

Profile of Patients with Hypertension Included in a Cohort with HIV/AIDS in the State of Pernambuco, Brazil

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Abstract

Background: Hypertension (HBP) is modifiable risk factor, whose control may reduce cardiovascular disease in patients with human immunodeficiency virus (HIV).

Objective: To estimate the prevalence of hypertension and describe the characteristics of patients with hypertension infected by HIV/AIDS.

Methods: A cross-sectional study aligned to a cohort of patients with HIV/AIDS. The study considered hypertension at levels $\geq 140/90$ mmHg or use of antihypertensive drugs and pre-hypertension at levels $> 120/80$ mmHg.

Results: Out of 958 patients, 388 (40.5%) were normotensive, 325 (33.9%) were pre-hypertensive, and 245 (25.6%) were hypertensive. Out of these 245 patients, 172 (70.2%) were aware of the fact there they were hypertensive, and 36 (14.8%) had blood pressure controlled. Sixty-two (62) patients (54.4%) were diagnosed with hypertension after HIV diagnosis. Lipodystrophy occurred in 95 (46.1%) patients; overweight/obesity in 129 (52.7%). Use of antiretrovirals occurred in 184 (85.9%), 89 (41.6%) with protease inhibitors (PI) and 95 (44.4%) without PI. Out of these patients, 74.7 used antivirals > 24 months. Age, family history of hypertension, waist circumference, body mass index and triglyceride levels were higher among hypertensive patients. Time of HIV infection, CD4 count, viral load, time and type of antiretroviral regimen were similar in hypertensive and prehypertensive patients.

Conclusion: The high frequency of uncontrolled hypertensive patients and cardiovascular risks in HIV-infected patients point out to the need for preventive and therapeutic measures against hypertension in this group. (Arq Bras Cardiol 2010; 95(5): 640-647)

Keywords: Hypertension/prevention & control; acquired immunodeficiency syndrome (AIDS); HIV: life style; risk factors; antihypertensive agents.

Introduction

While there has been a significant increase in the survival rate of patients with HIV/AIDS, due to control of infection by highly active antiretroviral therapy (HAART)¹, there has been evidence of an increased frequency of cardiovascular disease of atherosclerotic origin in this group, probably due to the combination of chronic viral infection and the side effects of antiretroviral drugs, which results in metabolic disorders (glucose intolerance, dyslipidemia, lipodystrophy) and endothelial damage². Thus, the onset of hypertension would bring an additional risk factor for the cardiovascular system

or, it would constitute, in itself, a consequence of the vascular damage determined by the HIV.

The data on the prevalence of systemic arterial hypertension (SAH) in patients with HIV/AIDS vary. Even though some authors have reported higher prevalence of high blood pressure³ and systemic arterial hypertension⁴ in this group, compared to the prevalence of SAH in subjects without infection, other studies have found similar prevalence of SAH between men and women with HIV and individuals without the infection⁴⁻⁶. Another aspect that also shows different results is the role of antiretroviral drugs in the genesis of SAH. Even though some authors^{4,7,8} have found a relationship between SAH and the longer time of use of antiretroviral drugs and the use of regimens containing protease inhibitors, other studies^{5,6,9} found no association between the onset of SAH and the use or employment of an antiretroviral regimen. In Brazil, these data are even scarcer, with the study by Diehl et al², which was conducted in the city of Londrina, state of Paraná, and

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which showed 32% prevalence of hypertension in HIV positive patients treated as outpatients², and the work of Magalhães et al¹⁰, who showed 41.4% prevalence of hypertension in HIV-infected individuals over the age of 50¹⁰.

The purpose of this work is to verify, diagnose and classify SAH in adult patients included in a cohort of patients living with HIV/AIDS, and to estimate the prevalence of risk factors and epidemiological characteristics present in hypertensive patients.

Methods

This is a cross-sectional study in progress in the city of Recife, state of Pernambuco, which is aligned with a cohort for the study of cardiovascular disease and metabolic disorders in individuals over the age of 18 with HIV/AIDS. The study was conducted from June 2007 to December 2008 and it included a baseline analysis of the first 1,000 patients included in the cohort. The subjects were treated in outpatient clinics of Oswaldo Cruz Hospital, of Pernambuco University, and in the outpatient clinics of Correa Picanco Hospital, of the Health Department of Pernambuco State, consecutively selected. They completed a questionnaire and their blood pressure (BP), weight, height and waist circumference were measured by trained technicians. A data collection form was filled out with information, contained in medical records, about how long the person had had the HIV infection, type of antiretroviral treatment, viral load and CD4 lymphocyte counts. A blood sample was collected for testing blood glucose, cholesterol and triglyceride levels.

To measure the blood pressure, we used a BD™ stethoscope and a Missouri™ mercury column sphygmomanometer, duly calibrated by INMETRO (Brazilian Institute of Metrology, Standardization and Industrial Quality). The diagnosis of SAH was confirmed on a second visit, paid after an interval of up to two months. On both visits, two measurements of the blood pressure were made on one of the upper limbs, and in the end, the mean systolic and diastolic pressures were used. The SAH was classified according to the classification of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7)¹¹, which considers four levels, in mmHg: normal (systolic BP < 120 and diastolic BP < 80); prehypertension (systolic BP between 120 and 139 or diastolic BP between 80 and 89); stage 1 hypertension (systolic BP between 140 and 159 or diastolic BP between 90 and 99) and stage 2 hypertension (systolic BP ≥ 160 or diastolic BP ≥ 100)¹¹.

The body mass index (BMI) was calculated by using the BMI formula = [weight (kg)] / [height (m)²]. Regular physical activity was defined as the practice of physical activity during work breaks or leisure time, calculated by the metabolic equivalent of the last week of the interview, according to the International Physical Activity Questionnaire (IPAQ)¹². All subjects who reported being a smoker at the time of the interview were considered smokers, regardless of the quantity of cigarettes. The consumption of alcohol was classified according to the standardized questionnaire intended for this purpose.

This study was approved by the Research Ethics Committee of Pernambuco University.

The statistical analysis of the data was carried out by using the statistical software "R" (The R Project for Statistical

Computing: www.r-project.org). For a comparative analysis of the categorical variables, we applied the chi-square test, and, when necessary, the Fisher's exact test. For the comparative analysis of continuous variables, we used the Student's t-test. p values < 0.05 indicate statistical significance¹³.

Results

One thousand (1,000) individuals with HIV/AIDS were consecutively evaluated. There was the loss of three patients (0.3%), because they were pregnant and 39 patients (3.9%) were excluded because the BP of such patients had been measured only once. Thus, the universe of this study consisted of 958 subjects. Out of this total, 584 patients (61%) were male and 374 were female (39%); 50% of them were 40 years-old or younger, and the other half were over 40 years of age. The average age of the cohort was 39.58 ± 10.03 years.

Figure 1 shows the distribution of respondents according to the classification of BP levels and the categories of hypertension. Among the individuals evaluated, 388 (40.5%) had blood pressure within the normal range, 325 (33.9%) were considered prehypertensive, and 245 (25.6%) were considered hypertensive. One hundred and seventy-two patients (70.2%) knew they had hypertension, and 95 of them (38.8%) used antihypertensive medication on a continuous basis. The blood pressure levels were controlled in only 36 (20.9%) patients that knew that they were hypertensive.

Out of the total of hypertensive patients, 156 (63.7%) were men, 145 (59.2%) were of mixed race; 63 (25.7%) were white; and 28 (11.4%) were black; 174 (71.0%) had a family history of SAH. Fifty-six (56) patients (23.1%) smoked, 139 (57.7%) ate fruit on a daily basis and 171 (71.2%) ate vegetables on a daily basis (Table 1).

Ninety-five (95) patients (46.1%) had lipodystrophy; 95 (38.8%) were overweight; and 34 (13.9%) were obese. The waist circumference was increased, according to criteria of NCEP-ATP III, in 72 (29.5%) patients and, according to the IDF's criteria, in 126 (51.6%) patients. Table 2 shows that, in relation to dyslipidemia, the total cholesterol level was > 200 mg% in 43 (30.9%) patients, the LDL-cholesterol level was ≥ 130 mg% in 24 (22.0%), the HDL-cholesterol level was < 40 mg% in 75 (52.1%), the triglyceride level was ≥ 150 mg% in 84 (60.0%) and the glucose levels were ≥ 110mg/dl in ten patients (7.1%).

The viral load was undetectable or < 10,000 copies in 54 patients (80.6%) and the CD4 lymphocyte levels were > 350 cells/mm³ in 80 patients (63.5%). Antiretroviral drugs were used in 184 patients (85.9%) and protease inhibitors (PI) in 89 (41.6%). However, 95 patients (44.4%) did not use PI. Approximately 127 patients (74.7%) had been using antiretroviral drugs for more than 24 months (Table 3).

A comparison between hypertensive and prehypertensive patients showed similarity in most risk factors, except for the fact that hypertensive patients were older, they had more cases of hypertension in their families, their waist circumference was larger, and their body mass index and triglyceride levels were higher. The physical activity of prehypertensive patients was more intense (Figure 2 and Tables 1, 2 and 3). With respect to the parameters related to HIV infection and treatment, such

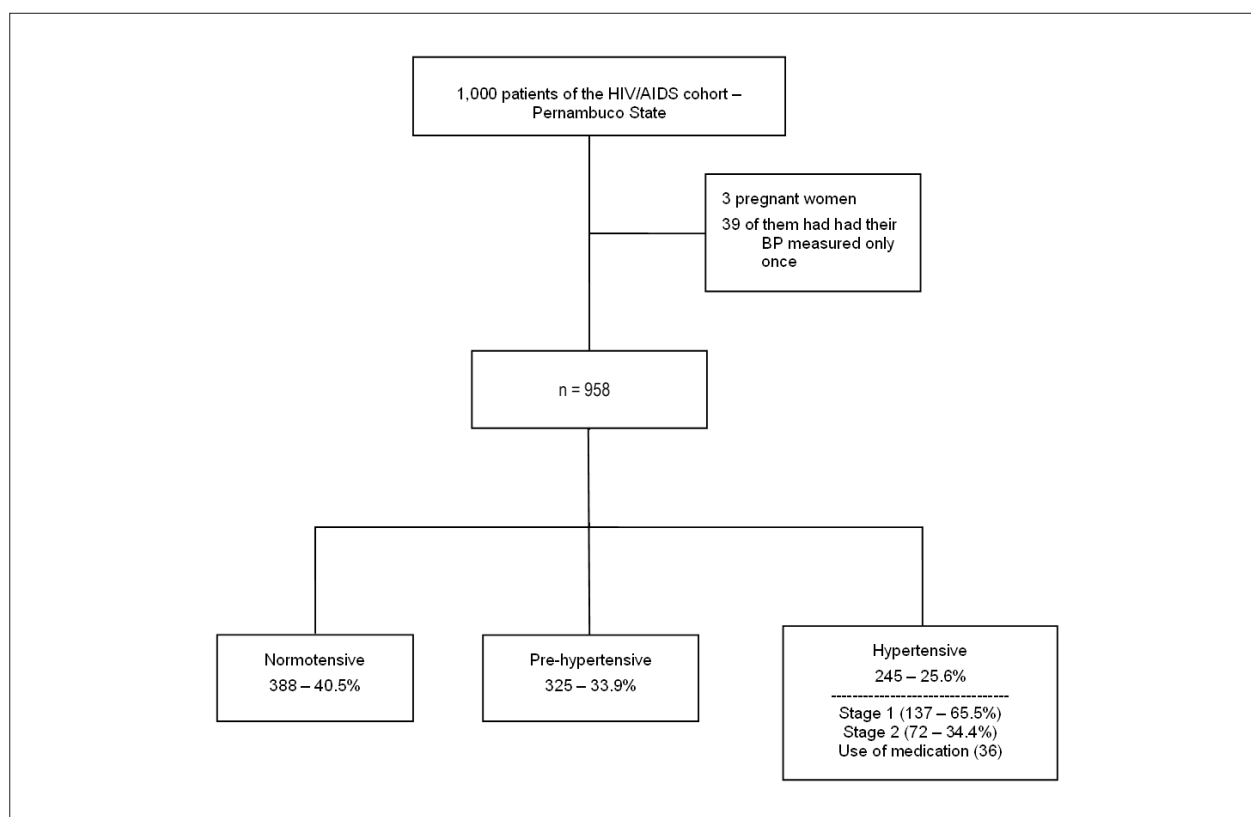


Figure 1 - Distribution of HIV/AIDS patients according to the classification of blood pressure levels established by JNC 7.

as viral load, CD4 lymphocyte counts, the use of antiretroviral drugs, the type of antiretroviral regimen and duration of use, there was no difference between hypertensive and prehypertensive patients (Table 3).

Discussion

This study included 958 HIV-infected individuals, most of whom were patients that had been previously diagnosed with AIDS and who had used antiretroviral drugs for more than 24 months. The study also revealed prevalence of 25.6% of hypertension and 33.9% of pre-hypertension. Even though most patients included in the study had already developed AIDS, the average CD4 lymphocyte count was 470 cells, and 80.6% of patients had a low or undetectable viral load. These data strongly suggest the effective use of antiretroviral drugs. Conversely, in relation to hypertension, the SAH was controlled in only 14.7% of hypertensive patients.

The newest edition of JNC 7¹¹ categorized blood pressure into normal, prehypertension, “stage 1” hypertension and “stage 2” hypertension. The new “prehypertension” category is a warning to physicians and patients, because it was found that the cardiovascular morbidity and mortality begin with these values or even at lower values¹¹. In our cohort, the blood pressure level of a large portion of individuals living with HIV/AIDS, i.e., 325 (33.9%), was within the pre-hypertension range, which indicates the importance of providing this population with guidance on how to lead a healthy lifestyle.

With respect to the prevalence of SAH, two important studies were conducted in Brazil to assess the prevalence of SAH in the general population. The first one deals with the compilation of studies on the prevalence of hypertension in different genders and age groups in different regions of Brazil, conducted between 1993 and 2004¹⁴. The second one, called “Hearts of Brazil” and conducted by the Brazilian Society of Cardiology, prospectively evaluated 2,550 individuals of different age groups, in several cities in Brazil from 2005 onwards¹⁵. In both studies, there was an overall prevalence of hypertension in about 28.5% of the individuals, and the highest prevalence was in the Northeast, where it reached 31.8%. Thus, one can conclude that the prevalence of SAH in patients with HIV/AIDS that accounted for 25.6% in this study was not different from that found in the Brazilian population.

In an Italian study that included 287 HIV-positive patients, who were on HAART, there was prevalence of 34.2% against 11.9% in patients in the control group ($p < 0.0001$)⁹. In the study called Data Collection on Adverse Events of Anti-HIV Drugs (DAD, 2005), a leading international cohort, it was concluded that high blood pressure in HIV-infected individuals is associated with traditional risk factors for hypertension⁹. There was no evidence of a risk associated with any of the classes of antiretroviral drugs⁹, although the use of NNRTI is “traditionally” associated with a low risk of developing hypertension. In the African study (Women’s Interagency HIV Study, 2007)⁶ conducted with a cohort

Table 1 - Biological characteristics, level of education, habits and history of pre-hypertensive and hypertensive patients with HIV/AIDS

Variables	Hypertensive		Pre-hypertensive		p value
	n	(%)	n	(%)	
Gender (male)	156/245	63.017	215/325	66.1	0.5987
Color					
Mixed race	145/245	59.2	170/325	52.3	0.5882
White	63/245	25.7	98/325	30.1	
Black	28/245	11.4	43/325	13.2	
Other	9/245	3.7	14/325	4.4	
Level of education (years)					
1 to 9	103/199	51.8	143/286	50.0	0.8840
10 to 12	68/199	34.2	104/286	36.4	
13 to 19	28/199	14.0	39/286	13.6	
Daily consumption (yes)					
Vegetables	171/240	71.2	232/318	73.0	0.7028
Fruits	139/241	57.7	203/318	63.8	0.1609
Alcohol consumption					
Abstainer/light drinker	201/228	88.2	259/304	85.2	0.3706
Heavy drinker/alcohol dependent	27/228	11.8	45/304	14.8	
Physical activity level					
High	71/245	29.0	128/325	39.4	0.0009
Moderate	45/245	18.3	29/325	8.9	
Low	129/245	52.7	168/325	51.7	
Smoking					
Smoker	56/242	23.1	77/316	24.4	0.7511
Former smoker	77/242	31.8	91/316	28.8	
Non-smoker	109/242	45.0	148/316	46.8	
Illicit drugs					
Cocaine (previous or current use)	17/244	7.0	30/322	9.3	0.8253
Crack (previous or current use)	11/244	4.0	18/324	5.5	0.8555
Medication for high blood pressure (yes)	59/110	53.6	18/80	22.5	<0.0001
Diagnosed with hypertension (yes)					
Before being diagnosed with HIV	58/123	47.1	11/40	27.5	0.0399
After being diagnosed with HIV	62/114	54.4	17/34	50.0	0.8696
Personal History (yes)					
Diabetes mellitus	20/243	8.2	15/316	4.7	0.2165
Angina pectoris	9/232	3.9	7/315	2.2	0.2604
Myocardial infarction	6/236	2.5	6/316	1.9	0.6193
Stroke	3/242	1.2	5/316	1.6	1.0000
Family history of hypertension (yes)	174/245	71.0	190/318	59.7	0.0027

χ^2 chi-square test.

composed of only HIV positive women, the prevalence of hypertension in 1,266 HIV-positive women was similar to the prevalence of hypertension in 368 HIV-negative women (26 versus 28%, $p = 0.3800$). In a recent study conducted

in 2008⁴, in a Norwegian cohort of 542 individuals with HIV/AIDS, hypertension was prevalent in 36.5% of the individuals, which is similar to the general population. A study in Spain¹⁶ detected high prevalence of hypertension in

Table 2 - Characteristics related to presence of lipodystrophy, waist circumference, body mass index (BMI), levels of total cholesterol, HDL cholesterol, LDL-cholesterol, triglycerides, dyslipidemia and glucose in pre-hypertensive or hypertensive patients with HIV/AIDS

Variables	Hypertensive		Pre-hypertensive		p value
	n	%	n	%	
Lipodystrophy (self-reported)	95/206	46.1	125/262	47.7	0.8030
Waist circumference					
NCEP-ATPIII* (Increased)	72/244	29.5	63/321	19.6	0.0086
IDF** (Increased)	126/244	51.6	125/321	38.9	0.0035
Body mass index (kg/m ²)					
< 25	116/245	47.3	205/325	63.1	0.0006
≥ 25 and < 30	95/245	38.8	94/325	28.9	
≥ 30	34/245	13.9	26/325	8.0	
Total cholesterol (mg/dl) (> 200)	43/139	30.9	45/187	24.1	0.2091
HDL-cholesterol (mg/dl) (< 40)	75/144	52.1	103/189	54.5	0.7440
LDL-cholesterol (mg/dl) (> 130)	24/109	22.0	18/130	13.8	0.1381
Triglycerides (mg/dl)					
< 150	56/140	40.0	106/196	54.9	0.0112
150 to 500	76/140	54.3	83/196	43.0	
> 500	8/140	5.7	5/196	2.1	
Blood glucose (mg/dl)					
American Diabetes Association (< 126)	4/140	2.9	3/194	1.6	0.4585
ATP III (< 110)	10/140	7.1	6/194	3.1	0.1184

* NCEP-ATPIII - increased waist circumference > 88cm for women and > 102 cm for men; ** IDF - increased waist circumference > 80cm for women and > 90cm for men; χ^2 Chi-square test.

the HIV group (25% versus 15%, $p < 0.001$) when compared to HIV-negative control patients.

With respect to the treatment of HIV infection in this study, it was found that the prevalence of PI-containing regimens in hypertensive patients was 41.6%, and the prevalence of regimens without PI was 44.4%. With respect to the type of antiretroviral regimens (containing PI or NNRTI) involved in the genesis of the SAH, even though the proportion of use of PI was greater among hypertensive patients than in the general population infected, the study design used does not allow reaching conclusions about the theme. It was also possible to notice that the use of different antiviral regimens, i.e. simple or complex regimens, does not preclude adherence to antiretroviral therapy, whereas the treatment of hypertension, in general, arouses less interest of the patient and even of the assistant physician, which explains why the hypertension was controlled in only 14.7% of the patients. It is a disease that is usually oligosymptomatic/asymptomatic and which, due to its high prevalence in the population, certainly creates less fear and fewer fantasies of death than the HIV.

Several lifestyle factors are likely to have a direct influence on blood pressure levels, both from the perspective of individuals and from the perspective of the population. Among these, the most important lifestyle factors are excess body fat (overweight/obesity), alcohol consumption,

insufficient physical activity, smoking, stress and a variety of dietary components¹⁷, such as inadequate consumption of fruits and vegetables¹⁸.

Knowing that smoking is an established risk factor for hypertension, if one observes Table 1, one will see that there is 23.1% prevalence of smoking in the sample, which is close to values found in another study in the Brazilian population¹⁴. A study with individuals with HIV/AIDS and patients with angina pectoris¹⁹ detected 24% of total prevalence of smokers in Pernambuco State, while Pupulin et al. found a rate of 35% in Paraná State²⁰.

The high prevalence of overweightness (overweightness/obesity) (52.7%) in this population of hypertensive patients with HIV/AIDS is in line with the alarming rates of overweightness described in the literature, which showed the prevalence of 53.7 to 58% of individuals with BMI above 25 in different populations^{21,22}. Among Brazilian workers, there was high prevalence of overweightness (approximately 46%) and SAH (approximately 30%), mainly among males²³.

The guidelines of JNC 7¹¹ recommend doing least thirty minutes of physical exercises on most days of the week. In our sample of 245 hypertensive patients, 129 of the respondents (52.6%) reported not doing physical exercises (inactive/little active), and only 106 of the total (47.4%) reported doing physical exercises on a regular basis (high/moderate

Table 3 - Time of infection, history of immunodeficiency, type and duration of antiretroviral treatment, values of CD4 lymphocytes and current viral load of prehypertensive or hypertensive patients with HIV/AIDS

Variables	Hypertensive		Pre-hypertensive		p value
	n	%	n	%	
Time patient has been diagnosed with the HIV infection					
< 12 months	19/153	12.4	24/200	12.0	0.8379
12 to 24 months	16/153	10.5	25/200	12.5	
> 24 months	118/153	77.1	151/200	75.5	
AIDS (yes)	182/221	82.3	257/295	87.1	0.1363
Use of antiretroviral drugs (yes)	184/214	85.9	252/289	87.2	0.1774
Time patient has been on antiretroviral therapy					
< 12 months	22/170	12.9	39/230	17.0	0.4409
12 to 24 months	21/170	12.3	32/230	13.9	
> 24 months	127/170	74.7	159/230	69.1	
Current antiretroviral regimen					
Without ARV	30/214	14.0	32/292	11.0	0.5163
With the use of PI	89/214	41.6	132/292	45.2	
Without the use of PI	95/214	44.4	128/292	43.8	
Average CD4 cells/mm ³ (mean ± SD)	126	467.9±242.5	168	436.6±229.3	0.2870
CD4 Lymphocytes (current) cells/mm ³					
≤ 200	16/126	12.7	24/168	14.3	0.8012
201 to 350	30/126	23.8	35/168	20.8	
> 350	80/126	63.5	109/168	64.9	
Viral Load (current) copies/ml					
up to 10.000	54/67	80.6	72	83.7	0.8531
10.000 to 100.000	8/67	11.9	9	10.5	
> 100.000	5/67	7.5	5	5.8	

NARTI - Nucleoside Analog Reverse Transcriptase Inhibitors; NNRTIs - Non-Nucleoside Reverse Transcriptase Inhibitors; PI - Protease inhibitors; PIR - Ritonavir Boosted Protease Inhibitors; χ^2 chi-square test.

physical activity). Other authors also found high prevalence of sedentary lifestyle in our country, ranging from 31.8% for adults to 58.0% for the elderly in the general population²⁴. There was significant difference between the physical activity levels of hypertensive patients and the levels of prehypertensive patients in this study, indicating that physical activity could be protecting, also in this population, against the emergence of higher pressure levels.

In this study, alcohol dependence or heavy consumption of alcoholic beverages was reported by 27 of the hypertensive patients (11.8%) and 45 of the pre-hypertensive patients (14.8%), with no difference between the groups. The excessive consumption of alcoholic beverages is associated with SAH, and the restriction of alcohol intake can lower blood pressure^{25,26}, which is a modification of lifestyle recommended by JNC 7¹¹.

With respect to the time when the hypertension was diagnosed, more than half (54.4%) learned they had hypertension after the HIV diagnosis, and many (29.8%)

did not know they had hypertension before this study was conducted. Moreover, only 21% of patients who knew they were hypertensive had their blood pressure levels adequately controlled. These findings seem to indicate that the patients were not warned by infectious disease specialists about the fact that they had hypertension, or that neither the patients nor the doctors had learned of the hypertension diagnosis, due to the “virological dictatorship,” i.e., all concerns are aimed at controlling the HIV. Or rather, the prolonged use of antiretroviral drugs could have been the determining factor for the onset of hypertension, which is an aspect that seems unlikely given the data presented here.

Conclusion

In conclusion, the evaluation of a population with HIV/AIDS, according to the new international classification of JNC 7, revealed prevalence of prehypertension and hypertension in over half of the population. It is important to warn clinicians who provide care to HIV/AIDS patients that such patients are

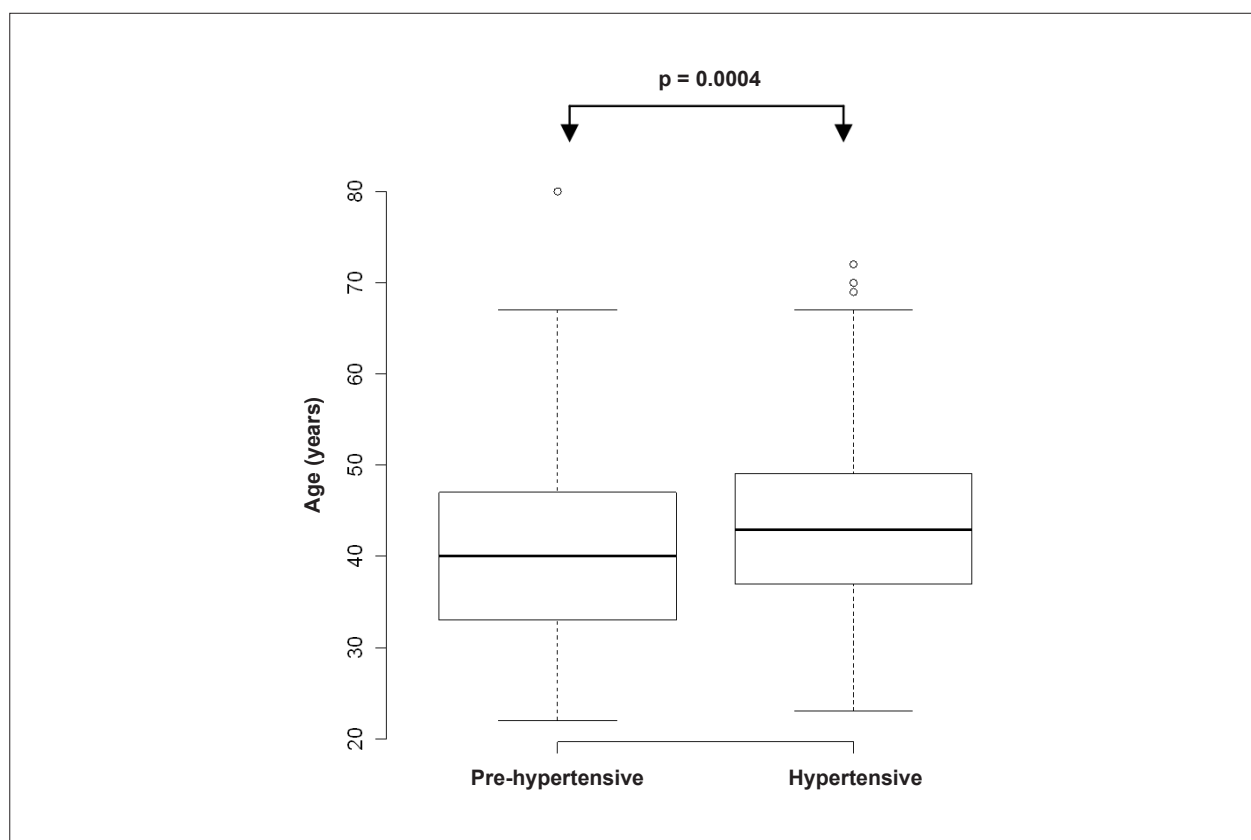


Figure 2 - Distribution by the average age of pre-hypertensive and hypertensive patients with HIV/AIDS included in a cohort.

not only individuals infected with a potentially fatal virus, but, despite the benefit of new antiretroviral therapies, they are also patients whose prognosis may be affected by comorbidities, such as hypertension.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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