Adherence to antiretroviral therapy and changes in body composition in people living with HIV and AIDS

Adesão a terapia antirretroviral e alterações da composição corporal em pessoas vivendo com HIV/AIDS

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ABSTRACT

Introduction: The successful treatment of human immunodeficiency virus (HIV) infection depends on adherence to antiretroviral therapy. Since the development of ART, there has been a significant increase in the survival of people living with HIV/AIDS. However, in the same way that it works in a positive way, the antiretroviral therapy has side effects that ultimately influence the rate of adherence to drug treatment. **Objective:** Evaluate adherence to antiretroviral therapy (ART) and changes in the body composition of adults diagnosed with HIV/AIDSon ART for at least 12 months. **Methods:** A cross-sectional study was conducted at an outpatient clinic for infectious-parasitic diseases at a teaching hospital that is a reference in the treatment of people living with HIV/AIDS. Socio-demographic and clinical data were collected from medical records. Weight, height, body mass index (BMI) and abdominal circumference (AC) were recorded. Bioelectrical impedance analysis was performed using the tetrapolar protocol to assess body composition. The "*Cuestionario para la Evaluación de la Adhesión al Tratamiento Antiretroviral*" was used to investigate adherence to ART. **Results:** Sixty-one patients (27 women and 33 men) participated in the study. Most were more than 40 years of age and were classified as overweight based on BMI. Most patients (86.8%) had been using ART for more than five years and 78.6% were classified as sedentary. Among the patients with an adequate AC, 82.3% were men. Among the 11 patients with low adherence to ART, 90.9% were men. Among the 33 with strict adherence, 69.6% were women. Mean percentage of fat mass was 28.63% among the men, and 40.82% among the women. **Conclusion:** Strict adherence to ART was seen in more than half of the study population. Women had more side effects from ART, as this group hadgreater adherence to treatment. The findings underscore the relationship between high rates of adherence to ART and changes in body composition, such as increased fat deposition and risk of associated diseases.

Keywords: therapeutic adherence; AIDS, antiretroviral therapy; body composition.

RESUMO

Introdução: O sucesso do tratamento da infecção pelo vírus da imunodeficiência humana (HIV) depende da adesão à terapia antirretroviral (TARV). Desde o desenvolvimento da TARV, houve aumento significativo da sobrevida das pessoas que vivem com HIV/Síndrome da Imunodeficiência Adquirida (AIDS). Porém, da mesma forma que atua de modo positivo, a terapia antirretroviral possui efeitos colaterais que acabam influenciando a taxa de adesão terapêutica ao tratamento medicamentoso. Esses efeitos incluem significativas alterações na composição corporal, resistência à insulina e dislipidemias. **Objetivo:** Avaliar a adesão à terapia antirretroviral e descrever alterações na composição corporal de adultos com diagnóstico de HIV/AIDS que usaram terapia antirretroviral por no mínimo 12 meses. **Métodos:** Estudo transversal realizado em um ambulatório de doenças infectoparasitárias em Hospital Universitário, referência no tratamento de pessoas que vivem com HIV/AIDS. Verificou-se dados sociodemográficos e clínicos nos prontuários. Foram registrados peso, altura, índice de massa corporal (IMC) e circunferência abdominal (CA). Realizou-se a bioimpedância segundo o protocolo da técnica tetrapolar para avaliação da composição corporal. Para avaliar a adesão terapêutica foi usado o *Cuestionario para la Evaluación de la Adhesión al Tratamiento Antiretroviral*. **Resultados:** Foram estudados 61 pacientes, 27 mulheres e 34 homens; a maior parte tinha acima de 40 anos e IMC classificado como sobrepeso. A maioria dos pacientes (86,8%) usavam TARV há mais de cinco anos e 78,6% se autodeclararam sedentários. Do total de pacientes que apresentaram circunferência abdominal adequada, 82,3% eram homens. Dos 11 pacientes que se classificaram como baixa adesão à TARV, 90,9% eram homens, e dos 33 que se classificaram como estritamente aderentes, 69,6% eram mulheres. Os homens apresentaram 28,63% de média de porcentual de massa gorda (%MG), enquanto as mulheres apresentaram 40,82%. **Conclusão:** A adesão estrita à TARV foi vista em mais da metade da população estudada. As mulheres apresentaram mais efeitos colaterais oriundos da TARV, visto que este grupo mostrou uma adesão maior ao tratamento. Isso reforça a relação entre altas taxas de adesão à terapia medicamentosa e alterações na composição corporal, como o aumento da deposição de gordura e riscos de doenças associadas.

Palavras-chave: adesão terapêutica; AIDS; terapia antirretroviral; composição corporal.

INTRODUCTION

More than one million cases of acquired immunodeficiency syndrome (AIDS) were reported in Brazil since the first case in 1980 to June 2020[1]. AIDSis caused by a human immunodeficiency virus (HIV), which attacks the immune system, causing progressive immunosuppression that results in opportunistic infections and characteristic clinical manifestations of the disease[2].

In the 1990s, there was the development of the potent antiretroviral therapy (ART), which is a combination of drugs with the aim of inhibiting the multiplication of HIV in the organism[3]. This discovery has led to the control of HIV infections, with improvement in the immunological profile and changes in nutritional status, providing patients with a better quality of life[4].

Despite the benefits, ARTis also associated with severe side effects[3], such as recurrent changes in the distribution of body fat and metabolic disorders, such as dyslipidemia, the abnormal homeostasis of

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glucose and insulin resistance. These factors can contribute to the development of diabetes mellitus and cardiovascular diseases in this group of patients[3,5].

The success of the ART, with the increase in the survival rate and reduction in the risk of the progression to AIDS, is directly related to adherence to therapy. Nevertheless, adherence poses a challenge due mainly to the side effects, the stigmatizing nature of the disease,among other factors[6].

The practice of exercise and diet are adjuvant therapies for people who live with HIV/AIDS, and help minimize the side effects of ART[6]. However, these types of therapy also pose a challenge in terms of adherence. Patients who do not adhere to these therapies may have high percentages of fat and an increase in body mass index, which contribute to the development of chronic noncommunicable diseases[7].

OBJECTIVE

Evaluate adherence to antiretroviral therapy, describe changes in the body composition of the population studied and determine a possible pattern related to sex.

METHODS

A descriptive cross-sectional study was conducted with people who live with HIV/AIDS at the infectious-parasitic diseases clinic of a university hospital that serves as a reference center for this population. All participants received clarifications regarding the objectives of the study, risks and benefits as well as the evaluations to which they would be submitted. The data were collected after approval from the Human Research Ethics Committee of the hospital (certificate number: 68068017.0.3001.8807) in accordance with Resolution N° 466/12, of the National Board of Health. Patients with a diagnosis of HIV and using antiretroviral therapy for at least 12 months were included. Individuals with edema, any limb amputation, the use of any prosthesis (metal or silicone), those who had ingested alcoholic beverages in the 48 hours prior to the test, those who practiced physical exercise in the 24 hours prior to the test, and women in the premenstrual or menstrual cycle were not included, in order to minimize the occurrence of errors on the bioelectrical impedance analysis (BIA), as suggested by the manufacturer of the equipment.

Anthropometric assessment

Questionnaires were administered for the collection of sociodemographic data. Information was also obtained from medical records. The anthropometric data were weight, height, waist circumference (AC) and body mass index (BMI). AC was interpreted using the recommendations of the World Health Organization (2004): ≥94 cm for men and ≥80 cm for women, increasing the risk of cardiovascular disease[8]. BMI was calculated by dividing weight in kilograms by height in meters squared and classified using the recommendations of the World Health Organization: BMI<18.5=underweight; BMI≥18.5 and <25=adequate weight; BMI≥25 and <30=overweight[9].

Evaluation of body composition

Body composition was measured using the Sanny® tetrapolar bioelectrical impedance equipment, employing the protocol proposed by Gray et al.[10] with recommendations proposed by Guedes[11]. The classification was based on the reference values for fat mass percentage (%FM) as proposed by Lohman et al.[12]: <5 for men and <8 for women=risk of diseases and disorders associated with malnutrition; 6 to 14 for men and 9 to 22 in women=below average; 15 for men and 23 for women=average; 16 to 24 for men and 24 to 31 for women=above average; >25 for men and >32 for women=risk of diseases associated with obesity.

Physical activity level

The short version of the International Physical Activity Questionnaire was administered for the classification of the physical activity level. Individuals who reported practicing moderate physical activities at least five times per week at least 30 minutes a day, and vigorous activities at least three times per week at least 20 minutes a day were classified as very active. Individuals who reported practicing moderate physical activities at least five times per week at least 30 minutes a day, or vigorous activities at least three times per week at least 20 minutes a day were classified as active. Individuals who reported performing physical activity, but not enough to be considered active, were classified as insufficiently active. Individuals who reported no involvement in any type of physical activity for at least 10 continuous minutes during the week were classified as sedentary[13].

Adherence to the ART

Adherence to ARTwas determined using the "*Cuestionario para la Evaluación de la Adhesión al Tratamiento Antirretroviral* (CEAT-VIH)" in its version translated, adapted and validated for use in Brazil. This questionnaire is composed of items that address compliance with treatment; factors that modulate adherence; interaction between healthcare provider and patient; patient's beliefs related to the effort and time of treatment; and an assessment of the severity of side effects. The structure is composed of 20 questions. The total is calculated by summing the items and ranges from 17 to 89 points, with higher scores denoting greater patient adherence to the medication. The degree of adherence was classified as "low/insufficient" (<77 points), "good/adequate" (≥77 and <83 points) or "strict" (≥83 points)[14].

Data analysis

A databank was created with double entry, and the consistence of the data was verified using the Data Compare module of Epi Info. The data were described using the frequency distribution (percentage) for categorical variables with the aid of the EPI INFO 7.2 program.

RESULTS

Sixty-one patients (27 women and 34 men) participated in the study. Most (78.7%) were older than 40 years of age (mean age: 47;

standard deviation: 8.089087299). Fifty-three participants made use of ART for five or more years (26 women and 27 men) (**Table 1**).

Regarding BMI, 37.7% of the patients were classified as overweight, and approximately 25%of the sample had an adequate BMI. In terms of physical activity level, 78.7% of the patients were classified as sedentary.

Table 2 displays the results of the body composition evaluation. A substantial difference was found between the sexes regarding abdominal circumference. Among the participants with an adequate AC, most were men (82.3%). A substantial difference between the sexes was also found for %FM, the mean of which was 40.82%for women and 28.63% for men. Among the 27 participants, only three had a %FM classifying them as not being at risk for diseases associated with obesity. Among the participants classified in the different categories of risk of diseases associated with obesity, 71% were men.

Table 1 – Sociodemographic characteristics and nutritional diagnosis of people living with HIV/AIDS in care at the infectious-parasitic diseases clinic of Oswaldo Cruz University Hospital (*Universidade de Pernambuco*).

Variables	Sex		Total
	Male	Female	
	% (N)	% (N)	% (N)
Sample (n)	55.7 (34)	44.3 (27)	100 (61)
Age (years)			
<40	14.7 (9)	6.6 (4)	21.3 (13)
≥40	41.0 (25)	37.7 (23)	78.7 (48)
BMI			
Adequate	18.0 (11)	9.8 (6)	27.8 (17)
Overweight	21.3 (13)	16.4 (10)	37.7 (23)
Grade I and II obesity	16.3 (10)	18 (11)	34.4 (21)
Physical activity level			
Sedentary	39.4 (24)	39.4 (24)	78.7 (48)
Insufficiently active	6.6 (4)	1.6 (1)	8.2 (5)
Active/very active	11.4 (7)	3.2 (2)	8.1 (5)
Duration of ART			
≥5 years	44.3 (27)	42.6(26)	86.9 (53)
3 years	6.6 (4)	-	6.6 (4)
1 year	4.9 (3)	1.6 (1)	6.5 (4)

BM: body mass index; ART: antiretroviral therapy.

Table 2 – Anthropometric characteristics of people living with HIV/AIDS in care at the infectious-parasitic diseases clinic of Oswaldo Cruz University Hospital (*Universidade de Pernambuco*).

Variables	Sex		Total
	Male	Female	
	% (N)	% (N)	N
AC			
Adequate	82.3 (14)	17.7 (3)	17
Risk of CVD	45.5 (20)	54.5 (24)	44
%FM			
Below average	50 (1)	50 (1)	2
Above average	81.8 (9)	18.2 (2)	11
Risk of DAO	50 (24)	50 (24)	48

AC: abdominal circumference; CVD: cardiovascular disease; %FM: percentage of fat mass; DAO: diseases associated with obesity.

In the analysis of adherence to ART, 18% of the patients had low/insufficient adherence, 27.8% had good/adequate adherence, and 54% had strict adherence. Among the 11 patients with low adherence to treatment, 10 were men. Among the 33 patients with strict adherence to treatment, 23 were women. These findings reveal a relationship between adherence and sex (**Table 3**).

Analyzing the points addressed on the adherence questionnaire separately, some findings stood out. A total of 73.7% of the participants reported making a considerable effort to follow treatment, whereas only 18% reported making little effort. Regarding the feeling of being able to follow treatment, 49% considered themselves to be poorly to fairly capable. A total of 80% reported very intense side effects and 65.5% reported having little or no information on the medications they were taking.

The individuals with higher mean %FM were women with a mean age of 50.1 years who underwent ART for more than five years and adhered strictly to treatment. In contrast, the men, despite being in treatment for a longer mean time, had lower adherence rates and lower mean %FM (**Table 4**).

DISCUSSION

Among the patients studied, the male sex predominated. This finding is in agreement with data from the 2020 HIV/AIDS epidemiological bulletin, which states that the ratio of men compared to women has always been higher than 1, regardless of the age group[1].

Table 3 – Adherence to treatment of people living with HIV/AIDS in care at the infectious-parasitic diseases clinic of Oswaldo Cruz University Hospital (*Universidade de Pernambuco*).

Adherence	Sex		Total
	Male	Female	
	% (N)	% (N)	% (N)
Low/insufficient	1.6 (1)	16.4 (10)	18.0 (11)
Good/adequate	4.9 (3)	22.9 (14)	27.8 (17)
Strict	37.7 (23)	16.4 (10)	54 (33)

Table 4 – Adherence rates and percentage of fat mass in people living with HIV/AIDS in care at the infectious-parasitic diseases clinic of Oswaldo Cruz University Hospital (*Universidade de Pernambuco*).

Adherence	Low/ insufficient adherence		Good/ adequate adherence		Strict adherence	
	Male	Female	Male	Female	Male	Female
	% (N)	% (N)	% (N)	% (N)	% (N)	% (N)
Below average	1.6 (1)	1.6 (1)	-	-	-	-
Above average	14.8 (9)	-	-	3.2 (2)	-	-
Risk of DAO	-	-	22.9 (14)	1.6 (1)	16.4 (10)	37.7 (23)
Total	16.4 (10)	1.6 (1)	22.9 (14)	4.9 (3)	16.4 (10)	37.7 (23)

DAO: diseases associated with obesity.

The mean age of the participants was similar to findings described in other studies conducted in Brazil, such as those by Beraldo et al.[15] (mean age: 44.3 years) and Zuge et al.[16] (mean age: 43.2 years). Most of the participants made use of ART for five years or more, which is in agreement with data from studies that report that the diagnosis of these patients is generally in the reproductive age range, as the main contagion route of the virus is sexual[6,17].

With regards to the practice of physical activity, which is an adjuvant treatment to ART, the majority of patients were sedentary. This finding underscores the importance of raising awareness regarding the benefits of physical exercise at reducing the side effects of drug treatment[18]. Recent studies state that the prescribed strength training for people who live with HIV/AIDSstimulates an increase in lean mass and strength levels, as well as a reduction in fat mass, better distribution of body fat and improvements in the immune system[6].

The BMI results revealed that overweight was prevalent in the sample. Analyzing the sexes comparatively, men and women had similar means. However, 88% of the women had a high AC. Beraldo et al.[15] also found that approximately 80% of the women in their studies had an AC placing them at risk for cardiovascular disease. AC is a measure of the deposition of central fat in the abdominal region and a high AC is associated with greater cardiovascular risk than generalized obesity classified based on the BMI[15], as abdominal adipose tissue synthesizes and secretes mediators and cytokines that contribute to mechanisms of hypertension, insulin resistance, atherosclerosis and dyslipidemias[19-21].

The women also had higher mean %FM compared to the men, which also indicates a greater risk of development of cardiovascular disease. It should be pointed out that there are somatic differences inherent to sex, as women have a greater quantity of subcutaneous adipose tissue and less developed muscle tissue, which is aggravated with age[22]. Belonging to the female sex is an independent risk factor for the development of metabolic syndrome and other diseases, such as lipodystrophy[23].

In the present study, the patients with a longer time on ART had higher percentages of fat mass, which is in agreement with data reported by other authors who evaluated the relationship between treatment time and changes in the body composition of patients. Analyzing 166 patients, Alikhani et al.[5] found an association between time in treatment and higher percentages of fat mass. In general, the evidence is that a longer treatment time is related to a greater occurrence of lipodystrophy (lipoatrophyand lipohypertrophy)[24-26].

Fat altering mechanisms in people living with HIV/AIDSare complex, multifactorial and not fully understood[27]. Much is discussed on the different classes of medications resulting in specific effects, and the combination of drugs causing such changes[28]. Reverse-transcriptase inhibitors and protease inhibitors have toxic effects on the mitochondria and endoplasmic reticulum, respectively[29]. As a result, changes occur in adipogenesis (increase in adipogenesis and the apoptosis of these cells), there are disturbances in the metabolism of cholesterol, neurodegenerative changes and an increase in serum levels of inflammatory cytokines. The sum of these effects results in changes in the distribution of body fat and the metabolism of people living with HIV/AIDS[28,29].

More than half (56%) of the patients adhered strictly to ART. Studies conducted within Brazil and abroad using the same assessment tool found divergent results with regards to adherence. Analyzing 179 patients in the country, Primeira et al.[14] found that only 16.8% adhered strictly to treatment. Remor[30] analyzed 652 patients in Colombia and found that only 15% had strict adherence.

Despite being aware of the benefits of therapy, the lack of understanding with regards to treatment, the stigmatizing nature of the disease, the side effects of treatment, anger, and the use of licit and illicit drugs can exert an influence on adherence[23]. Gir et al.[31] analyzed 200 people and found that the side effects of the medications were cited as the main complicating factors of adherence to treatment, the most frequent of which were nausea, vomiting, headache, diarrhea and skin rash[6]. Following a psychosocial bias, another relevant factor described in the literature is the need for an effort to follow treatment and the extent to which patients feel capable of following it. In the present study, most participants reported making a considerable effort to follow treatment, whereas approximately half considered themselves to be poorly to fairly capable of following it. Almeida et al. and Primeira et al. discuss the association between less adherence and both a greater effort and a lower feeling of capacity[6,15].

Comparing the sexes, the majority of individuals with strict adherence to treatment were women, whereas men adhered little to treatment. The low adherence of the male sex is widely discussed in the literature. The culture of masculinity, which perpetuates the notion that men are the strong sex, induces men to take care of themselves less, leading them to seek healthcare services only when in need of curative treatment. In contrast, women pay more attention to their health and there is greater incentive on the part of the media for preventive health care and female health, leading women to seek health services more often and making them active agents in the treatment and cure process[23,32].

Besides the physiological differences in the distribution of body mass between the sexes, women are expected to suffer more side effects of ART, as they adhere more to treatment. Women had higher AC and %FM compared to patterns considered healthy.

The present findings are relevant and underscore the need for interventions regarding adherence to drug treatment and adjuvant therapies, such as the practice of physical exercise and nutritional counseling. The multidisciplinary group should be prepared to promote better care to minimize the side effects resulting from the combination of the disease and the ART to ensure better quality of life for people living with HIV/AIDS.

The strengths of this study were the identification of adherence to ART at a reference center; a nutritional assessment was performed beyond classic anthropometry; and differences between the sexes were found regarding both adherence to treatment and body composition. The results reveal that adherence to ART is very good at this service, but shows a need for better follow-up for women on antiretroviral therapy.

The main limitation of this work is the fact that it is a descriptive study with a small number of participants.

CONCLUSION

Most people living with HIV/AIDSunder treatment at the reference service where this study was conducted adhered to antiretroviral

treatment. Women had more side effects resulting from ART, as this group adhered more to treatment and there is a relationship between high rates of adherence to ARTand changes in body composition, such as an increase in fat disposition, characterizing a greater risk of diseases associated with obesity.

Approval by the Human Research Ethics Committee:

The data were collected after approval from the Human Research Ethics Committee of the HUOC/PROCAPE hospital complex (certificate number: 68068017.0.3001.8807) in accordance with Resolution N° 466/12 of the National Board of Health.

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Conflict of interests

The authors declare no conflicts of interests.

Participation of each author

Fernanda Carneiro Gomes Ferreira: conceived the project, participated in the data collection and interpretation of the results and final writing of the article.

Sofia Oliveira de Souza: conceived the project, participated in the data collection and interpretation of the results and final writing of the article.

Érica Priscila Carneiro Ouriques de Vasconcelos: wrote the project, conducted the data collection, participated in the interpretation of the results and final writing of the article.

Ana Célia Oliveira dos Santos: planned and supervised the work and corrected the writing of the manuscript in all phases.

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