

Assessment of climate syndrome in women living with HIV/AIDS in a reference center

Avaliação da síndrome climatérica em mulheres vivendo com HIV/AIDS em um centro de referência

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ABSTRACT

Introduction: Women living with HIV (MVHIV) have a lower mean age at menopause than the general population, in addition to more exuberant symptoms during this period. These factors can further reduce the quality of life of this population during perimenopause and negatively affect antiretroviral therapy (ART). Understanding this risk is important for medical advice at this stage, as well as for evaluating the initiation of hormonal therapy, when necessary. **Objective:** To evaluate the climacteric syndrome in women living with HIV/AIDS. **Methods:** During an endocrinological medical consultation, a clinical examination was performed, including an anthropometric physical examination, in addition to the application of a questionnaire to assess the symptoms of the climacteric syndrome and collection of hormonal values, viral load and serum CD4 cell values of 44 women, aged between 35 to 65 years old, living with HIV/AIDS. **Results:** The mean age at spontaneous menopause was 47.44 years, there was an association between FSH, LH and estradiol hormones and perimenopause phases. Anxiety and/or nervousness was present in 84.1% of patients and slowing of thinking in 72.7%. Skin dryness was also shown to be a significant symptom, with 75% of recurrence. Furthermore, women with skin dryness had higher FSH and LH compared to those without the symptom. **Conclusion:** Women living with HIV in Belém-PA had menopause 3.76 years before the expected national average and presented a high prevalence of symptoms related to cognition and mood. Other similar studies, with a larger sample size, are needed in the region to establish more reliable results.

Keywords: HIV; Early menopause; Climacteric symptoms; ART.

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RESUMO

Introdução: Mulheres vivendo com HIV têm idade média de menopausa menor que a população em geral, além de sintomas mais exuberantes nesse período. Esses fatores podem reduzir ainda mais a qualidade de vida dessa população durante a perimenopausa e afetar negativamente a terapia antirretroviral (TARV). Entender esse risco é importante para o aconselhamento médico nesta etapa, bem como para a avaliação do início da terapia hormonal, quando necessária. **Objetivo:** Avaliar a síndrome climatérica em mulheres vivendo com HIV/AIDS. **Métodos:** Durante consulta médica endocrinológica, foi realizado exame clínico, incluindo exame físico antropométrico, além da aplicação de questionário para avaliação dos sintomas da síndrome climatérica e coleta dos valores hormonais, carga viral e valores de células CD4 séricos de 44 mulheres, com idade entre 35 e 65 anos, vivendo com HIV/AIDS. **Resultados:** A idade média da menopausa espontânea foi 47,44 anos, houve associação entre os hormônios FSH, LH e estradiol e as fases da perimenopausa. A ansiedade e/ou nervosismo esteve presente em 84,1% das pacientes e a lentificação do pensamento em 72,7%. O ressecamento de pele também se mostrou um sintoma significativo, com 75% de recorrência. Ademais, as mulheres com ressecamento de pele apresentaram FSH e LH mais elevados comparadas com as que não possuíam o sintoma. **Conclusão:** Mulheres vivendo com HIV de Belém/PA apresentaram a menopausa 3,76 anos antes da média nacional esperada e apresentam alta prevalência de sintomas relacionados à cognição e humor. Outros estudos similares, com maior número amostral, são necessários na região para estabelecer resultados mais confiáveis.

Palavras-chave: HIV; Menopausa precoce; Sintomas climatéricos; TARV.

INTRODUCTION

Early menopause refers to menopause occurring between the ages of 40 and 45 years, and premature menopause refers to menopause occurring before the 40 years old. Several reports have shown that the average age of menopause in women living with HIV (WLHIV) is lower than the general population, with a greater risk of developing early and premature menopause¹.

HIV infection and the use of ART can impair ovarian functions and fertility in women, culminating in early menopause². Pacheco et al. (2020)³ demonstrated this association by revealing that mild, moderate, and severe menopausal symptoms were more intense in middle-aged women with HIV infection.

Although there is evidence to infer that these women experience menopause at an earlier age and they experience more exacerbated symptomatology than women without HIV, there is no clear consensus on the impact of HIV on menopause and its symptomatology in the literature. Little

information exists about the predictors of menopausal symptoms, nor the impact of these symptoms on behavior, well-being, and health maintenance in this group of women. In addition, menopausal symptoms in women with HIV may not be recognized by healthcare providers and women themselves, and there is little data on symptom management in this population⁴. Therefore, the study aimed to evaluate the climacteric syndrome in women living with HIV/AIDS.

METHODS

STUDY'S TYPE AND RESEARCH LOCATION

It is a descriptive, cross-sectional study and is classified, as to its purpose, as applied research, used two comparison groups of women: pre-menopausal and post-menopausal. The procedures adopted were field research and documental research. This study was realized in the Endocrinology Service of the Jean Bittar Hospital, located in Belém do Pará, Brazil.

POPULATION STUDIED

The target population included female patients, attended at the Endocrinology Service of the Jean Bittar Hospital, between 35 and 65 years old, who live with HIV. The sample consisted of 44 women who agreed to participate by signing a Free and Clarified Consent Term. Female patients were included, aged between 35 and 65 years, with positive serology for HIV and using ART. Women who were using hormonal therapy, or who had difficulty in communication or who did not wish to continue as subjects of the research were excluded.

DATA COLLECT

Personal and clinical data relevant to the research were collected through a questionnaire applied by the researchers in addition to anamnesis, medical records, and physical examination performed during the outpatient consultation. The information collected were: age, race, weight, height, waist circumference, medications in use and physical activity, time of menopause, HIV viral load, time of HIV diagnosis, CD4+ T lymphocyte count, antiretroviral regimen in use, symptoms relating to the climate.

PHYSICAL EXAM

In the physical examination, anthropometric data were collected: height, weight, and waist circumference. Was used the following formula to calculate the body mass index: $BMI = \text{Weight}/\text{Height}^2$ (kg/m^2 unit). Patients were classified according to BMI as thinness grade III ($BMI < 16 \text{ kg}/\text{m}^2$); grade II thinness ($16 \text{ kg}/\text{m}^2 \leq BMI < 17 \text{ kg}/\text{m}^2$); grade I thinness ($17 \text{ kg}/\text{m}^2 \leq BMI < 18.5 \text{ kg}/\text{m}^2$); normality ($18.5 \text{ kg}/\text{m}^2 \leq BMI < 25 \text{ kg}/\text{m}^2$); overweight ($25 \text{ kg}/\text{m}^2 \leq BMI < 30 \text{ kg}/\text{m}^2$); obesity grade I ($30 \text{ kg}/\text{m}^2 \leq BMI < 35 \text{ kg}/\text{m}^2$); and obesity grade II ($35 \text{ kg}/\text{m}^2 \leq BMI < 40 \text{ kg}/\text{m}^2$); and grade III obesity ($BMI \geq 40 \text{ kg}/\text{m}^2$).⁵ The abdominal circumference was measured in the middle of the distance between the iliac crest and the lower costal margin, with a waist circumference between 80 and 88 cm already suggesting risk factors for coronary disease, and greater than 88 already constituting abdominal obesity, being included as one of the criteria for metabolic syndrome⁶.

SYMPTOMATOLOGICAL INTERROGATION

The interview was conducted with the purpose of investigating the main symptoms of the weather syndrome. In perimenopausal patients, was evaluated the presence of symptoms. While in postmenopausal patients, it was evaluated whether there were symptoms during the climacteric period.

The climacteric symptoms were evaluated in six areas: vasomotor symptoms (hot flashes, flushing, chills, and sweating), sleep disorders (non-restorative sleep, nocturnal awakening, and insomnia), cognition and mood (irritability, memory impairment, slowed thinking, sadness and nervousness or anxiety), genitourinary symptoms (vaginal dryness, vaginal atrophy, vaginal itching, and urinary incontinence), sexuality (dyspareunia and loss/decreased libido) and general symptoms (hair loss or change in hair

appearance, loss of appetite, muscle or joint pain, headache, dry skin, and nausea/vomiting).

In addition to the symptoms related to the climacteric, symptomatological interrogation evaluated the gynecological history reported by the patients: sexually transmitted infections, pregnancy, abortion, annual prevention, regularity of the menstrual cycle, date of the last menstruation, use of contraceptives, polycystic ovary syndrome, endometriosis, therapy hormone replacement therapy (HRT), oophorectomy and ovarian cyst.

LABORATORY EXAMS

Blood samples were collected at Jean Bittar Hospital for hormone evaluation levels of prolactin, estradiol, LH and FSH. The CD4 tests and viral load were brought from the HIV/AIDS reference centers (Centro de Atenção à Saúde em Doenças Infecciosas Adquiridas – Casa Dia – Centro de Testagem e Acolhimento da Unidade de Referência Especializada em Doenças Infecciosas Parasitárias Especiais – CTA UREDIPE) by patients for consultation at Jean Bittar Hospital. The following reference values were used:

- **Luteinizing Hormone (LH)** – in mIU/mL: Follicular Phase: 1.9 to 9.92; Peri-ovulatory phase: 6.1 to 49.1; Lutein phase: 1.3 to 10.8; Post-menopause; No hormone therapy: 15.4 to 53.3; With hormone therapy: 0.7 to 52.7.
- **Follicle Stimulating Hormone (FSH)** – in mIU/mL: Follicular Phase: 3.5 to 9.2; Lutein phase: 1.7 to 5.6; Post-menopause; No hormone therapy: 13.9 to 103.1; With hormone therapy: 1.7 to 96.8.
- **Estradiol** – in pg/mL: Follicular phase: <10 to 122; Peri-ovulatory phase: 53.6 to 361; Luteal Phase: 30.9 to 197; Post Menopause; No hormone treatment: <10.

DATA ANALYSIS

Qualitative and quantitative results were stored in electronic spreadsheets using Microsoft Excel 2013 software, and analyzed using BioEstat 5.3, Epi-Info (version 3.5.2), and Jamovi (version 1.6.23 solid) software. Qualitative variables were presented as absolute and relative frequency measures, quantitative variables were presented as measures of central tendencies, such as mean and median, as well as measures of variability, standard deviation, and quartiles, respectively.

To analyze the normality of the sample, the D'Agostinho and Kolmogorov-Smirnov tests were performed. Then, analysis of variables was performed using Student's T test and Mann-Whitney U test, according to the normal or non-normal distribution of the sample, respectively. The sample summary T Test (one sample) and the Spearman Correlation Test were also used. The alpha level of rejection of the null hypothesis was considered to be 0.05 (5%).

RESULTS

In this study, 26 patients (59.1%) had already gone through menopause. Of the remaining, 11 (25%) had menstrual

irregularity, while 7 (15.9%) had a regular menstrual cycle. The mean age of spontaneous menopause (n=18) was 47.44 ± 3.81 years, with a minimum age of 40 years and a maximum of 55 years, while the median was 47.5 years. The minimum and maximum years old of spontaneous menopause in the present study were 40 and 55 years, respectively. It is important to note that patients who reported surgical menopause were excluded from this analysis (n=8).

In our study, when the mean age at menopause of the Brazilian population was compared with the mean age of WLHA (women with spontaneous menopause without hormonal contraceptive use in this period), there was a significant difference (Table 1). Of these women who entered menopause spontaneously, 15 began menopause at a younger age than the national average, with an average of 46.26 ± 2.97 years for their last menstrual period.

The study covered 44 women, of whom the minimum and maximum age were respectively, 33 and 65 years old, with a mean age of 51.4 years (± 8.91 years). Regarding the time of HIV infection, the minimum time of infection was one year, and the maximum time was 30 years, with an average of 12 (± 7.94) years of infection. Regarding the time of treatment with ART, the minimum and maximum time of treatment were 0.6 and 25 years, respectively, with a mean of 11.2 years.

A correlation between the time of HIV and the time of treatment with ART with the age of menopause (Table 2) was made to verify if there was a correlation of these parameters with the age of onset of menopause of the patients, resulting in the no correlation meant.

Also, were described the CD4 cell count and viral load of the patients. Of the patients in the study, it was observed that eight had CD4 < 200 and 30 CD4 ≥ 200. It was not possible to obtain this data from six women. Regarding viral load, nine had a detectable viral load, and 33 had an undetectable viral load. It was not possible to obtain these data from two women. Patients with detectable viral load (n=9) started ART, on average, about 3.62±3.36 years after the beginning of this study. The median was 2 years, with a minimum of 0.66 years and a maximum of 10 years. All of

these patients had already been using antiretroviral therapy for more than 6 months.

Regarding the class of ART used by the participants, it was observed that the regimens with nucleoside reverse transcriptase inhibitors (NRTIs) + Protease inhibitors (PI) were the most used (n=18), followed by non-nucleoside reverse transcriptase inhibitors (NNRTI) + NRTI (n=10), NRTI + Integrase Inhibitors (II) (n=7), Protease Inhibitors (PI) + II (n=2), NRTI (n=2), NRTI + PI + II (n=1), IP + II +Fusion Inhibitors (FI) (n=1) and NRTI + II + NNRTI (n=1). Regarding the ART regimen by class in women who used hormone replacement therapy (n=8), the most used class was NRTI + IP (n=3), followed by NNRTI + NRTI (n=2), NRTI + PI + II (n=1), PI + II +FI (n=1) and NRTI (n=1).

About the gynecological profile of the patients in this study, none reported previous diagnosis of endometriosis, and only 3 (6.8%) reported a previous diagnosis of polycystic ovary syndrome. Twenty-four (54.5%) underwent preventive in the last two years. Twenty-one (47.7%) use or used oral contraceptives when they had climacteric symptoms. Only 8 (18.2%) had already undergone hormone replacement therapy (HRT) because they had symptoms of the syndrome.

After analyzing the symptomatologic questionnaire, it was possible to establish a first clinic profile of the climacteric syndrome in the patients. Symptoms were divided into six areas: vasomotor symptoms, sleep, cognition and mood, genitourinary symptoms, sexuality, and general symptoms.

In terms of vasomotor symptoms, hot flashes were present in 30 patients (68.2%) and flushing in 28 (63.6%), these being the most prevalent symptoms. Chills were present in 22 women (50%) and sweating in 27 (61.4%). Concerning sleep disorders symptoms, the nocturnal awakening was the most prevalent, with 28 women (63.6%). Non-restorative sleep and insomnia occurred in 24 (54.5%) and 25 (56.8%) patients, respectively. The results on cognition and mood were quite expressive in all variables studied. Twenty-nine patients (65.9%) had irritability, 30 (68.2%) had memory impairment, 32 (72.7%) had slowed thinking, and 31 (70.5%) had sadness and or symptoms of depressants. The most expressive variable was anxiety and or nervousness, with 37 patients (84.1%) presenting the symptom.

Table 1. Comparison between the mean age at menopause of the Brazilian population and the mean age at menopause in women living with HIV/AIDS in Belém/PA in 2021.

	Average of the Brazilian population	Sample mean (n=18)	p-value*	CI 95%
Age of Menopause (in years)	51,20	47,44	0,0006	45,54 – 49,33

Legend: *Sample summary t test - one sample.

Table 2. Relationship between Time of HIV (in years) and Time of ART (in years) with age at menopause (in years) of women living with HIV/AIDS in Belém/PA in 2021.

	Spearman's Coefficient	(p)	Number of pairs
Time of HIV*	0,05	0,81	18
Time of ART*	0,15	0,54	18

Legend: *Spearman correlation test.

In the genitourinary symptoms, vaginal dryness was the most mentioned symptom by 32 women (72.7%). Vaginal atrophy was referred by 22 women (50%), urinary incontinence by 21 (47.7%), and vaginal itching by 7 (15.9%). In the symptoms related to sexuality, loss/decreased libido was reported by 29 (65.9%) of the women. Dyspareunia was present in only 13 patients (29.5%). Regarding nonspecific symptoms, the highest

prevalence was noticeable in dry skin in 33 patients (75%) and hair loss and or change, present in 32 patients (72.7%). Muscle and or joint pain was present in 59.1% (n=26) and headaches in 63.6% (n=28). The percentages of 20.5% (n=9) by nausea/vomiting and 34.1% (n=15) by appetite loss were discreet compared to the other general symptoms. In Figure 1, this information is detailed.

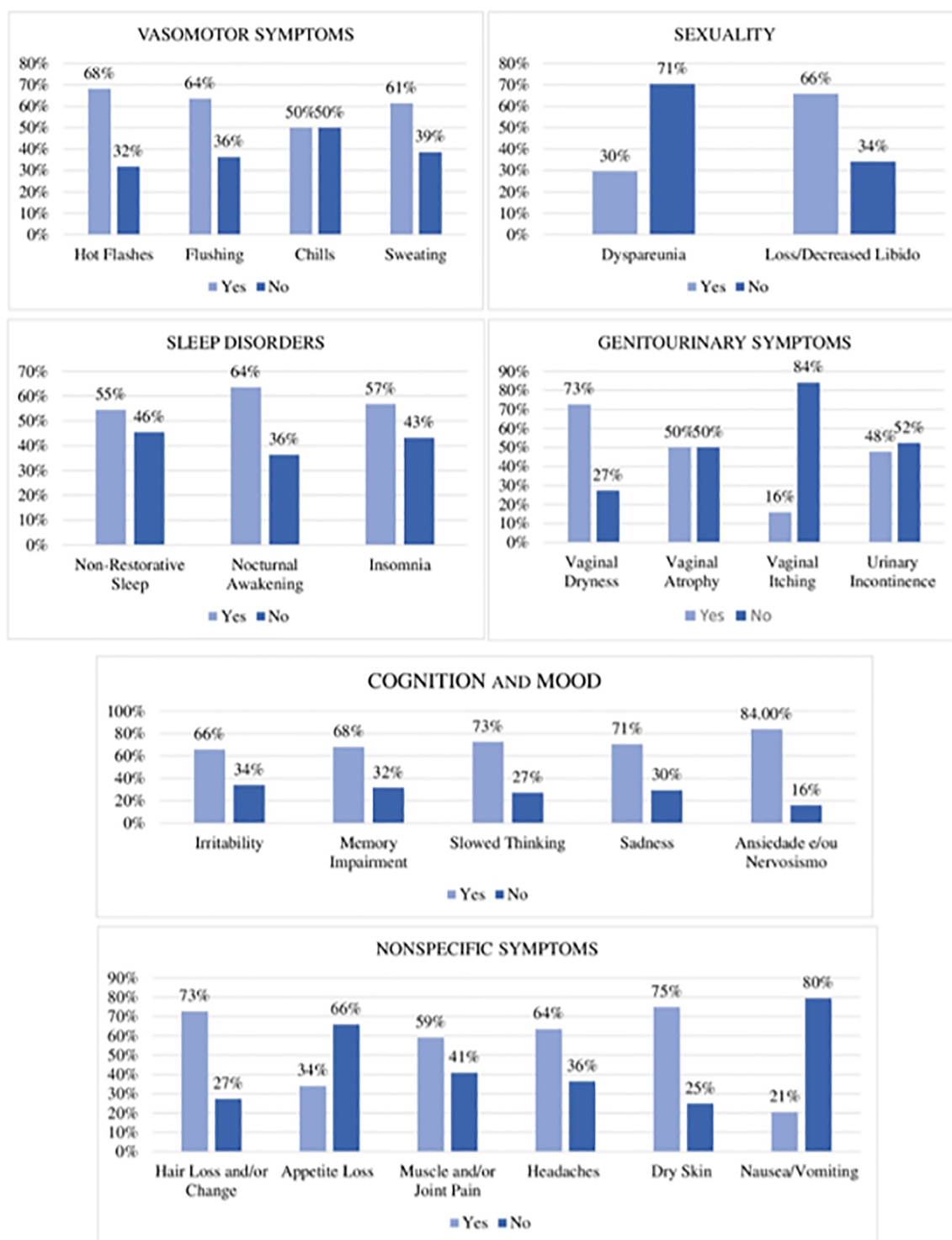


Figure 1. Graphs on vasomotor symptoms, sleep, cognition and mood, genitourinary symptoms, sexuality, and general symptoms in women living with HIV/AIDS in Belém/PA in 2021. Source: Elaborated by authors.

Regarding lifestyle habits, only 15 women in the study (34.1%) practiced physical activity at least three times a week. Regarding the anthropometric profile of the studied patients, it was observed that the mean Body Mass Index (BMI) and Abdominal Circumference (AC) were, respectively, 28.6 kg/m² and 92.7 cm. It was observed that the profile of women in this study (Table 3) consisted primarily of women with an average BMI who were overweight and whose WC was above the limit value of 88 cm by the World Health Organization. In table 3, it is also possible to identify the anthropometric profile separated by menopausal stage, noting that overweight is the most common nutritional status, both in pre- and post-menopausal patients.

The profile of the patient's hormones was also investigated. The FSH, LH, and estradiol exams were chosen to correlate with the research objective as they have a direct relationship with the menstrual cycle and ovarian failure. The levels of LH, FSH, and estradiol in the pre- and post-menopause phases were showed in table 4. Patients who used both contraceptive therapy and HRT at the time of data collection were excluded.

Tables 5, 6 and 7 refer only to data from patients already menopausal. Patients who used HRT were also excluded. In this table, only the most prevalent symptoms from each symptom area were selected – vasomotor symptoms, sleep disorders, cognition and mood, genitourinary symptoms, sexuality, and general symptoms. Due to the sample size of the groups studied, it was not possible to perform a statistical analysis of the relationship between FSH - vaginal dryness and estradiol - loss of libido.

DISCUSSION

According to the Climacteric Protocol of Fortaleza Federal University and the Assis Chateaubriand Maternity

School⁷, the national average for menopause is 51.2 years. In our study, women are starting menopause about 3.76 years earlier than the expected age for the uninfected population. Thus, it is possible to infer that the viral status of women living with HIV (WLHIV) may have some influence on this climacteric syndrome symptomatic precocity.

The proximity between the estimated mean time of HIV infection (12 years) and the start of ART (11.2 years) is a good indicator of public health. It is known that Brazil's HIV treatment and prevention policy has already reached a excellence level and achieved international recognition, since the performance of the Sistema Unico de Saúde (SUS) is able to guarantee effective testing, regular monitoring of diagnosed patients and free ART distribution. According to Villarinho et al. (2013)⁸, efforts guaranteed by law and public health policies, are encouraged by the federal government itself, through a wide care network that supports and ensures the broad exercise of the health right for PLHIV. This approach is essential to promote early acceptance of treatment as well as effective long-term adherence to therapy.

In the present study, many patients have little or no data about their immunological profile. These difficulties present a limiting factor for the present research, since without the immunological variables it is not possible to evaluate the effectiveness of the antiretroviral regimens used and to provide possible changes.

The distribution of the ART regimen divided by class is also noteworthy, as only 21.4% of patients use regimens that do not have NNRTIs or PIs in their combinations. Among the patients who use ART concomitantly with HRT (n=8 [18.2%]), only one (12.5%) does not use a regimen with either NNRTI or PI. According to Howells et al. (2019)⁹, caution should be exercised when associating these two classes of ARTs with HRT, since possible drug interactions of ART with contraceptive drugs do not allow the conclusion that

Table 3. General nutritional status and menopausal period in women living with HIV/AIDS in Belém/PA in 2021.

BMI (kg/m ²)*	Underweight (BMI 17-18)	Normal (18,5-25)	Overweight (IMC ≥ 25)	Obesity I (IMC ≥ 30)	Obesity II (IMC ≥ 35)	Obesity III (IMC ≥ 40)
 Geral (n=44)	1 (2,27%)	9 (20,45%)	22 (50%)	8 (18,18%)	2 (4,54%)	2 (4,54%)
Pre-menopausal (n=18)	-	3 (16,6%)	10 (55,5%)	1 (5,55%)	1 (5,55%)	-
Post-menopausal (n=26)	1 (3,84%)	6 (23,07%)	12 (46,15%)	4 (15,38%)	1 (3,84%)	2 (7,69%)

Legend: *Women with spontaneous and surgical menopause were included in this table.

Table 4. LH, FSH, and estradiol levels in the pre-menopausal and post-menopausal stages of women living with HIV/AIDS in Belém/PA in 2021.

Hormone	Pre-menopausal (n=11)	Post-menopausal (n=18)	p-value
FSH mUI/ml (Average ± SD)*	42,18 ± 37,56	89,66 ± 26,57	0,0004
LH mUI/ml (Average ± SD)*	19,27 ± 15,98	30,05 ± 10,56	0,03
Estradiol pg/ml (Median ± Interquartile Deviation) **	46 ± 95,4	13 ± 6,6	0,0007

Legend: *T test; **Mann-Whitney test.

Table 5. Relation between FSH and frequent symptoms of climacteric syndrome in women living with HIV/AIDS in Belém/PA in 2021*.

SYMPTOMS	N	FSH (mUI/MI)			
		Average	SD	p*	CI 95%*
With hot flash	15	90	24,36	0,9	-34,70 – 38,70
No hot flash	3	88	42,88		
With nocturnal awakening	10	91,8	22,71	0,7	-22,64 – 32,22
No nocturnal awakening	8	87	32,19		
With sadness	12	92,41	25,13	0,55	-20,45 – 36,95
No sadness	6	84,16	30,91		
With slowing of thought	15	89,53	24,94	0,96	-37,52 – 35,92
No slowing of thought	3	90,33	40,55		
With Vaginal Dryness	16	87,56**	27,52**
No Vaginal Dryness	2	106,50**	0,70**
With loss of libido	16	86,25	25,97	0,12	-71,13 – 9,63
No loss of libido	2	117	14,14		
With dry skin	14	96,28	26,19	0,04	0,89 – 58,67
No dry skin	4	66,5	10,34		
With Anxiety/Nervousness	16	91	26,04	0,56	31,08 – 55,08
No Anxiety/Nervousness	2	79	39,59		

Legend: *T test; **Mann-Whitney test.

Table 6. Relation between LH and frequent symptoms of climacteric syndrome in women living with HIV/AIDS in Belém/PA in 2021*.

SYMPTOMS	N	LH (mUI/MI)			
		Average	SD	p*	CI 95%*
With hot flash	15	31,06	9,49	0,37	-8,17 – 20,30
No hot flash	3	25	16,46		
With nocturnal awakening	10	30,30	11,68	0,91	-10,39 – 11,49
No nocturnal awakening	8	29,75	9,76		
With sadness	12	31,66	10,54	0,37	-6,42 – 16,08
No sadness	6	26,83	10,77		
With slowing of thought	15	30,46	10,8	0,72	-12,07 – 17,0
No slowing of thought	3	28	11,13		
With Vaginal Dryness	16	28,93	10,38	0,21	-26,53 – 6,40
No Vaginal Dryness	2	39	9,89		
With loss of libido	16	29,31	10,91	0,41	-23,63 – 10,25
No loss of libido	2	36	5,65		
With dry skin	14	34	8,04	0,0008	8,65 – 26,84
No dry skin	4	16,25	4,99		
With Anxiety/Nervousness	16	30,81	10,6	0,4	-10,11 – 23,74
No Anxiety/Nervousness	2	24	11,31		

Legend: *T test; **Mann-Whitney test.

Table 7. Relation between estradiol (E2) and frequent symptoms of climacteric syndrome in women living with HIV/AIDS in Belém/PA in 2021*.

SYMPTOMS	N	E2 (pg/mL)			
		Average	SD	p*	CI 95%*
With hot flash	15	13,12	4,03	0,26	-2,34 – 7,92
No hot flash	3	16,25	2,3		
With nocturnal awakening	10	13,27	4,27	0,45	-2,47 – 5,26
No nocturnal awakening	8	11,87	3,83		
With sadness	12	13,0	4,37	0,61	-3,15 a 5,15
No sadness	6	12	2,82		
With slowing of thought	15	13,0	4,13	0,43	-3,23 – 7,23
No slowing of thought	3	11	2		
With Vaginal Dryness	16	12,47	3,59	0,5	-8,27 – 4,21
No Vaginal Dryness	2	14,5	7,77		
With loss of libido	16	13,11**	3,90**
No loss of libido	2	9,0**	0**		
With dry skin	14	12,66	3,82	0,97	-4,85 – 4,68
No dry skin	4	12,75	4,78		
With Anxiety/Nervousness	16	12,68	4,07	0,58	-4,69 – 8,06
No Anxiety/Nervousness	2	11	2,82		

Legend: *T test; **Mann-Whitney test.

there is complete safety in this association with estrogens and/or progestogens, even in hormone replacement. Taking into account that the mean age of the patients studied is 51.4 years, being this age one of the most affected by the symptoms of the climacteric syndrome and these being eligible for the use of HRT, it is important to carefully monitor these patients to prevent possible pharmacological interactions, such as ethinylestradiol, norethindrone and norgestimate, with antiretrovirals, such as PIs and NNRTIs (except rilpivirine), as described by the Health Ministry¹⁰.

The study's anthropometric measurements also proved to be important, since the mean BMI was 28.6 kg/m² and the mean waist circumference was 92.7 cm. According to Coelho and Vassimon (2015)¹¹, these measures corroborate the metabolic and body composition changes expected for patients with HIV on ART, called lipodystrophy, in this case, lipohypertrophy, in which adiposity accumulates in different parts of the body. Only 34.1% of the study patients performed physical activity more than 3 times a week, which may contribute even more to the HIV metabolic syndrome. Another factor that may explain the high percentages of body mass and abdominal fat in the study is the predisposition to anxiety and depression of WLHIV, triggering an increase in food intake, and consequently a continuous cycle of low self-esteem and binge eating.

Hot flashes, hot flushing, sweating, night awaking, vaginal dryness and loss of libido – classic climacteric symptoms – were quite prevalent complaints, corresponding to what was expected in this syndrome. When evaluating the

general symptoms, it is necessary to emphasize that these symptoms, as they are non-specific and present in several clinical situations, should not be analyzed individually to avoid any inappropriate conclusions.

An important addition should be made regarding cognition and mood symptoms, as all were extremely prevalent in this study. According to Looby et al. (2018)¹², the menopausal transition itself is capable of causing psychological changes, especially depression and anxiety, due to variation in hormone levels, presence of vasomotor symptoms, decreased life quality and stress factors. These factors, in association with the social stigma that the HIV diagnosis carries, can negatively influence the psychological aspects of these women.

In the hormonal profile investigation, statistically significant values were found between follicular hormones and the menopausal stages (pre and post menopause). According to the study by Navarro et al. (2012)¹³, in which a hormonal profile was investigated in seronegative women in the city of Havana, the FSH found in perimenopause was 34.69 ± 11.24 IU/L, while in post menopause it ranged between 75.43 ± 26.3 IU/L and 73.08 ± 56 IU/L in two groups surveyed ($p = 0.003$) – the study divides postmenopausal patients into early and late stages. In our study, FSH values were higher in both phases. With regard to LH, the study by Navarro et al. (2012)¹³ presented a perimenopause value of 20.78 ± 10.33 IU/L, and a postmenopause value ranging from 37.59 ± 19.33 IU/L and 32.44 ± 18.3 IU/L, according to two groups ($p < 0.001$).

However, in our work, the LH values were slightly lower in both situations. For estradiol, this same study carried out in Havana found a value for perimenopause of 54.75 ± 12.25 IU/L, while postmenopause had a dose value of 31.87 ± 10.89 IU/L in the first group and in the second group, of 21.86 ± 4.68 IU/L ($p = 0.379$). In our study, the patients' estradiol was also lower than all these variables, especially in postmenopausal women.

This disparity may suggest that although the menopausal process follows a unique trend in all women, HIV seropositivity can differentiate the hormonal profile of patients. According to Bull et al. (2018)¹⁴, some factors that can cause this ovarian dysfunction in WLHIV include opportunistic infections and effects of the virus itself on the ovaries and pituitary gland, as well as the effects on the neuroendocrine axis, which can alter both the natural history and the menopausal symptoms due to the persistent inflammatory state caused by HIV.

Relating the most prevalent symptoms and follicular hormones, it is clear that the presence or absence of skin dryness was relevant for both LH and FSH. According to Monteleone et al. (2018)¹⁵, what occurs is a progressive collagen loss, with an average decrease of 2.1% per year in postmenopausal women and with a loss of up to 30% in the first five years after the last menstrual period. Consequently, skin thickness decreases at a rate of 1.13% and elasticity at a rate of 1.5% per year. In addition, this skin dryness can be exacerbated by the atrophy of the dermal vascular network that occurs after menopause, resulting in reduced nutrients and hormones supply. This explanation is also valid for hair loss/change symptoms, which was quite prevalent in this study.

It is well postulated in the literature that HIV infection has a significant influence on the modulation of the climacteric syndrome, either maximizing the symptoms or advancing the onset of symptoms. However, it is still not possible to clearly highlight the specific factors that are involved in this process, due to the scarcity of recent studies that analyze this relationship.

It is important to emphasize that this study is limited by the small sample used in the research. Therefore, further studies should be carried out to further clarify the climacteric syndrome in women living with HIV/AIDS.

CONCLUSION

Our study found that the women living with HIV in the present study presented menopause at 47.44 years of age, 3.76 years earlier than the expected national average. The women living with HIV/Aids in the study had the hormone dosage expected for the age group and menopausal period but with a slightly different dosage when compared to seronegative women in other studies.

The most prevalent climacteric syndrome symptom in the present study was skin dryness, present in 75% of the patients. In these women, the levels of FSH ($p=0.04$) and

LH ($p=0.0008$) were higher when compared to those who did not have the same symptoms. Among the symptoms related to cognition and mood, anxiety and/or nervousness were the most prevalent (84.1%), as well as slowed thinking (72.7%).

Most of the women in the present article who are on HRT (87.5%) while using ART use associations that may not be safe in the drug interaction between the two therapies.

AUTHORS' CONTRIBUTIONS

The authors' contributions are structured according to the taxonomy (CRediT) described below:

The following participated in developing the theme, carrying out the bibliographic survey, empirical research and preparation of the article: Henrique Otavio Coutinho Sanches and Hugo Siqueira Diniz. *The following participated in the theoretical discussion, writing and preparation of the final version of the article:* Thirza Damasceno Ramos Oliva, Isabella Mesquita Sfair Silva, Rosana Maria Feio Libonati and Flávia Marques Santos. *The following participated in reviewing the text and preparing the final version:* Gisele Alves Morikawa Caldeira. All authors discussed, read and approved the final version of this article.

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REFERENCES

1. Andany N, Kennedy VL, Aden M, Loutfy M. Perspectives on menopause and women with HIV. *Int J Womens Health*. 2016;8:1-22. DOI: <https://doi.org/10.2147/IJWH.S62615>.
2. Hernández-Angeles C, Castelo-Branco C. Early menopause: A hazard to a woman's health. *Indian J Med Res*. 2016 Abr;143(4):420-7. DOI: <https://doi.org/10.4103/0971-5916.184283>.
3. Cutimanco-Pacheco V, Arriola-Montenegro J, Mezones-Holguin E, Niño-García R, Bonifacio-Morales N, Lucchetti-Rodríguez A, et al. Menopausal symptoms are associated with non-adherence to highly active antiretroviral therapy in human immunodeficiency virus-infected middle-aged women. *Climacteric*. 2020;23(3):229-36. DOI: <https://doi.org/10.1080/13697137.2019.1664457>.
4. Tariq S, Anderson J, Burns F, Delpuch V, Gilson R, Sabin C. The menopause transition in women living with HIV: current evidence and future avenues of research. *J Virus Erad*. 2016;2(2):114-6.
5. WHO Consultation on Obesity (1999: Geneva, Switzerland) & World Health Organization. (2000). Obesity : preventing and managing the global epidemic : report of a WHO consultation. World Health Organization. 2000:894:i-xii, 1-253.

6. I Diretriz Brasileira de Diagnóstico e Tratamento da Síndrome Metabólica. *Arq Bras Cardiol.* 2005 Apr;84:3–28. DOI: <https://doi.org/10.1590/S0066-782X2005000700001>
7. Lucena AF, Sena MCF, Coelho RA. Sistema de Gestão da Qualidade. Climatério. Protocolo clínico. Universidade Federal do Ceará. Hospitais Universitários Federais (EBSERH). Protocolo de Medicina e Ginecologia. 2018;010:1-9.
8. Villarinho MV, Padilha MI, Berardinelli LMM, Borenstein MS, Meirelles BHS, Andrade SR de. Políticas públicas de saúde face à epidemia da AIDS e a assistência às pessoas com a doença. *Rev Bras Enferm.* 2013;66(2):271-7. DOI: <https://doi.org/10.1590/S0034-71672013000200018>.
9. Howells P, Modarres M, Samuel M, Taylor C, Hamoda H. Experience of hormone replacement therapy in postmenopausal women living with HIV. *Post Reprod Health.* 2019 Jun;25(2):80-85. doi: 10.1177/2053369119838737. Epub 2019 Mar 21. PMID: 30895862
10. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Departamento de Vigilância, Prevenção e Controle das Infecções Sexualmente Transmissíveis, do HIV/Aids e das Hepatites Virais. Protocolo Clínico e Diretrizes Terapêuticas para Manejo da Infecção pelo HIV em Adultos / Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância, Prevenção e Controle das Infecções Sexualmente Transmissíveis, do HIV/Aids e das Hepatites Virais. Brasília: Ministério da Saúde; 2018.
11. Coelho I, Vassimon H. Excesso de peso em portadores do HIV assintomáticos: uma nova realidade e desafio. *Rev Bras Nutr Clin.* 2015;30(2):111-5.
12. Looby SE, Psaros C, Raggio G, Rivard C, Smeaton L, Shifren J, et al. Association between HIV-status and psychological symptoms in perimenopausal women. *Menopause.* 2018;25(6):648-56. DOI: <https://doi.org/10.1097/GME.0000000000001058>.
13. Navarro D, Acosta A, Robles E, Díaz C. Hormone Profile of Menopausal Women in Havana. *MEDICC Rev.* 2012;14(2):13. DOI: <https://doi.org/10.37757/MR2012V14.N2.5>.
14. Bull L, Tittle V, Rashid T, Nwokolo N. HIV and the menopause: A review. *Post Reprod Heal.* 2018;24(1):19-25. DOI: <https://doi.org/10.1177/2053369117748794>.
15. Monteleone P, Mascagni G, Giannini A, Genazzani AR, Simoncini T. Symptoms of menopause - Global prevalence, physiology and implications. *Nat Rev Endocrinol.* 2018;14(4):199-215. DOI: <https://doi.org/10.1038/NREND0.2017.180>.

