people diagnosed with HIV in the United States in 2018 were over the age of 50². Due to the success of antiretroviral therapy and changes in lifestyle, an increase in the number of elderly people living with HIV has been observed³. In Brazil, the increase in PLHIV notifications over 50 years old was 257 % between 2007 and 2019⁴. PLHIV has a tendency towards premature aging, and therefore, is able to

develop signs of aging about 10 years earlier when compared to people not infected by the virus⁵⁻⁷.

According to the World Health Organization (WHO), an individual aged 60 years or older is considered elderly⁸. However, studies involving the elderly infected by HIV, show divergences regarding the age of these individuals, and often the age group defined for the elderly group is from 50 years old⁹, 55 years old¹⁰ or even 60 years¹¹ which results in making it difficult to compare the results obtained.

It is well established in the literature that aging is associated with the presence of physiological, tissue, molecular, and ce-

llular changes¹². According to Maanen; Wilting; Jansen, physiological changes related to aging can affect pharmacokinetic parameters¹³. Additionally, the elderly population, compared to the general population, is at increased risk for certain comorbidities such as liver, kidney, cardiovascular, and/or metabolic diseases, such as diabetes mellitus and obesity. These diseases often occur due to the decline of physiological functions and cellular aging⁶, which can affect vital functions performed by specialized organs and, in this aspect, biochemical markers stand out as useful tools to characterize the aging process.

Thus, considering that the physiological alterations present in the elderly are capable of affecting the pharmacokinetics of antiretroviral drugs and compromising the therapeutic results in this specific population¹⁴, This study aims to compare biochemical and hematological markers in different age groups in order to propose a cutoff point for defining elderly people with HIV, thus providing support for decision-

-making about the management of antiretroviral therapy in clinical practice.

MATERIALS AND METHODS

Study design

This is a cross-sectional, population-based study, structured based on the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE), using data collected from patients' medical records.

Study participants

The study was carried out between October 2019 and March 2021, at the Specialized Assistance Service (*Serviço de Assistência Especializada - SAE*) in Divinópolis, in the Brazilian state of Minas Gerais (MG), with the population defined as in Figure 1.

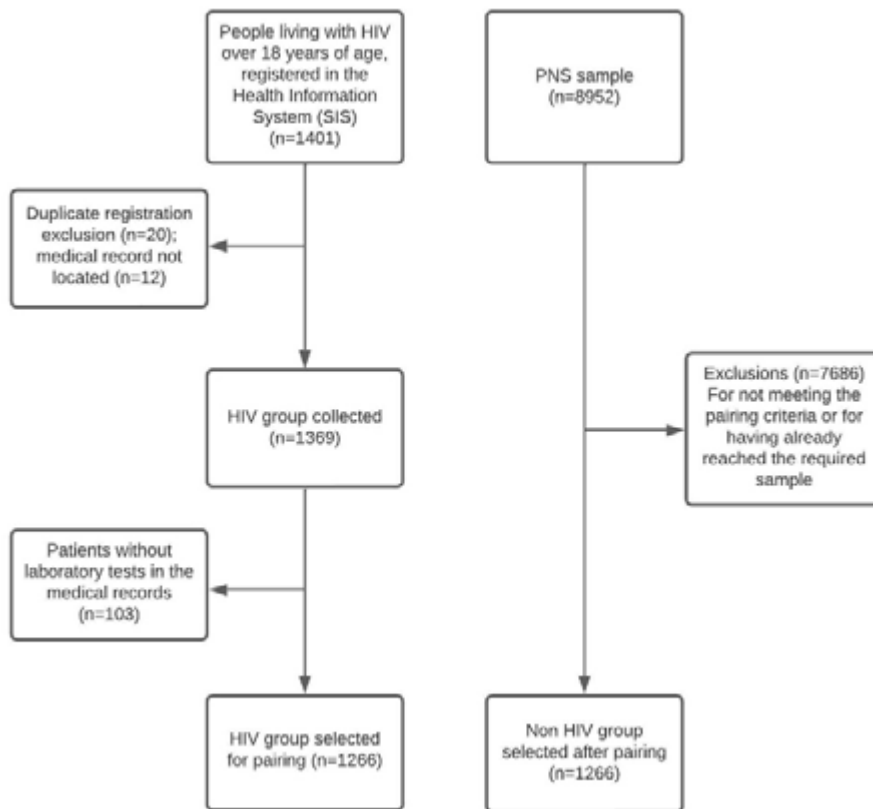


Figure 1 - Diagram of selection of study participants and pairing.

The non-HIV group was selected from the 2013 National Health Survey (*Pesquisa Nacional de Saúde - PNS*) database, carried out by the Oswaldo Cruz Foundation (FIOCRUZ), with the collaboration of the Brazilian Institute of Geography and Statistics (IBGE). The PNS is a household-based, nationwide survey that aims to understand the health profile of the Brazilian population. It uses socio-spatial, health status, lifestyle, and health care indicators to characterize these individuals¹⁵.

For each patient in the HIV group, one person from the non-HIV group was selected and, for this pairing, the criterion of gender and age was used (considering a variability of three years).

Data collection

Data collection was performed using a Microsoft Excel 2019® spreadsheet to obtain the variables of interest:

- Sociodemographic characteristics: age, education, gender;
- Pharmacotherapeutic characteristics: date of initiation of current antiretroviral therapy, current antiretroviral therapy, medications for continuous use other than antiretrovirals;
- Clinical characteristics: date of diagnosis, viral load, T CD4⁺ cells, weight, height, blood pressure, erythrogram (red blood cells, hemoglobin and hematocrit) and platelets, leukogram (white blood cells)

and differential: neutrophils, lymphocytes, monocytes, eosinophils and basophils), lipid profile (total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) and triglycerides), glycemic profile (fasting blood glucose), renal function (creatinine, urea, and filtration rate). The most recent laboratory data were collected and evaluated according to the patient's age at the time of the exams.

The estimate of the glomerular filtration rate was calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation¹⁶, using the nephrological calculator on the website of the Brazilian Society of Nephrology¹⁷.

Data analysis

Patients were categorized into age groups: 18 to 49 years old, 50 to 59 years old, and over 60 years old for some comparisons. In other analyses, patients were categorized into two groups: over 50 years and over 60 years.

Descriptive data analysis was performed using frequency distribution, mean, standard deviation, median and 25th and 75th percentiles, according to the characteristics of the data. To verify the normality of the data, the Kolmogorov-Smirnov test was used.

To compare the groups, the ANOVA test with Hochberg's GT2 post hoc test and Student's t test were performed for parametric data; while Kruskal-Wallis with Dunn-

-Bonferroni post test and the Mann-Whitney U test were used for non-parametric data. The Statistical Package for the Social Sciences® (version 19.0) and Epi Info software were used for the analyses, with a significance level of $p < 0.05$ being set.

Ethical considerations

The study was approved by the Ethics Committee in Research Involving Human Beings of the Federal University of São João del-Rei, Campus Centro-Oeste Dona Lindu (CEPES/CCO/UFSJ: CAAE 18521219.3.0000.5545) and authorized by the Municipal Health Department of Divinópolis (MG). The entire study was conducted in accordance with resolution 466/2012, which regulates research involving human beings. In addition, all researchers related to the data of this research signed a data confidentiality agreement; no personal identification of the patients was collected, thus ensuring greater confidentiality of the data.

RESULTS

The sociodemographic and clinical characteristics of the individuals participating in this study are shown in Table 1. The median age of the patients was 44 years (IQR25 %: 34; IQR75 %: 53). Regarding gender, the males were predominant, being 59.6 % of the patients. With regard to education, incomplete elementary education was more prevalent in both groups.

Table 1: Sociodemographic and clinical characteristics of patients treated at the SAE in Divinópolis (MG), (n=1266) and individuals from the PNS database (n=1266), from October 2019 to March 2021.

Variables	HIV		Non-HIV		p-value
	N	%	N	%	
Age					
Median (IQR 25% - IQR 75%)	44	(34-53)	44	(34-53)	0.964*
Gender					
Male	754	59.6	754	59.6	1.000**
Female	512	40.4	512	40.4	
Education					
Illiterate	52	4.1	73	5.8	0.559**
Incomplete junior school	549	43.4	578	45.7	
Complete junior school	229	18.1	243	19.2	
Complete High school	267	21.1	306	24.2	
Graduation completed	54	4.3	65	5.1	
Not informed	115	9.0	1	0.1	
Weight					
Median (IQR 25%-75%)	67.80	(58.70-78.00)	70.60	(61.25-80.00)	<0.001*
Hight					
Median (IQR 25%-75%)	1.65	(1.58-1.73)	1,64	(1.57-1.72)	0.179*

*Nonparametric data expressed as median and IQR 25% - IQR 75%. Statistics: Mann-Whitney;
**Chi square.

Regarding the therapeutic regimens of patients, the association of tenofovir, lamivudine and efavirenz stands out with 38.9 %

of use, followed by the association of tenofovir, lamivudine and dolutegravir, with 18.9 % of use among patients (Table 2).

Table 2: Therapeutic regimen in use by people living with HIV treated at the SAE in Divinópolis (MG), n=1266, from October 2019 to March 2021.

Antiretroviral Therapy	N	%
TDF + 3TC + EFV	492	38.9
TDF + 3TC + DTG	240	18.9
TDF + 3TC + ATV + RIT	224	17.7
AZT + 3TC + EFV	144	11.4
OTHER THERAPIES	142	11.2
NOT INFORMED	24	1.9

Abbreviations: TDF: Tenofovir, 3TC: Lamivudine, EFV: Efavirenz, DTG: Dolutegravir, ATV: Atazanavir, RIT: Ritonavir, AZT: Zidovudine.

When evaluating the biochemical data by age group of PLHIV, there was a significant difference between the median of total cholesterol, red blood cells, and blood glucose of patients aged 50 to 59 years, compared to patients aged 18 to 49 years. In contrast, patients aged over 60 years old did not show any difference

with the group from 50 to 59 years old in these same parameters. When analyzing the median of creatinine and hemoglobin, there was a significant difference only between the groups from 18 to 49 years old and the group over 60 years old. Regarding glomerular filtration rate (GFR), there was a difference in all groups (Table 3).

Table 3: Laboratory characteristics of people living with HIV treated at the SAE in Divinópolis (MG), n=1266, from October 2019 to March 2021.

Biochemical and hematological markers	18 to 49 years	50 to 59 years	Over de 60 years	P value
GFR (min/1.73m ²)	99.00 (83.00-113.00) N=721	86.00 (72.00-99.00) N=222	73.00 (61.00-91.00) N=125	<0.001**d
Creatinine (mg/dL)	0.90 (0.80-1.04) N=759	0.90 (0.80-1.05) N=249	0.96 (0.80-1.11) N=139	0.042**b
Blood glucose (mg/dL)	86.00 (80.00-94.00) N=634	92.00 (83.00-102.00) N=214	95.00 (86.00-106.50) N=126	<0.001**ab
Total cholesterol (mg/dL)	172.00 (149.00-203.00) N=627	194.00 (167.00-230.40) N=219	194.00 (174.75-227.85) N=126	<0.001**ab

HDL (mg/dL)	45.00 (37.12-56.00) N=300	47.00 (39.00-58.50) N=128	46.50 (42.00-57.00) N=56	0.164**
LDL (mg/dL)	98.50 (78.00-122.00) N=250	115.00 (93.00-152.00) N=111	108.00 (85.50-135.75) N=50	<0.001**a
Red blood cells (million cells/mm ³)	4.52 (3.97-4.92) N=456	4.22 (3.85-4.70) N=125	4.10 (3.71-4.61) N=85	<0.001**ab
Hematocrit (%)	42.34 (+/-5.29) N=643	41.81 (+/-5.52) N=219	40.37 (+/-4.65) N=125	0.001*bc
Hemoglobin (g/dL)	14.30 (13.00-15.50) N=737	14.05 (12.90-15.00) N=242	13.60 (12.60-14.80) N=139	0.002**b
White blood cells (cells/ μ L)	5900 (4784-7248) N=737	5700 (4500-7000) N=243	5815 (4800-7025) N=138	0.296**
Neutrophils	3128.00 (2394.00-4200.00) N=627	3130.00 (2307.50-4128.42) N=202	3160.00 (2347.90-4200.00) N=111	0.795**
Platelets (cells/ μ L)	225000 (187000-266500) N=730	224000 (188000-266000) N=243	217000 (182000-259500) N=133	0.404**

Abbreviations: GRF: Glomerular Filtration Rate, HDL: High-Density Lipoproteins, LDL: Low-density lipoprotein.

*Parametric data expressed as mean and standard deviation. ANOVA and Hochberg's GT2 post test, **Nonparametric data expressed as median and IQR 25% - IQR 75%. Kruskal-Wallis with Dunn-Bonferroni post test. a = G1 different from G2. b= G1 different from G3. c= G2 different from G3. d= All are different from each other.

Table 4 presents the comparison of biochemical data between the HIV and non-HIV groups of different age groups. When analyzing GFR, creatinine, and white blood cells, the 18 to 49 years old, HIV and non-HIV groups showed a statistically significant difference when compared; while the groups from 50 to 59 years old and over 60 years old showed no difference in these same parameters.

When analyzing the GFR, there was a significant difference between people living with HIV over 50 years of age and people in the non-HIV group over 60 years of age; while the group over 60 years old HIV and non-HIV showed no difference. Regarding the values of total cholesterol, LDL, and red blood cell count, all groups showed a statistically significant difference. Regarding creatinine, hemoglobin, platelet, and white blood cell values, all groups were the same (Table 5).

Table 4: Comparison of laboratory parameters by age group, of the groups: HIV treated at the SAE in Divinópolis (n=1266) and non-HIV from the PNS database (n=1266), from October 2019 to March 2021.

Biochemical and hematological markers	18 to 49 years		P Value	50 to 59 years		P Value	Over 60 years		P Value
	HIV	Non-HIV		HIV	Non-HIV		HIV	Non-HIV	
GFR (min/1.73m ²)	99.00 (83.00-113.00) N=721	104.00 (90.50-115.00) N=721	<0.001**	86.00 (72.00-99.00) N=222	87.00 (75.00-100.00) N=222	0.185**	73.00 (61.00-91.00) N=125	78.00 (62.00-91.00) N=125	0.642**
Creatinine (mg/dL)	0.90 (0.80-1.04) N=759	0.90 (0.70-1.00) N=759	<0.001**	0.90 (0.80-1.05) N=249	0.90 (0.80-1.00) N=249	0.340**	0.96 (0.80-1.11) N=139	0.90 (0.80-1.10) N=139	0.709**
Total cholesterol (mg/dL)	172.00 (149.00-203.00) N=627	167.00 (147.00-197.00) N=627	0.041**	194.00 (167.00-230.40) N=219	183.00 (162.00-204.00) N=219	0.001**	194.00 (174.75-227.85) N=126	181.00 (165.00-198.50) N=126	<0.001**
HDL (mg/dL)	45.00 (37.12-56.00) N=300	42.00 (36.00-50.00) N=300	<0.001**	47.00 (39.00-58.50) N=128	44.00 (37.00-53.00) N=128	0.026**	46.50 (42.00-57.00) N=58	43.50 (37.00-50.75) N=58	0.008**
LDL (mg/dL)	98.50 (78.00-122.00) N=250	92.00 (75.00-114.00) N=250	0.007**	115.00 (93.00-152.00) N=111	102.50 (87.00-123.00) N=111	0.005**	108.00 (85.50-137.75) N=50	100.00 (79.00-123.00) N=50	0.056**

Red blood cells (million cells/mm ³)	4.52 (3.97-4.92) N=456	4.80 (4.43-5.15) N=456	<0.001**	4.22 (3.85-4.70) N=125	4.62 (4.36-5.03) N=125	0.000**	4,10 (3,71-4,61) N=85	4,60 (4,29-4,95) N=85	<0,001**
Hematocrit (%)	42.34 (+/-5.29) N=643	43.68 (+/-4.61) N=643	<0.001*	41.81 (+/-5.52) N=219	43.73 (+/-4.23) N=219	0.000*	40,37 (+/-4,65) N=125	43,06 (+/-4,44) N=125	<0,001*
Hemoglobin (g/dL)	14.30 (13.00-15.50) N=737	14.20 (13.10-15.20) N=737	0.330**	14.05 (12.90-15.00) N=242	14.00 (13.00-15.00) N=242	0.991**	13,60 (12,60-14,80) N=139	13,70 (12,85-15,00) N=139	0,285**
White blood cells (cells/μL)	5900 (4787-7248) N=737	6300 (5025-7500) N=737	0.003**	5700 (4500-7000) N=243	5900 (4800-7400) N=243	0.069**	5815 (4800-7025) N=138	6100 (4700-7460) N=138	0,241**
Platelets (cells/μL)	225000 (187000-266500) N=730	220000 (189000-259000) N=730	0.373**	224000 (182250-244750) N=243	212500 (182250-244750) N=243	0.027**	217000 (182250-244750) N=243	212000 (182250-244750) N=243	0,337**

Abbreviations: GRF: Glomerular Filtration Rate, HDL: High-Density Lipoproteins, LDL: Low-density lipoprotein.

*Parametric data expressed as mean and standard deviation. Student's t test **Nonparametric data expressed as median and IQR 25% - IQR 75%. Mann-Whitney U test

Table 5: Comparison of laboratory parameters of the groups: HIV treated at the SAE in Divinópolis (n=1266) and non-HIV from the PNS database (n=1266), over 50 and 60 years old, from October 2019 to March 2021.

Biochemical and hematological markers	HIV	Non-HIV	P Value	HIV	Non-HIV	P Value
	>50 years	>60 years		>60 years	>60 years	
GFR (min/1.73m ²)	83.00 (67.00-96.00) N=349	78.00 (62.00-91.00) N=125	0.005**	73.00 (61.00-91.00) N=125	78.00 (62.00-91.00) N=125	0.642**
Creatinine (mg/dL)	0.91 (0.80-1.10) N=391	0.90 (0.80-1.10) N=139	0.638**	0.96 (0.80-1.11) N=139	0.90 (0.80-1.10) N=139	0.709**
Total cholesterol (mg/dL)	194.00 (170.00-228.00) N=347	181.00 (165.00-198.50) N=126	0.000**	194.00 (174.25-227.85) N=126	181.00 (165.00-198.50) N=126	<0.001**
LDL (mg/dL)	115.00 (88.50-144.80) N=162	100.00 (79.00-123.00) N=50	0.027**	108.00 (85.50-137.75) N=50	100.00 (79.00-123.00) N=50	0.056**
Red blood cells (million cells/mm ³)	4.16 (3.78-4.64) N=211	4.60 (4.29-4.95) N=85	0.000**	4.10 (3.71-4.61) N=85	4.60 (4.29-4.95) N=85	<0.001**
Hematocrit (%)	41.28 (+/-5.26) N=344	43.06 (+/-4.44) N=125	0.001*	40.37 (+/-4.65) N=125	43.06 (+/-4.44) N=125	<0.001*
Hemoglobin (g/dL)	14.00 (12.80-15.00) N=384	13.70 (12.82-15.00) N=139	0.830**	13.60 (12.60-14.80) N=139	13.70 (12.85-15.00) N=139	0.285**

White blood cells (cells/ μ L)	5785 (4600-7000) N=384	6100 (4700-7460) N=138	0.172**	5815 (4800-7025) N=138	6100 (4700-7460) N=138	0.241**
Platelets (cells/ μ L)	221500 (186000-261750) N=376	212000 (181000-242000) N=133	0.071**	217000 (182000-259500) N=133	212000 (181000-242000) N=133	0.337**

Abbreviations: GRF: Glomerular Filtration Rate, LDL: Low-density lipoprotein.

*Parametric data expressed as mean and standard deviation. Student's t test

**Nonparametric data expressed as median and IQR 25% - IQR 75%. Mann-Whitney U test

DISCUSSION

Much is said about the elderly living with HIV, but data are conflicting about when PLHIV can be considered elderly, especially considering the physiological changes that impact medication dose adjustment^{9-11,18,19}. Therefore, the present study compared the renal, metabolic, and hematological profile of PLHIV with data from the general population and observed different age cutoff points for each of the functions studied.

First, when considering renal function in PLHIV, there was a difference between all age groups for the GFR parameter, with a reduction in the parameter as age advanced. Corroborating this finding, the study by Pontes *et al.*²⁰ analyzed factors associated with chronic kidney disease in PLHIV and observed that patients over 40 years of age are more likely to develop kidney disease. This can be explained because biological aging is characterized by changes in organs and systems, with renal aging being marked by a decline in GFR, due to the progressive loss of nephrons²¹.

When comparing the HIV and non-HIV groups, the groups from 50 to 59 years old and over 60 years old showed no difference in the GFR variable in the same age groups. However, for the age group 18 to 49 years, there was a difference, and the HIV group had a reduced GFR. This finding is similar to that found by Guaraldi *et al.*²², which shows a higher prevalence of kidney disease in HIV-infected individuals when compared to the general population. This fact can be explained by the constant inflammation caused by the virus and nephrotoxic effects of antiretroviral therapy²³. However, according to the results of the present study, this difference is neither sustained nor accentuated as the patient ages.

When a cutoff point of 50 years was established, compared with those over 60 years of age, renal function was different between the HIV and non-HIV groups, while the groups over 60 years of age in our study showed no difference. Thus, with regard to GFR, the age cutoff would be from 60 years old. It can be highlighted that aging is multifactorial, and an age equal to or greater than 50 years can impact the im-

mune response and survival of people living with HIV²⁴. In contrast, this information is extremely important when considering the concern for dose adjustment of medication in the elderly, especially for hydrophilic drugs, excreted unchanged by the kidney, such as antiretroviral nucleoside analogue reverse transcriptase inhibitors such as tenofovir, didanosine, lamivudine and zidovudine²⁵.

Evaluating total cholesterol among the different age groups in the HIV group, the profile was very similar to that of the GFR, with patients belonging to the group aged 50 to 59 years having values equal to the group over 60 years and lower in younger people living with HIV. Other authors found similar data demonstrating that age interferes with the levels of this metabolic; the study by Vance *et al.*²⁶ demonstrated that when comparing people aged 50 to 59 years living with HIV with a group over 60 years old, there was a higher prevalence of hypercholesterolemia, diabetes, and kidney disease in the older group. Thus, greater care with these patients is essential, since the number of elderly people with HIV tends to increase even more.

In comparing total cholesterol with the non-HIV group, there was a difference between the groups in all comparisons. However, an interesting fact in these comparisons is that the total cholesterol levels of the non-HIV group were lower than in the HIV group. This data can be explained by increases in total cholesterol levels caused by antiretroviral therapy in the group of people living with HIV, a finding explained in the study by Guimaraes *et al.*²⁷, where HIV patients were followed up before and after starting antiretroviral therapy; an increase in the level of this metabolic was observed after therapy.

Evaluating HDL cholesterol in the HIV and “non-HIV” groups, it was possible to see that there was a difference between all age groups, with the HIV group showing higher levels of HDL. The presence of high levels of high-density lipoprotein (HDL) in HIV patients in this study may have been influenced by the use of antiretroviral therapy. The drug efavirenz has a positive impact on the preservation of HDL, as demonstrated by Fernandes *et al.*²⁸. The impact of HIV infection on metabolic dysfunction has not been fully elucidated. However, the study by Hann evaluated HIV patients taking ART, HIV patients not taking ART and a control group without HIV, over 36 months, found a slight decrease in HDL levels in the HIV-negative group and a slight increase in the HIV-positive group, but this difference disappeared during the follow-up period²⁹. It is worth highlighting that our study did not evaluate some factors that are important when analyzing dyslipidemia, such as lifestyle, dietary quality and genetic characteristics that could influence these metabolic factors³⁰. Therefore, new studies evaluating lipid profiles in HIV patients are extremely important.

Finally, when analyzing the hematological data only for the HIV group, the red blood cell values of the group aged 50 to 59 years were equal to those of the group over 60 years, while the hemoglobin in the group of 18 to 49 years was different only from the group over 60 years of age. At the same time, the hematocrit of the 18-49 age group was the same as the 50-59 age group. All these data had progressive declines with increasing age. When comparing the HIV and non-HIV groups in terms of red blood cells and hematocrit, all groups showed a statistically significant difference, with HIV patients showing lower values. This find-

ing is in disagreement with that found by Daminelli *et al.*³¹, where when analyzing hematocrit of the HIV group and the control group, although the control group presented higher values, these were not statistically significant. However, this result may be due to the reduced power of the sample in the study (n=48).

Education has been identified as an indicator of the socioeconomic level of the population, with lower levels of education associated with worse health prognoses^{32,33}. In this study, most people living with HIV (42.6 %) had not completed elementary school, which is in agreement with the study by Antonini *et al.*³⁴, carried out in the interior region of São Paulo state, Brazil, where individuals with less schooling had a greater chance of late diagnosis in the condition of AIDS. These findings reinforce the importance of health promotion and education actions aimed at this population, in order to prevent new infections and improve adherence to antiretroviral therapy in people living with HIV.

This study has some limitations and, in addition to those mentioned above, the use of secondary data stands out, which does not provide a complete profile of the patients. Some medical records did not have all the data, and sometimes they were not organized. The non-HIV group also has some limitations, such as individuals assessed with a different sociodemographic profile from those in the HIV group and the use of other methodologies for determining laboratory parameters. Such differences between the two groups evaluated in the present study may partially explain unexpected results, such as for example, no difference in hemoglobin values between the groups, lower glucose values and higher HDL values for the HIV group. Howev-

er, these limitations do not invalidate the results of this research, and the strengths outweigh the limitations. The strengths of this research are the use of the entire adult population served at the referral service, with a significant number of participants in all age groups. Furthermore, this is the first national survey to carry out comparisons of biochemical and hematological data between different age groups of people living with HIV, which we are aware of.

CONCLUSION

After analyzing the data of the present study, it is concluded that in relation to renal function, the ideal age cutoff to consider the elderly individual, in people living with HIV, would be from 60 years old. A progressive decline in GFR was observed, demonstrating that greater care is needed with the dosage of medications prescribed to people living with HIV at older ages and periodic monitoring of renal function. In contrast, with regard to metabolic parameters, total cholesterol, and blood glucose, the age cutoff would be from 50 years old. Finally, in relation to hematological parameters, the patterns were different; in relation to red blood cells, the ideal age cutoff would be from 50 years old, while hematocrit would be from 60 years old. Our findings reinforce the importance of further studies, since aging is heterogeneous and multifactorial, and it is not possible to provide a precise definition for all parameters.

REFERENCES

1. UNAIDS. ESTATÍSTICAS GLOBAIS SOBRE HIV 2021 [Internet]. 2021 [cited 2021 Oct 3]. Available from: <https://unaids.org.br/estatisticas/>
2. CDC. Diagnoses of HIV Infection in the United States and Dependent Areas, 2018 (Updated) [In-

- ternet]. 2018 [cited 2022 Apr 24]. Available from: <http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>.<http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html><http://wwwn.cdc.gov/dcs/ContactUs/Form>
3. Cabrera DM, Diaz MM, Grimshaw A, Salvatierra J, Garcia PJ, Hsieh E. Aging with HIV in Latin America and the Caribbean: a Systematic Review. *Curr HIV/AIDS Rep*. 2021 Feb 1;18(1):1. Available from: [/pmc/articles/PMC8059362/](https://pubmed.ncbi.nlm.nih.gov/358059362/)
 4. BRASIL. Boletim epidemiológico [Internet]. Brasília; 2019. Available from: <http://www.aids.gov.br/pt-br/pub/2019/boletim-epidemiologico-de-hiv-vaids-2019>
 5. Schank M, Zhao J, Moorman JP, Yao ZQ. The impact of hiv-and art-induced mitochondrial dysfunction in cellular senescence and aging. *Cells*. 2021 Jan 1;10(1):1–21.
 6. Gabuzda D, Jamieson BD, Collman RG, Lederman MM, Burdo TH, Deeks SG, et al. Pathogenesis of aging and age-related comorbidities in people with HIV: Highlights from the HIV action workshop. *Pathog Immun*. 2020;5(1):143–74.
 7. Maciel RA, Klück HM, Durand M, Sprinz E. Comorbidity is more common and occurs earlier in persons living with HIV than in HIV-uninfected matched controls, aged 50 years and older: A cross-sectional study. *International journal of infectious diseases*. 2018 May 1;70:30–5. Available from: <https://pubmed.ncbi.nlm.nih.gov/29476902/>
 8. OMS. Active Ageing – A Police Framework. A Contribution of the World Health Organization to the second United Nations World Assembly on Aging. Vol. 11. Madrid, Spain; 2002.
 9. McMillan JM, Krentz H, Gill MJ, Hogan HB. Managing HIV infection in patients older than 50 years. Vol. 190, *CMAJ*. Canadian Medical Association; 2018. p. E1253–8.
 10. Magaki SD, Vinters H V., Williams CK, Marinov S, Khanlou N, Said J, et al. Neuropathologic Findings in Elderly HIV-Positive Individuals. *J Neuropathol Exp Neurol*. 2022 Jul 1;81(7):565. Available from: [/pmc/articles/PMC9425852/](https://pubmed.ncbi.nlm.nih.gov/39425852/)
 11. Haeuser E, Serfes AL, Cork MA, Yang M, Abbas-tabar H, Abhilash ES, et al. Mapping age- and sex-specific HIV prevalence in adults in sub-Saharan Africa, 2000–2018. *BMC Med*. 2022 Dec 1;20(1).
 12. Ferrucci L, Gonzalez-Freire M, Fabbri E, Simon-sick E, Tanaka T, Moore Z, et al. Measuring biological aging in humans: A quest. Vol. 19, *Aging Cell*. Blackwell Publishing Ltd; 2020.
 13. Drenth-van Maanen AC, Wilting I, Jansen PAF. Prescribing medicines to older people—How to consider the impact of ageing on human organ and body functions. *Br J Clin Pharmacol*. 2020 Oct 1;86(10):1921–30. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1111/bcp.14094>
 14. Back D, Marzolini C. The challenge of HIV treatment in an era of polypharmacy. *J Int AIDS Soc*. 2020 Feb 1 [cited 2023 Dec 16];23(2):e25449. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1002/jia2.25449>
 15. PNS. Pesquisa Nacional de Saúde [Internet]. Fiocruz/IBGE. 2013 [cited 2021 Aug 28]. Available from: <https://www.ibge.gov.br/estatisticas/sociais/saude/9160-pesquisa-nacional-de-saude.html?=&t=o-que-e>
 16. Levey AS, Stevens LA, Schmid CH, Zhang Y, Castro AF, Feldman HI, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009 May 5;150(9):604–12. Available from: [/pmc/articles/PMC2763564/?report=abstract](https://pubmed.ncbi.nlm.nih.gov/18762364/)
 17. SBN. Calculadoras nefrológicas - SBN [Internet]. 2020 [cited 2020 Aug 3]. Available from: <https://www.sbn.org.br/profissional/utilidades/calculadoras-nefrológicas/>
 18. M H, M D, C A, C J, MA V, A C, et al. Impact of Age-related Comorbidities on Five-year Overall Mortality among Elderly HIV-Infected Patients in the Late HAART Era--Role of Chronic Renal Disease. *J Nutr Health Aging*. 2016 Apr 1;20(4):408–14. Available from: <https://pubmed.ncbi.nlm.nih.gov/26999241/>
 19. Nevedal A, Neufeld S, Luborsky M, Sankar A. Older and Younger African Americans' Story Schemas and Experiences of Living with HIV/AIDS. *J Cross Cult Gerontol*. 2017;32(2):171–89.
 20. Pontes PS, Ruffino-Netto A, Kusumota L, Costa CRB, Gir E, Reis RK. Factors associated to chronic kidney disease in people living with HIV/AIDS. *Rev Lat Am Enfermagem*. 2020 Jul 15;28:1–10. Available from: <http://www.scielo.br/j/rlae/a/SFVvX8L6gKD-fvkqW3pq5T7L/?lang=en>
 21. Denic A, Mathew J, Lerman LO, Lieske JC, Larson JJ, Alexander MP, et al. Single-nephron glomerular filtration rate in healthy adults. *New England Journal of Medicine*. 2017 Jun 15;376(24):2349–57. Available from: <http://www.nejm.org/doi/10.1056/NEJMoa1614329>
 22. Guaraldi G, Orlando G, Zona S, Menozzi M, Carli F, Garlassi E, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. *Clinical Infectious Diseases*. 2011;53(11):1120–6.
 23. da Mata GF, Fernandes DE, de Paiva Luciano E, Sales GTM, Riguetti MTP, Kirsztajn GM. Inflammation and kidney involvement in human viral disease

- ses caused by SARS-CoV-2, HIV, HCV and HBV. Vol. 27, *Journal of Venomous Animals and Toxins Including Tropical Diseases*. Centro de Estudos de Venenos e Animais Peconhentos; 2021.
24. Brañas F, Galindo MJ, Torralba M, Antela A, Vergas J, Ramírez M, et al. Different profiles among older adults with HIV according to their chronological age and the year of HIV diagnosis: The FUNCFRIL cohort study (GeSIDA 9817). *PLoS One*. 2022 Mar 1;17(3 March).
25. Naicker S, Rahmanian S, Kopp JB. HIV and chronic kidney disease. *Clin Nephrol*. 2015;83:S32–8.
26. Vance DE, Mugavero M, Willig J, Raper JL, Saag MS. Aging with HIV: a cross-sectional study of comorbidity prevalence and clinical characteristics across decades of life. *J Assoc Nurses AIDS Care*. 2011;22(1):17–25. Available from: <https://pubmed.ncbi.nlm.nih.gov/20471864/>
27. Guimaraes NS, Caporali JF de M, Reis PV do CC, Tanajura PR, Guimaraes AR, Tupinambás U. Alterações metabólicas e estimativa de risco cardiovascular em pessoas vivendo com HIV/AIDS doze meses após o início da TARV. *Revista Médica de Minas Gerais*. 2017;27(1):38–43. Available from: <http://www.rmmg.org/artigo/detalhes/2215>
28. Fernandes AC da S, Cesar JJ, Bonolo P de F, Souza CR de, Ceccato M das GB. Perfil lipídico em pessoas iniciando a terapia antirretroviral com regimes baseados em efavirenz ou dolutegravir em um centro de referência no Brasil: um estudo de coorte. *Research, Society and Development*. 2022 Apr 15;11(5):e55811528662.
29. Low H, Hoang A, Pushkarsky T, Dubrovsky L, Dewar E, Yacovo MS Di, et al. HIV disease, metabolic dysfunction and atherosclerosis: A three year prospective study. *PLoS One*. 2019 Apr 1;14(4).
30. American Heart Association. Guidelines Pocket Guides - Professional Heart Daily | American Heart Association. 2023. Available from: <https://professional.heart.org/en/guidelines-and-statements/guidelines-pocket-guides>
31. Daminelli EN, Tritinger A, Spada C. Alterações hematológicas em pacientes infectados pelo vírus da imunodeficiência humana submetidos à terapia antirretroviral com e sem inibidor de protease. *Rev Bras Hematol Hemoter*. 2010 Feb;32(1):10–5. Available from: <http://www.scielo.br/j/rbhh/a/74LSZ-mkpXCwVQ6fDnfG8WNC/?lang=pt>
32. Iqbal S, Maqsood S, Zafar A, Zakar R, Zakar MZ, Fischer F. Determinants of overall knowledge of and attitudes towards HIV/AIDS transmission among ever-married women in Pakistan: Evidence from the Demographic and Health Survey 2012-13. *BMC Public Health*. 2019 Jun 21;19(1).
33. Campos I de O, Cezar da Cruz DM, Magalhães YB, Rodrigues D da S. Escolaridade, trabalho, renda e saúde mental: um estudo retrospectivo e de associação com usuários de um Centro de Atenção Psicossocial. *Physis: Revista de Saúde Coletiva [Internet]*. 2021 Nov 15;31(3):e310319. Available from: <https://www.scielo.br/j/physis/a/ky8t9hcYM7BLhB-N9XJ3WfWg/>
34. Antonini M, Gerin L, Melo ES, Pontes PS, Arantes LMN, Ferreira GRON, et al. PREVALENCE AND FACTORS ASSOCIATED WITH LATE DIAGNOSIS OF THE HIV INFECTION IN A MUNICIPALITY OF SÃO PAULO. *Texto & Contexto – Enfermagem*. 2022 May 13;31. Available from: <http://www.scielo.br/j/tce/a/YLRkCrwHQpXMFsRZJ74yhWx/?lang=en>

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